The ORION

Medical Journal

Vol-18, May-August 2004

Multi Discipline Vol - 18 : 161 - 192, 02 May 2004, International ISSN 1606 - 9722

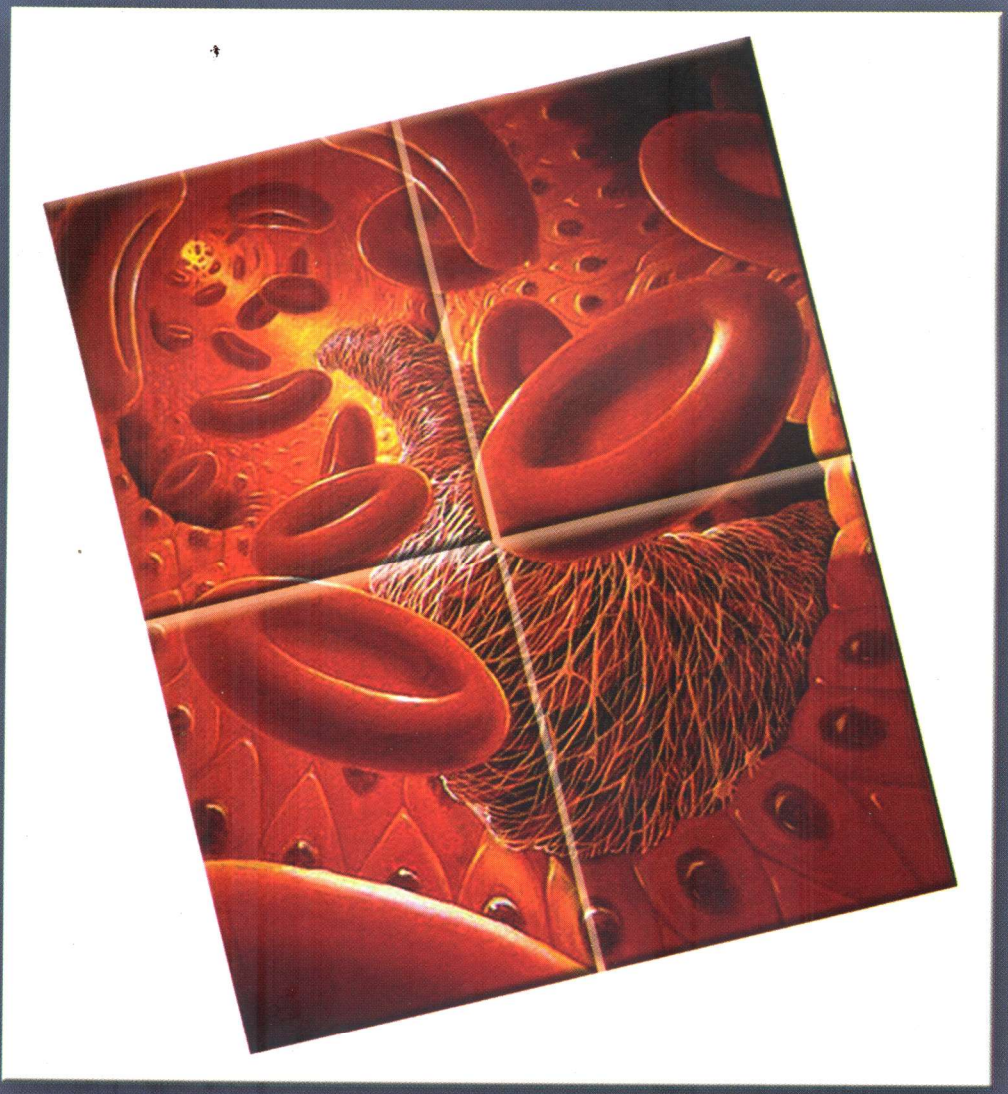
Dedicated to Continued Medical Education Program

www.orion-group.net/journals

Clognil *Plus*

Clopidogrel INN 75 mg & Aspirin USP 75 mg

Two captains
with one mission



Provides excellent synergistic effect to inhibit platelet *aggregation*

ORION
LABORATORIES LTD.
In Search of Excellence

REGISTERED TO ISO 9001:2000 NO. 7868
URS
Orion Laboratories Limited
UKAS QUALITY MANAGEMENT 043

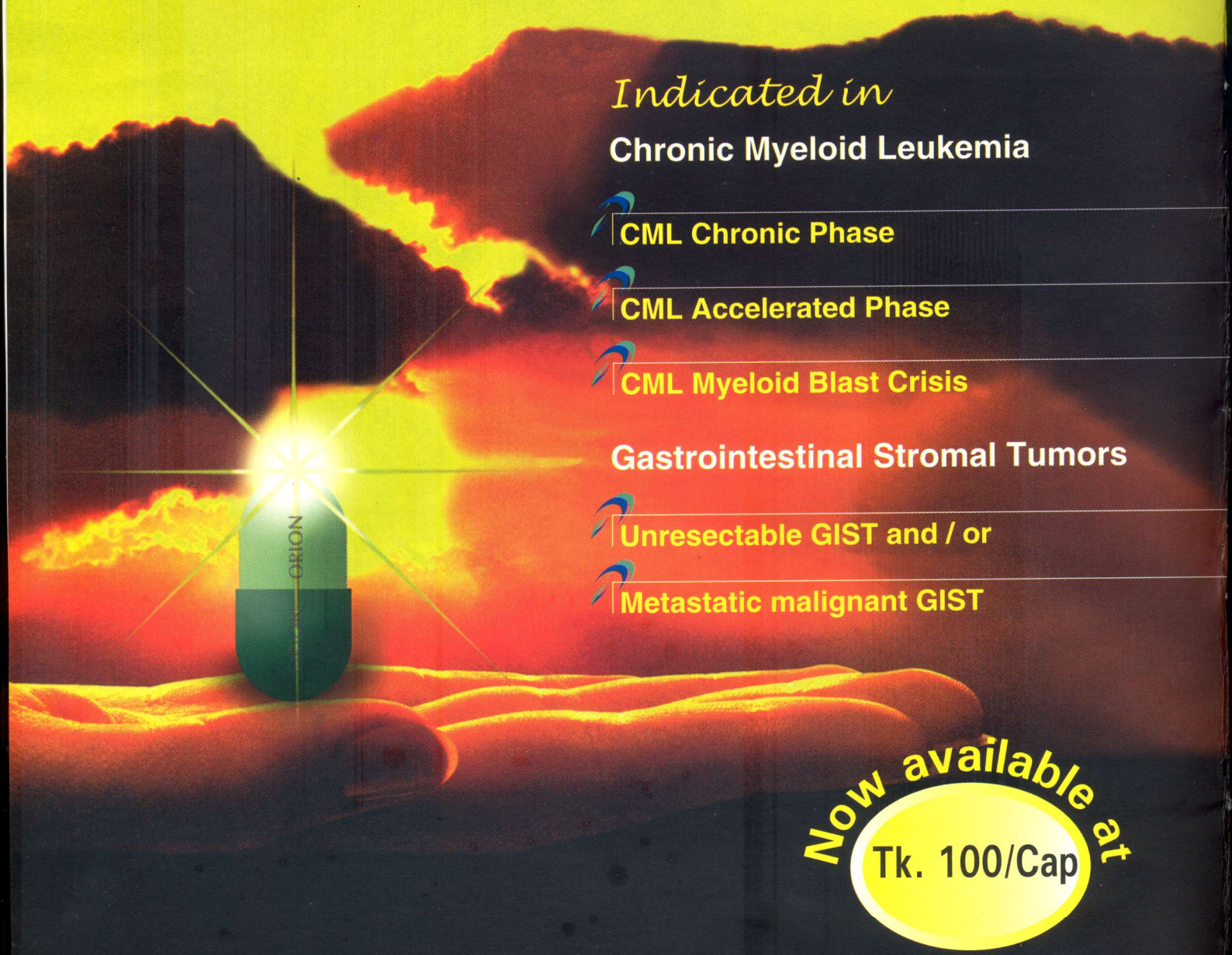
Printed by : Fair Printing Press
7160680, 7169896

1st of Its Kind in Bangladesh

Enliven

Imatinib INN 100 mg

... New Light ... New Hope



Indicated in

Chronic Myeloid Leukemia

- CML Chronic Phase
- CML Accelerated Phase
- CML Myeloid Blast Crisis

Gastrointestinal Stromal Tumors

- Unresectable GIST and / or
- Metastatic malignant GIST

Now available at Tk. 100/Cap

Founded September 1998 • Published quarterly • Volume 18• Sunday 02 May 2004

The ORION Medical Journal

Editor's Choice

The ORION, salute the arduous effort

The consummate dominion of The ORION medical journal owes to reflect the arduous efforts of the authors and the continuous support of the valued readers. This superlative enthuses The ORION for successive progression to be arrayed into broad medical spectrum. Therefore, this issue is congregated with valuable topics like "Trimetazidine: An innovative approach to ischemic heart disease"(P-173-174) discussing about a unique way of management of ischemic heart diseases that enlighten a new hope to prevent cardiovascular death.

The editorial (P-162) of this issue points out the importance of psychiatric training at primary health care delivery level in order to achieve early diagnosis and to treat the mental disorders patients with more excellence.

An original article on "Apathy in neuropsychiatric disorders' (P- 167-172) nicely sketches the differential diagnosis of apathy, addresses issues related to the assessment and treatment of apathy in neuropsychiatric patients. A review article on "Management of thyroid carcinoma" (P- 163-166) cites an update profile of etiology, diagnosis and treatment of thyroid carcinoma.

The article on "Non operative treatment modalities of clubfoot" (P-175-176) is focused on conservative treatment of clubfoot. The article on "Diagnosis of irritable bowel syndrome; A review" (P-177-178) gives an modern information for diagnosis and treatment of the disease.

The review article on "Plain radiography : Yet an important diagnostic modality" (P-179-181) flushes the importance of plan radiography as an important diagnostic tool in diagnosis various diseases. The article on "Disseminated intravascular coagulation in obstetrics" (P-182-184) reveals the details information of the disease and its management.

The article on "Imaging hepatobiliary and pancreatic system by ERCP" (P-185-186) confers on significant development of diagnostic tool in evaluation of hepatobiliary and pancreatic diseases.

The case report on "Successful correction of total anomalous pulmonary venous connection (TAPVC type-1): A case report" (P-187-188) nicely documents a very common and interesting cardiac anomaly and successful operative correction of the case.

Furthermore, The ORION is happy to offer the valued readers a worldwide access through the Internet website www.orion-group.net/journals where all the issues of The ORION are available. All the esteemed readers can also access The ORION from anywhere around the world through other international web search options like MSN, Yahoo, Google etc.

The opinion and suggestion of the valued readers are always appreciated to make The ORION medical journal upgraded day by day.

May the Almighty bless all in the spirit of good health.

The ORION wishes all a very happy and colorful "Bangla New Year - 1411" and prosperous life in every moment.

DR. MOHAMMAD ZAKIRUL KARIM
Chief Editor, The ORION
and Manager,
Medical Services Department, ORION Laboratories Ltd.

Role of consultation-Liaison psychiatry in primary health care in Bangladesh

Sobhan M A[1]

The ORION 2004 ; 18 : 162

It is a well-known fact that the great majority of patients with psychological difficulties are first seen by the primary care physicians, working in public or private sectors. Nearly one third of these patients do not suffer from organic disorders rathter they complain of the somatic manifestations of their psychological difficulties. These complaints like Headache, aches and pains, tiredness, weakness and functional symptoms affecting several organs or systems are vague in nature. Depression and/ or anxiety usually underlie such complaints with substance absue being more rarely involved.

Non psychiatrist specialists also see many patients who come to them with conviction that the specialists is the right person they need, infact those patients are suffering from psychological disorder, with somatic manifestations in the specialist's field of specialty.

Another group of patients are seen by the specialists with physical illness also have a concomitent psychological disorder who needs paralell treatment.

Psychological recovery is usually associated with improvement in the patients physical conditions.

The Magnitude of the need of service in the mental health in the community is enormous. Few national surveys depict the picture. At a cross sectional study conducted by a specialist physician MN Alam et all in 1978 in an urban area (Dhaka city) showed that 29% of population had psychiatric morbidity. Among them neurotic disorder scored highest, mood disorder being second. Another study by Khan LR et all in primary health care center in rural area showed that 23.1% had psychiatric disorder, among them 47.6% depressive disorder, 30.8% anxiety disorder, 13.3% somatoform disorder, 5.2% had substance abuse disorder.

On an average 30-40% of the patients attending general practioners, specialists and primary health centers suffer from mental illness. Vast majority of these cases present with various somatic complaints. These group of patients are under diagnosed and are treated with psychotropic medication aiming the objectives to relief symptoms. In absence of adequate training of mental health aspects in diagnostic practice in under-graduate and post-graduate level of training is responsible for this condition.

Consultation-Liasoin psychiatry is the solution to improve this situation both for inpatient and out patient set up covering all specialities.

Small packge of training with the objective of establishing a proper diagnosis should be developed and implemented for the general physicians and specialists. This will enable physicians and specialists to achieve a proper diagnsis and treat the patients with more excellence. Quality of life of patients will be improved and chronicity of mental disorders will be prevented.

1. **Prof. M.A. Sobhan,** MBBS, DPM
Fellow WHO
Chairman, Dept. of Psychiatry, BSMMU

Bangladesh Association of psychiatrists can take the initiative in collaboration with Training institutions and sponsorships of WHO, DGHS, pharmaceutical industries.

References

1. Alam MN. Psychiatric morbidity in general practice. Bangladesh Med Res Counc Bull 1978 ; 4 : 38-42.

Medical justification for putting kids on antidepressants!

The rate at which antidepressants were prescribed to children rose about 10 percent annually between 1998 and 2002, with preschoolers accounting for the sharpest increase, according to a new study. The study, which looked at prescriptions written for some 2 million pediatric patients nationally, found 2.4 percent were prescribed antidepressants in 2002, up from 1.6 percent five years earlier. That amounts to a 49 percent increase in the number of people under 18 prescribed antidepressants, according to the study in Psychiatric Services, a medical journal published by the American Psychiatric Association.

Among children 5 and under, the increase was even higher, with antidepressant use among girls doubling and among boys rising by 64 percent. Overall, the increase was highest among girls: 68 percent, compared to 34 percent among boys. The growth in prescriptions written for children occurred even though antidepressants -- with the exception of Prozac -- were never approved for anyone younger than 18. Prozac was approved as a treatment for children, but only two years ago -- after the rise in juvenile prescriptions began. The findings come amid a widening controversy over antidepressants and alleged links to suicidal behavior and thoughts, especially among children. Last month, the Food and Drug Administration asked drug makers to add explicit warnings to their product labeling. "This adds to the data showing many children are using these drugs," said Tom Delate, research director at Express Scripts, a pharmacy benefits manager that conducted the study. "The safety and efficacy have to be examined more closely. This may add some impetus."

He cited off-label use as the reason more children are prescribed the drugs. Off-label use refers to a common practice among doctors to write prescriptions even though regulators have not approved a medicine for a specific use. Many doctors and families contend antidepressants have saved lives. This argument is also cited by drug makers, which deny their pills, including Zoloft, Paxil and Effexor, lead to suicide. The manufacturers include Wyeth, GlaxoSmithkline, Eli Lilly and Pfizer. Last year, though, British authorities warned doctors not to prescribe the drugs, except for Prozac. They pointed to newly disclosed data showing one drug, Glaxo's Paxil, wasn't effective and could increase the risk of suicide. Last week, two congressional committees launched a probe into the FDA's handling of the controversy. They want to know why the agency didn't take more action, such as urging doctors not to prescribe the pills.

The committee also wants the FDA to explain why one of its own medical reviewers was prevented from presenting data at a February hearing convened to explore safety risks. The hearing garnered national publicity after many parents testified their children committed suicide after taking an antidepressant. Consumer advocates, meanwhile, are stepping up calls for the companies that make antidepressants to release all unpublished clinical trial data. Drug makers aren't required to disclose this information, which critic's say allows negative findings to remain suppressed. "Frankly, I call this child abuse," said Vera Sharav of the Alliance for Human Research Protection, a consumer advocate. "There is no medical justification for putting preschoolers on such drugs. And there's nobody protecting the children. It's just a free-for-all." *www.nj.com/business/ledger*

Management of thyroid carcinoma

Alauddin M[1], Joarder A H[2]

The ORION 2004 ; 18 : 163-166

Overview

The two most common forms of thyroid cancer, papillary and follicular thyroid cancer, together termed differentiated thyroid cancer (DTC), comprise the majority of thyroid cancers and have the best prognosis[1]. Experts believe that DTC has increased in many places around the world over the past three decades, yet this has been associated with a significant fall in mortality rate in some countries. In our experience we also found that the incidence of DTC is increasing in Bangladesh.

Epidemiology

Although thyroid nodules are extremely common, malignant lesions derived from thyroid epithelial cells are relatively rare. Clinically recognized thyroid carcinomas constitute less than 1% of all human malignant tumors. The annual incidence of thyroid cancer varies worldwide from 0.5 to 10 per 100,000 populations. It is the most common endocrine malignant lesion (90% of all endocrine cancers) and is responsible for more deaths than all other endocrine cancers combined. Exact incidence of thyroid cancer in Bangladesh is not known. One study at INM & Thyroid Clinic in IPGMR Dhaka reviewed 2629 Thyroid patients from January 1994 to June 1995, and found Thyroid carcinoma in 2.58%[2]. The American Cancer Society estimates that 17,000 new cases of thyroid cancer are diagnosed annually in the United States and that 1,300 thyroid cancer-related deaths occur annually[3]. Nevertheless, with appropriate treatment the survival rate from thyroid cancer is very high. In the United States, an estimated 190,000 patients are thyroid cancer survivors, some for more than 40 years after diagnosis.

Etiology

Exact etiology of thyroid cancer is unknown. Radiation to head and neck and thorax in small doses in childhood is liable to induce thyroid cancer in later life. Irradiation of the cervical lymph node in Hodgkin's disease may predispose for thyroid malignancy in late life. Endemic goiter predisposes for Follicular carcinoma[4].

Classification of malignant thyroid tumors

Primary

- Follicular epithelium : differentiated
  -Papillary carcinoma
  -Follicular carcinoma
- Follicular epithelium : undifferentiated
  -Anaplastic carcinoma
- Parafollicular cells
  -Medullary carcinoma
- Lymphoid cells
  -Lymphoma

Secondary

-Metastatic carcinoma
-Local infiltration.

Though there are various types of thyroid cancer as seen in the above list, the present article will be dedicated in discussing management of Papillary and Follicular Carcinoma. There is difference of opinion among Surgeons about the extent of thyroid resection. Managing differentiated (papillary and follicular) thyroid carcinoma can be a challenge because there have been no prospective randomized trials of treatment. Results from randomized trials that are under consideration will not be available for many years given the typically prolonged course. This account for much of the disagreement in managing differentiated thyroid carcinoma.

Diagnosis

At the time of initial assessment, most patients with thyroid cancer have a palpable neck mass, either a primary intrathyroidal tumor or metastatic regional lymphadenopathy. In some patients, however, the tumor may be clinically occult, and the impalpable lesion may first be recognized at the time of surgical intervention for presumed benign thyroid disease. Unfortunately, even thorough history taking and physical examination rarely allow the definitive diagnosis of thyroid cancer. The diagnosis of thyroid cancer necessitates cytological or histological confirmation. FNA biopsy is the most cost-effective method of distinguishing benign from malignant thyroid nodules preoperatively. The diagnosis of thyroid cancer must be substantiated by careful pathologic examination of surgically excised thyroid tissue. This verification is particularly important in cases of cellular follicular lesions described by cytologists as "suspicious" for follicular cell neoplasm (also known as follicular neoplasms or microfollicular lesions). For accurate diagnosis of follicular carcinoma, one must clearly demonstrate tumor invasion through the capsule of the nodule or tumor invasion of blood vessels (angioinvasion). This process requires multiple serial sections through the excised paraffin-fixed specimens and careful evaluation for the presence or absence of such microinvasion. Intraoperative frozen section is often inadequate for this purpose. Papillary thyroid carcinoma (PTC) constitutes 75 to 80% of cases of clinically recognized thyroid cancer and can often be diagnosed with confidence by FNA biopsy[3].

Prognosis and recurrence of differentiated thyroid carcinoma

In the NCDB (National Cancer Data Base, USA) study, the 10- year relative survival rates for patients with papillary and follicular were 93% and 85%, respectively[5]. Although anaplastic thyroid carcinoma is uniformly lethal, most thyroid carcinoma deaths are from papillary and follicular carcinomas, which account for nearly 95% of all thyroid carcinoma cases.

Age, stage, and gender at diagnosis[5]

Although many factors influence the outcome for patients with papillary and follicular thyroid carcinomas, the two most important and consistently demonstrable are patient age at the time of initial therapy and tumor stage.

1. **Prof. M Alauddin,** FRCS (Glas), FCPS (BD), FCPS (Pak), DLO (London)
Prof. and Chairman, Dept. of Otolaryngology, BSMMU.

2. **Dr. Abul Hasnat Joarder,** MBBS, FCPS
Assoc. Prof. of Otolaryngology, BSMMU.

A significant number of studies show that age is an important prognostic variable for cancer mortality. Thyroid carcinoma is more lethal after age 40, increasing in severity thereafter with each subsequent decade of life and rising dramatically after age 60. However, tumor recurrence rates show a remarkably different age pattern. Rates are highest (40%) before age 20 and after age 60. Recurrence for other ages is approximately half this rate. Children typically present with more advanced disease and have more tumor recurrences after therapy than adults, yet their prognosis for survival is good. Prognosis is less favorable in men than in women, but the difference is usually small.

Tumor variables affecting prognosis[5]

Certain tumor features have a profound effect on prognosis. Perhaps the most important features are tumor histology, primary tumor size, local invasion, and metastases.

Histology

Although survival rates with typical papillary carcinoma are quite good, cancer-specific mortality rates vary considerably with certain histological subsets of tumors. A graver prognosis is associated with **1.** anaplastic tumor transformation and tall-cell papillary variants, **2.** columnar variant papillary carcinoma, **3.** diffuse sclerosing variants. Follicular-variant papillary carcinoma, which is recognized by its follicular architecture and typical papillary cytology, dose not appears to have a worse prognosis than the more common pure papillary lesions. Follicular carcinoma is typically a solitary encapsulated tumor that may be more aggressive than papillary carcinoma. It usually has a microfollicular histologic pattern. It is identified as cancer by follicular cell invasion of the tumor capsule and/or blood vessels. The latter has a worse prognosis than capsular penetration alone.

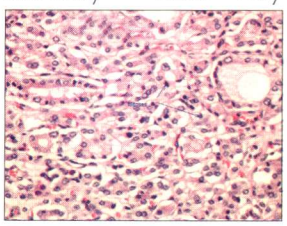


Fig 1 : Follicular Carcinoma of Thyroid

Primary tumor size

Papillary carcinomas smaller than 1cm, termed "microcarcinomas," are typically found unexpectedly after surgery for benign thyroid conditions. Their recurrence and cancer specific mortality rates are near zero. Small (less than 1.5 cm)but clinically apparent papillary of follicular carcinomas almost never cause distant metastases. Furthermore, rates of recurrence after 30 years are one-third those associated with larger tumors and 30 year cancer-specific mortality is 0.4% compared to 7% for tumors 1.5cm or larger. In fact, the prognosis for papillary and follicular carcinomas is incrementally poorer as tumors increase in size.

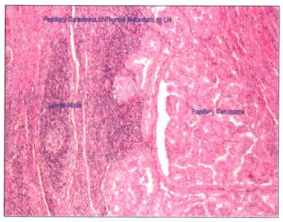


Fig 2 : Papillary Carcinoma of Thyroid

Local tumor invasion

Up to 10% of differentiated thyroid carcinomas grow directly into surrounding tissues, increasing both morbidity and mortality. The invasion may be microscopic or gross and can occur with both papillary and follicular carcinomas. Recurrence rates are two times higher with invasive than noninvasive tumors. Up to one-third of patients with invasive tumors die of cancer within a decade.

Lymph node metastases

In one review, nodal metastases were found in 36% of 8,029 adults with papillary carcinoma, in 17% of 1,540 patients with follicular carcinoma, and in up to 80% of children with papillary carcinoma. An enlarged cervical lymph node may be the only sign of thyroid carcinoma. In these patients, multiple nodal metastases are usually found at surgery. The prognostic importance of regional lymph node metastases is controversial. Some studies find that the presence of regional lymph node metastases has no impact on recurrence or survival. Other studies find nodal metastases are a risk factor for local tumor recurrence and cancer specific mortality and correlate with distant metastases, especially if there are bilateral cervical or mediastinal lymph node metastases or if the tumor invades through the lymph node capsule. In one study, 15% of patients with cervical ode metastases died of thyroid carcinoma while all patients without cervical node metastases survived. Another study of patients with distant metastases from papillary carcinoma who had cervical or mediastinal lymph node metastases had a significantly higher 30- year cancer-specific mortality (10%) than patients without metastases (6%).

Distant Metastases

Distant metastases are the principal cause of death from papillary and follicular carcinomas. Almost 10% of patients with papillary carcinoma and up to 25% of those with follicular carcinoma develop distant metastases. About half of these metastases are present at the time of diagnosis. The sites of reported distant metastases among 1,231 patients in 13 studies were lung (49%), bone (25%), both lung and bone (15%), and thecentral nervous system or other soft tissues (10%). Although some patients, especially younger ones, with distant metastases survive for decades, about half die within 5 years regardless of tumor histology. Even so, some pulmonary metastases are compatible with long-term survival.

Tumor staging and prognostic scoring strategies

Several staging and clinical prognostic scoring strategies use patient age over 40 as a major feature to identify cancer mortality risk from differentiated thyroid carcinoma. When applied to the papillary carcinoma data from the Mayo Clinic, four of the schemes using age (EOTRC/European Organization for Research and Treatment of Cancer, TNM/tumor characteristics, lymph node involvement, and distant metastatic lesions, AMES/age of patient, presence of distant metastatic lesions, and extent and size of the primary cancer, and AGES/patient age and tumor grade, extent, and size), were effective in separating low-risk patients, in whom the 20 year cancer-specific mortality was 1%, from high-risk patients, in whom the 20 year cancer-specific mortality was 30% to 40%. With incrementally worsening metastasis, age, completeness of resection, invasion, and size (MACIS) scores of less than 6; 6 to 6.99; 7 to 7.99; and 8+; the 20-year survival rates were progressively lower: 99%, 86%, 59%, and 24%, respectively. The American Joint Commission on Cancer (AJCC) TNM staging approach, which is perhaps the most widely used

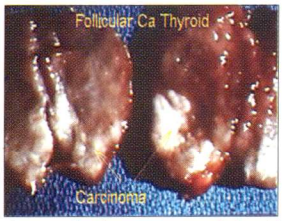


Fig 3 : Follicular Carcinoma of Thyroid

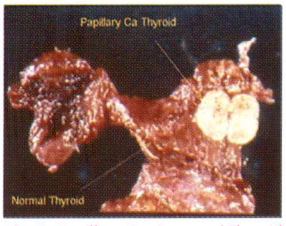


Fig 4 : Papillary Carcinoma of Thyroid

schemes, classifies tumors in all patient under age 45 as stage I and stage II (i.e., low risk), even those with distant metastases. Although. it has been widely verified to predict cancer mortality, TNM staging does not forecast the high number of recurrences that occur in patients diagnosed before age 20, which is true of all prognostic scoring systems that lend heavy weight to age[5].

In the Otolaryngology Department of Bangabandhu Sheikh Mujib Medical University at Dhaka we define low and high risk in following order. Here, in papillary carcinoma a low risk patient means a case which has got, **a.** age between 15 to 40 years, **b.** intrathyroidal growth, **c.** tumor size less than 4 cm. and **d.** no nodal or distant metastasis; and a high risk patient means a case having **i.** age below 15 year and over 40 years, **ii.** extra thyroid growth, **iii.** tumor size 4 cm. or more and **iv.** with nodal or distant metastasis. All follicular carcinoma are kept in high risk group irrespective of age of patient, extent & size of tumor and metastasis. The above criteria has a close similarity with NCCN (National comprehensive cancer network, USA) criteria in regard to papillary carcinoma but different to NCCNs low and high risk types, we categorize all follicular carcinoma as high risk ones.

Primary treatment-

Papillary thyroid carcinoma (PTC)

No prospective clinical trials have clearly determined the "best treatment'' of patients with PTC. In most cases, a preoperative diagnosis of PTC established by FNA allows appropriate surgical planning. Total ipsilateral thyroid lobectomy is generally thought to be the minimal surgical procedure for a unilateral, possibly malignant thyroid nodule. Unilateral total lobectomy may be an appropriate definitive procedure for patients with minimal thyroid cancers. Most surgeons agree that total thyroidectomy is the preferred operation for high-risk patients with PTC- as defined by the AMES, AGES, TNM EORTC, or MACIS classification system. For several reasons, however, opinions differ about the extent of thyroid resection for patients with low-risk PTC. Most of these patients have an excellent prognosis as long as gross tumor is completely resected. One group of surgeons prefer total thyroidectomy where as other group prefer Lobectomy & Isthmusectomy. The arguments advanced in favor of total thyroidectomy are that PTC is often multifocal in origin and may spread throughout the thyroid by lymphatic drainage. Total thyroidectomy facilitates the postoperative use of I131to ablate residual thyroid tissue and to identify and treat residual or distant tumor. After total thyroidectomy, Tg is a more sensitive indictor of residual disease. Whereas the proponents of Lobectomy & Isthmusectomy urgues that total thyroidectomy has a increased chance of recurrent laryngeal nerve injury and hypoparathyroidism, contralateral disease is not clinically relevant, survival rate is nearly equivalent for low risk patients, I131 ablation and Thyroglobulin level estimation is not necessary for most patients. Lymph node metastatic lesions are present in about 40% of adult patients with PTC; where complete lymphadenectomy of involved nodes is recommended.

In children and young adults, clinical node involvement is more common. Nodal metastatic lesions increase the risk for subsequent nodal recurrences but have little effect on survival. Surgeons should remove all enlarged lymph nodes in the central and lateral neck areas. In the central neck, removal is essential because reoperations in this area are more difficult and are associated with a higher risk of complications. When enlarged nodes are identified in the lateral aspect of the neck, most surgeons perform an ipsilateral functional (modified radical neck) dissection and remove all the perijugular nodes from the clavicle to the hyoid, including the nodes along the spinal accessory nerve. During this operation, the spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle should be preserved. Prophylactic lateral neck dissection is not recommended, and radical neck dissections that result in loss of function are rarely indicated for patients with PTC unless direct muscle invasion is present. We offer Lobectomy & Isthmusectomy for low risk PTC.Then thyroxine is prescribed for lifelong. The high risk PTC are offered total thyroidectomy. Additionally, Neck dissection and treatment /removal of metastases is offered when nodal or distant metastases are present.These is followed by radio iodine ablation & thyroxine. We found good results in relation to recurrence and mortality.

Follicular cell carcinoma

Most follicular cell neoplasms are large (2- to 5-cm), relatively soft, solitary thyroid nodules. Typically, FNA cytological findings are reported as "indeterminate or suspicious for follicular cell neoplasm''. About 80% of follicular cell neoplasms are benign; larger follicular cell neoplasm's are more likely to be malignant, especially in men and patients older than age 50 years. Unfortunately, follicular adenomas and carcinomas usually cannot be distinguished at the time of surgical intervention. Therefore, most surgeons recommend a total thyroid lobectomy with isthmusectomy for "follicular cell neoplasm.'' When the lesion is benign, no further therapy is needed. When the tumor is malignant, completion (total) thyroidectomy may be indicated to facilitate subsequent radioactive iodine (RAI) scanning and therapy. Risk group assignments classifies low and high risk cases of follicular carcinoma in a similar way to papillary one. Similar to papillary carcinoma, NCCN guide line advocate that the low risk follicular carcinoma should be treated by lobectomy with isthmusectomy; and high risk follicular carcinoma should be treated by total thyroidectomy. As mentioned earlier, we designate all follicular carcinoma as high risk class. And our way is to do total thyroidectomy in all cases of follicular carcinoma. This is followed by scanning, radio iodine ablation and thyroxin treatment.

Ipsilateral lymph node metastatic lesions occur in only about 10% of patients with follicular thyroid cancer (FTC). When lymphadenopathy is extensive in a patient with a follicular neoplasm as determined by FNA cytology, the tumor is usually a follicular variant of PTC. Enlarged lymph nodes in the central neck area should be removed. A functional lateral neck dissection is indicated for patients with clinically palpable nodes.

Adjuvant therapy

Thyroid Hormone The administration of supraphysiologic doses of thyroid hormone to suppress serum TSH in patients with Follicular Cell-Derived Cancer (FCDC) has been a mainstay of therapy for more than 40 years. Growth of FCDC cells depends on TSH; suppression of endogenous TSH is thought to deprive these cells of an important growth-promoting influence. Traditionally, the goal of levothyroxine therapy has been complete suppression of pituitary secretion of TSH.

Radioiodine remnant ablation

Many patients with FCDC receive RAI to ablate residual thyroid tissue postoperatively (RRA). RRA is defined as "the destruction of residual macroscopically normal thyroid tissue after surgical thyroidectomy." RRA is used as an adjunct to surgical treatment when the primary FCDC has been completely resected. This technique is contrasted with RAI therapy, in which larger doses of I are administered in an attempt to destroy persistent neck disease or distant metastatic lesions.

External irradiation

External irradiation is rarely used as adjunctive therapy in the initial management of patients with FCDC. It may be beneficial, however, in patients with poorly differentiated (higher histologic grade) tumors that do not concentrate RAI. It also may be considered in the postoperative management of patients with FCDC who have gross evidence of local invasion and who are presumed to have microscopic residual disease after primary surgical treatment.

Long-term follow-up-

Diagnostic scanning

For whole-body scanning with Radioactive iodine, an increased serum TSH level (generally >25microIU/mL) is necessary to thyroid cells to accumulate the radio-iodine. This state is usually accomplished by the withdrawal of thyroid hormone therapy. Newly advocated recombinant human TSH does not not require withdrawal of thyroid hormone.

Thyroglobulin

Thyroid tissue is the only source of circulating Tg. Serum Tg levels may be high in thyrotoxicosis, thyroiditis, iodine deficiency, and benign thyroid adenomas as well as in thyroid cancer. Tg is a highly specific tumor marker for differentiated thyroid cancer and has a pivotal role in follow-up of patients with such cancers. After thyroidectomy and successful radioiodine ablation, serum Tg should be undetectable (generally, <2 ng/ mL). After a unilateral lobectomy, serum Tg is usually less than 10 mg/mL during thyroid hormone therapy in the absence of metastatic disease.

Reference

1. Mazzeferri EL, Massoll N. Management of papillary and follicular (differentiated) thyroid cancer: New paradigms using recombinant human thyropin. Endocrine-Related cancer (2002) 9 227-247
2. Alam MN et al. Spectrum of thyroid disorders in IPGMR, Dhaka.Bangladesh J Medicine 1995; 6: 53-58
3. AACE (American Association of clinical Endocrinologist) guidelines. Thyroid Carcinoma guidelines, Endocr Pract. 2001;7 (No. 3)
4. Shaheen O, Thyroid neoplasm Scott-Browns otolaryngology, 5th ed. Alan G Kerr. 1987, p. 301-14.
5. NCCN (National comprehensive cancer network), Practice Guidelines in Oncology-v.1.2002,Thyroid Carcinoma

Apathy in neuropsychiatric disorders

Firoz AHM[1], Rahman AHMM[2]

The ORION 2004 ; 18 : 167-172

Abstract

Apathy is a common neurobehavioral feature in a variety of neuropsychiatric disorders. Apathy is often interpreted as a sign of deppression or as a nonspecific symptom of other medical conditions. However, recent research indicates that the essential meaning of apathy is lack of motivation. This article presents a frame work for the classification and differential diagnosis of apathy and addresses issues related to the assessment and treatment of apathy in neuro phychiatric patients.

Introduction

To most clinicians, apathy is a vaguely defined symptom suggesting a lack of interest or emotion. Patients who present with these and related symptoms (eg. lack of feeling or concern, indifference, flat affect and/or emotional unresponsiveness) are often described as being apathetic. In the clinical setting, apathy is commonly interpreted as a sign of depression or as a non-specific symptom of a variety of other medical disorders.

The prevalence of apathy in different neuropsychiatric populations and research data indicating that apathy may occur in the absence of other depressive symptoms have led to the development of a framework for classification and differential diagnosis of apathy1. Additionally, criteria for diagnosing apathy as a clinical syndrome have been proposed [2,3].

Definition of Apathy

Defining apathy as a lack of emotion or interst leads to ambiguity because emotion and interests are related but clearly not the same. More recently, apathy has been defined as lack of motivation[1-3]. Lack of motivation is operationalized as the "simultaneous decrease in the overt behavioral, emotional, and cognitive concomitants of goal-directed behaviors"[3]. The central role of gole-directed behavior in the definition indentifies apathy with the domain of psychological functioning concerned with motivation. The diagnsis of apathy requires a diminution in observable goal-directed behavior relative to a person's age and culture. Apathy under the above definition also requires evidence of a descrease in emotional reactivity. For example, patients with apathy will show diminished emotinal distress in response to pleasant or unpleasant event. Finally, thought content must be considered. The diagnosis of apathy requires diminition of goal-realated cognitions such as diminished goals for the future, diminished interest.

Syndrome of Apathy

The application of the above definition of apathy to clinical practice requires guidelines for distinguishing apathy as a symptom and syndrome. According to the American Psychiatric Association[4], a syndrome is a recurring and discriminable pattern of symtoms that has heuristic value for diagnosing and treating patients. Once the presence of apathy has been determined, therefore, the next question is whether to regard as a symtptom of some other syndrome or as a syndrome itself.

Table 1: Criteria for the syndrome of Apathy

A. Lack of motivation relative to the patient's previous level of functioning or the standards of his/her age and culture, as evidenced by all three of the following:

I. Diminished goal-directed behavior

- Lack of productivity
- Lack of effort
- Lack of time spent in activities of interest
- Lack of initiative or perseverance
- Compliance/dependency on others to structure activity
- Diminished socialization or recreation

II. Diminished goal-directed cognition

- Lack of interests, lack of interest in learning new things, lack of interest in new experiences
- Lack of concern about one's personal health or functional problems
- Diminished importance or value attributed to such goal-related domains as socialization, recreation, productivity, initiative, preseverance, curiosity.

III.Diminished emotional concomitants of goal-directed behavior

- Unchanging affect
- Lack of emotional responsitivity to positive and negative events
- Euphoric or flat affect
- Absence of excitement or emotional intensity

B. Lack of motivation is the dominant feature of the clinical presentation. If the lack of motivation is not the dominant feature, then apathy is a symptom of some other syndrome such as dementia, delirium, or depression.

Definition of Apathy

As a general rule, apathy is considered to be a symptom if the apathy is mild relative to other symptom. In such cases, the patient is described syndromally in terms of the other syndrome and apathy is considered a symptom of that syndrome. Examples include syndromes of intellectual impairment (eg. dementia) and syndromes of impaired level of consciousness (eg, delirium).

The esential feature of the syndrome of apathy is diminished goal-directed behavior due to a lack of motivation[1-3]. The extent to which apathy dominates the clinical picture determins the presence of a syndrom of apathy. In other

1. **Prof. Dr. A. H Mohammad Firoz,** MBBS, DPM, MAPA, MCPA, MBA, FCPS, MRCP, FRCP
Professor of Psychiatry, Director, National Institute of Mental Health, Dhaka

2. **Dr. AHM Mustafizur Rahman**
Asstt. Professor of Psychiatry, National Institute of Mental Health, Dhaka

words, apathy is considered a syndrom when lack of motivation is not attributable to such other syndromes as dementia, delirium, or depression. Deciding whether apathy is secondary to some others syndroms depends on the process of evaluating a patient's overall clinical state and judging which symptoms are most prominent. For example, if a patient with diminished interests is intensely dysphoric, a diagnosis of depression would be more likly. The criteria for diagnosing the syndrome of apathy[3] are summarized in table-1.

Patients may show the syndrom of apathy and another syndrome simultaneously, eg, in Parkinson's disease and Alzheimer disease. Patients with Parkinson's disease often present with both apathy and dementia, while patients with Alzheimer disease may exhibit apathy, dementia, and psychosis. In each case, the patients exhibit diminished motivation, but the symptoms meet criteria for some other syndrome, eg, dementia.

Assessment of Apathy

Recognition of apathy has important implications for clinical care because motivation is essential for adaptive behavior. Comprehensive medical assessment may be needed to evaluate many psychiatric, neurologic, and medical condition that can produce apathy. Taking a through psychosocial history is necessary to determine whether apathy has been present throughout child hood or adult life, whether it is a symptom of a personality disorder or whether it represents a change in personality.The level of motivation must be interpreted in the context of the individual's cultural background and personal experiences.
Apathy is considered to be clinically significant when:
(1) there is evidence of diminished motivation relative to the norms of one age and culture; and (2) the lack of motivation is severe enough to interfere with psychosocial functioning[3]. In evaluating motivation, it is to remember that apathy need not be prevasive or incapacitating. In fact, adaptive functioning requires selectivity of choices. Healthy individuals are, of necessity, relatively or selectively apathetic about some goal in comparison with others.

Characterizing the individual's skill accomplishments, goals and aspirations, emotional relationship, and social interactions will help distinguish apathy that is adaptive (having functional significance) and selective (making a carefully chosen response) from that which is defensive (meaning response that is protective but not necessarily functional) and pervasive (meaning always present.)

Apathy Evaluation Scale (AES)[5] is the most widely used and extensively validated rating scale for measuring the presence and severity of apathy. This 18-item instrument is specifically designed to assess the elements of apathy's operational definition, namely a decrease in the behavioral , cognitive and emotional concomitants of goal-directed behavior. Self-informant, and clinician-rated versions of the AES have been developed. The validity of the AES has been confirmed in studies of patients with stroke[6] and Parkinson's disease. Psychometric analyses have also demonestrated that the AES discriminates between apathy and depression symptoms. Some patients have shown significant apathy without elevation of depression scores, a pattern consistant with the proposed concept of the syndrome of apathy[8]. Taken together, these and other research findings[3] strongly confirm the discriminability of apathy and depression in neuropsychiatric populations.

A recent study[8] determined that four items of the Hamilton Depression Rating Scale (HDRS-17 items) may be used to estimate apathy. Apathy is assessed by deriving a subtotal score using the following HDRS items : (1) lack of interest; (2) psychomotor retardation; (3) lack of energy; and (4) lack of insight. The correlation between the AES and HDRS total scores in this study is significantly reduced when the four "apathy items" are excluded from the HDRS total score. This finding supports the notion that this HDRS subtotal score can serve as a measure of apathy when more specific instruments of apathy are not used.

Differential diagnosis of Apathy

Depression

The essential difference between apathy and depression is that apathy is a syndrome of diminished motivation, whereas depression is defined by disturbances in mood[1]. Difficultly differentiating the syndromes of apathy and depression is understandable, as both are associated with diminished motivation, often in depression and always in apathy. The most useful features for differentiating apathy and depression occur in the emotional and cognitive areas. Depression is, by definition, a dysphoric state, whereas patients with a syndrome of apathy do not report dysphoria. The emotional response of depressed patients also differs from that of patients with apathy. Whereas apathetic patients show attenuated emotional responses to both positive and negative rewards, depressed patients are biased to perceive and respond selectively to negative events. In the cognitive dimension, individuals with depression often report negative thoughts about the self, the present, and the future[9]. In apathy, a lack of concern is present, with diminution in goals interests, and curiosity. Furthermore, in depressed patients who claim to lack interest, careful assessment generally reveals that their lack of interest actually reflects despair, hopelessness, and pessimism. Thus, the lack of interest of the depressed individual is due to diminished expectancy of achieving goals that, if anything, are now overvalued. In contrast, patients with apathy value their goals less than they used to and are therefore truly unconcerned.

Delirium

Apathy is a common symptom of delirium. Persons with delirium who are sedate, drowsy, or hypoactive are likely to be characterized as apathetic. Presumably, the mechanism of apathy in these cases is suppression of the reticular activating system by the metabolic effects of medical conditions, or the effects of gross brain disease on the neural connections or blood supply of this system or structures mediating attention.

Dementia

Dementing diseases, particularly those involving the frontal lobes and basal ganglia, often cause apathy. Alzheimer disease may produce apathy, but does not necessarily do so in the earliest stages of the disease. It may cause apathy by impairing the cognitive basis of motivation (via deterioration of frontal lobes and association areas): by disrupting the right parietotemporal circuits involved in perceiving emotional significance of information; or by impairing the subcortical mechaisms necessary for normal mood and drive.

Abulia

Individuals with abulia associated with mesial frontal (ie. anterior cingulate) damage show diminished will or motivation. Abulia is associated with damage to the anterior cingulate gyrus, which is part of the mesial frontal system in the brain. In clinical practice, abulia generally refers to patients who are fully awake but otherwise severely impaired in their ability to communicate

and to initiate and self-regulate purposeful behavior. Apathy and abulia have been viewed as part of a continuum of motivational impairment, with abulia representing the more severely impaired patients[1-2] .Consistent with this, the gross brain lesions that cause abulia may cause apathy when they are smaller and less completely destructive, or evaluated during the recovery stage.

Akinesia

Akinesia is primarily a disorder of movement, not motivation. However, the two syndromes are not necessarily unassociated. A mildly akinetic patient can be severely apathetic, and a severely akinetic patient can be highly motivated. Akinetic patients show diminution or loss of the initiation of speech and actions. Basal ganglia disease and use of neuroleptic medications, the most prominant causes of akinesia, also cause apathy.

Aprosodia

Aprosodia is a disorder of emotion in which patients show impaired ability to perceive, interpret, or express emotion. Aprosodias are generally attributed to disease of the right hemisphere. Flat affect and inappropriate cheerfulness can occur in both apathy and aprosodia. Therefore, apathy and aprosodia may be difficult to distinguish from each other on the basis of emotional responsivity.

Neural substrates of apathy

The neural mechanisms of apathy in neuropsychiatric disorders have been described in a review by Mega and Cummings[10]. Clinical research suggests that dopaminergic activity mediates diminished motivation in a number of conditions, such as subcortical diseases, frontal lobe syndromes, negative symptoms of schizophrenia, and postpsychotic depression. Thus, increasing dopaminergic activity is the primary strategy or the pharmacologic treatment of patients with apathy[8]. Apathy, however, should not be viewed simply as a problem of dopaminergic hypoactivity[11].

Dopamine systems

Apathy has been associated with hypofunctionality of the frontal cortex[10]. The mesocortical dopaminergic system arises in the ventral tegmental area of the mesencephalon and innervates the cerebral cortex, particularly the frontal cortex. Increased mesocortical dopaminergic function associated with dopamine against or stimulant therapy is presumed to be an important source of clinical improvement in patients whose apathy is primarily associated with frontal rather than subcorticl dysfuncton[8].

The mesolimbic dopaminergic system, which also emerges from the ventral tegmental area, innervates the nucleus accumbens, amygdala, hippocampus, ventral pallidum and other forebrain structures. These and other interconnected structures (eg, the medial dorsal nucleus of the thalamus, the prefrontal cortex, and the pedunculopontine region of the brainstem) comprise a highly integrated series of circuits that represent the motivational state of the organism. This network translates motivition into action[12]. Output of this motivation circuitry depends substantially on the pedunculopontine region and its connection to the basal ganglia and reticulospinal system. The benefit of dopamine aganist therapy in cases of subcortical disorders are believed to result from an increase in mesolimbic dopaminergic activity[8].

Frontal-Subcortical circuits

Three syndromes produced by frontal lobe damage are associated with apathy. Each frontal region is part of a specific cortical-subcortical circuit involving the thalamus, basal ganglia and forebrain[10, 13,14]. Damage affecting the anterior cingulate/mesiofrontal region produces a clinical syndrome of apathy. Dorsolateral prefrontal dysfunction is associates with impairment in the executive cognition necessary for planining and monitoring goal-directed behavior. Patients with damage to the lateral orbitoforntal cortex present with charges in personality marked by irritability, angry outbursts, or disinhibited sexual behavior. In these patients, however, there is often an underlying background of abulia and apathy that pervades the clinical picture.[15] These frontal regions are connected to specific regions of caudate nucles, nucles accumbens, globus pallidus, and medical dorsal nucleus of the thalamus. Injury to any component of these three circuits produces the behavioral, emotional, and/or cognitive symptoms of that circuit.

Clinical causes of apathy

Clinically significant apathy can be due to primary neurologic processes and medical conditions that alter the neural systems subserving motivation. Table-2 lists clinical conditions associated with apathy.

Alzheimer disease

Apathy is a pervasive neurobehavioral disturbance in Alzheimer disease[16]. The prevalence and severity of the syndrome of apathy increases with the progression of Alzheimer disease, with prevalence reports varying from 29% to 88%.[17-19] Functional imaging studies suggest that the syndrom of apathy in this patient group is related to the severity of prefrontal and anterior temporal dysfunction[20].

Frontal lobe dysfunction

Neurologic diseases of any etiology affecting the frontal lobes produce changes in cognition and behavior in which motivational loss is often sufficiently prominent to be characterized as a syndrome of apathy. Multiple sclerosis, Pick's disease, other non-Alzheimer frontal dementias, frontal tumors, stroke, and hydrocephalus are examples of patholigic processes that may produce frontal lobe syndromes[21]

Basal ganglia disease

The syndrom of apathy has been associated with damage to the ventral striatum and globus pallidus[10,14]. Systematic investigations of basal ganglia disease have focused primarily on Parkinson's disease[7, 20, 22], Huntington's disease[17, 18] Progressive supranuclear palsy[23] and human immunodeficiency virus HIV) infection.[24] In these and other subcortical diseases, loss of motivation often occurs in association with symptoms of mood disturbance and cognitive loss. HIV infection can leadto significant neuronal cell loss in the basal ganglia. Clinical studies indicate that apathy may reach syndromal proportions in the latter stages of disease progression[24]. A recent study examined the relationship between apathy, depression and neurocognitive functioning during the asymptomatic stage of HIV infection[25]. The study results showed that psychomotor slowing was associated with an increase in apathy but not depression in this cohort. These findings support the notion that apathy symptoms may be one of the earliest clinical manifestations of central of nervous system involvement in HIV-infected patients.

Diencephalic and amygdala damage

Dysfunction of the diencephalon and amygdala may also produce the syndrome of apathy. The best known of the conditions affecting these areas of the brain is Korsakoff's syndrome. Tumor, stroke, and trauma injuring the diencephalon may also produce a syndrome of apathy. The

role of the amygdala in motivation is reflected by the Kluver-Bucy syndrome, which is, in part, characterized by blunted affect and apathy.

Hemispheric stroke

Apathy is a frequent finding among patients with acute stroke lesions and may coexist with other emotional and cognitive poststroke disturbances[6]. Apathy is more common after focal right hemispheric stroke. In one investigation, a reaction of indifference occured in approximately 25% of patients with right hemispheric stroke.[26] In another study a syndrome of apathy was detected in 23% of patients with right hemispheric stroke and 11% of patients with left hemispheric stroke.[5] A notable finding was that these patients presented with elevated apathy scores but did not show elevated HRDS depression scores.

Depression

Apathy is well recognized as a symptom of depression. It has been reported frequently in adolescent depression,[27] and is often a sailent feature of late-life depressive dieorders [2, 28,29] A substantial percentage of cases of subsyndromal depression in the elderly may actually be apathy cases, because the features generally attributed to depression may actually reflect a syndrome of apathy. Accurately diagnosing such subsyndromal "depressions" as apathetic states has important implications for assessment and treatment. In all age groups, identifying apathy as an accompainment of depression can improve outcome by making recovery of motivation a critical goal of antidepressant treatment and, by implication, a criterion for evaluating adequacy of treatment.

Psychotic disorders

Apathy is well known in choronic schizophrenia. The clinical improvement of negative symptoms (motivational impairment) in schizophrenia is critical in that unmotivated patients have adverse social and functional prognoses. Postpsychotic depression is usually believed to be a depressive syndrome that follows remission from acute schizophrenia or other psychotic disorders. Multiple studies of postsphychotic depression suggest, however, that it often present as a syndrome of apathy rather than dysphoria[1].

Current medications

Drugs disrupting the dopaminergic systems of the brain share the ability to produce apathy. The most familiar form of drug-induced apathy is associated with neuroleptics. Commonly, such apathy occurs as part of neuroleptic-induced akinesia. Selective serotonin reutake inhibitors (SSRIs) may also produce varying degrees of a syndrome of apathy. Some patients exprience a disabling or distressing loss of motivation[30], while others show an attenuation of emotional responsivity that may actually contribute to the reduction in dyphoria in that is part of the antidepressant benefit[31].

Other medical conditions

Apathy is commonly viewed as a nonspecific symptom of various medical conditions. It may be a prominent symptom in hypoaroused cases of delirium. Patients with chronic fatigue syndrome and Lyme diesease will present with a syndrome of apathy, although the prominence of anergia and fatigability in these patients is distinctive. In addition, a syndrome of apathy has been described in some elderly patients with hyperthyroidism[32]. It also result from pseudohypoparathyrodism, presumable as a result of associated central dopamonergic abnormalties[33].

Table 2 : Conditions associated with the syndrome of apathy

Alzheimer disease
Frontal lobe dysfunction
Conditions affecting the frontal-subcortical circuit involving the anterior cingulate gyrus and associated globus pallidus, nucleus accumbens, and medial dorsal nucleus of the thalamus

Basal ganglia disease
Parkinson's Disease, Huntington's disease, progresive supranuclear palsy, HIV infection, etc.

Diencephalic and amygdala damage
Kluver-Buch syndrome, Korsakoff's syndrome, tumor, stroke, etc.

Right hemispere damage
Stroke, tumors and other conditions involving the inferior parietal lobule and its connections to the frontal lobe

Other neuroligic disorders
Conditions affecting any of the above neural structures

Partially treated depression
Schizophrenia
Deficit syndrome (enduring negative symptoms)

Drug-induced conditions
Neuroleptics, selective serotonin reuptake inhibitors, chronic marijuana use, amphetamine or cocaine withdrawal.

Treatment approaches-

Medication history

In all patients with apathy , it is important to consider the presence of neuroleptic drugs or SSRIs' either of which may include or exacerbate symptoms of loss of motivation. The SSRIs presumably produce apathy because of serotonergic modulation of the brainstem dopaminergic systems[34]. In patients with apathy receiving neuroleptics or SSRIs, dose reduction or drug discontinuation is often an essential first step in managment. Other psychoactive agents, such as benzodiazepines and anticholinergic drugs, may impair motivation indirectly because of their effects on attention and memory. Pharmacologic interventions for the treatment of negative symptoms associated with schizoohrenia are under investigation. Atypical anti psychotic medication may be particularly useful in schizophrenia and other patiant groups with prominent negative symptoms.

Psychiatric assessment

Apathy is commonly, but not always, seen in major depression. Formal ratings of apathy and depression may help clarify the extent to which motivational loss accounts for a patient's functional deficits. It is important to keep in mind that apathy symptoms along may account for significant elevation of depression rating scores. Apathy in the setting of depression is generally best treated by selecting the most effective antidepressant regimen for the patient's mood disorder. If apathy is particularly prominent, several modifications of treatment may be considered[35]. In the case is otherwise uncomplicated stimulating antidepressants, those with dopamine uptake blocking selectivity may be preferable. Sertraline, in comparison with other SSRIs, has relative strong dopaminergic uptaje blocking activity. Bupropion also has some selectivity for dopaminergic reuptake mechanisms.

Following a proper antidepressant treatment trial, some deoressed patients show resoluting of vegetative symptoms of depression, but continue to show symptoms of a syndrome of

apathy (such as a lack of ir:erest, anergy, dimished emotioal reactivity, and diminished initiative). In these patients, treatments with methy phenidate or an amphetamine should be cosidered[36]. If an SSRI was used initially, dose reduction is sometimes sufficient to provide optimal outcome. When apathy is prominent in the context of depression, thepatients should also be evaluated carefully for the presence of coexisting frontal-subcortical diseases. It is not uncommon for such patients to be mistakenly diagnosed as depressed and treated for depression without benefit Looking at such patients in retrospect, it is often clear that depression-specific symptoms (eg, depressed mood, guilt, suicidal ideation) are absent or minimal.

Neurologic assessment

In neuroligic disease, apathy may be the dominant component of the clinical picture or it may occur in association with other symptom clusters (such as dementia or depression). In either case, its presence should be carefully discriminated. Subtle extrapyramidal findings are often important clues to conditions affecting basal ganglia and related frontal-subcortical circuits. An apathetic patient with an underlying neurologic disorder commonly requires separate treatment for apathy. Increasing dopaminergic function by reducing the neuroleptic dosage, switching to an atypical antipsychotic, or adding a dopamine aganist is often indicated for apathy.

Neuropsychological assessment

Apathy has been asscoiated with executive dysfunction. An assessment of the patient's cognitive capacity will identity the extent to which executive function and other cognitive impairment account for difficulties in planning, intiating, and executing daily activities. Individuals without evidence of more widespread dementia symptoms (eg, impairments in language, visuospatial function, memory) tolerate drug therapy better. One therapeutic approach[35] treat such patients with stimulant drugs (eg, methylphenidate). Indirect dopamine agonists (eg, bromocriptine) also may be tried in this setting, although these are generally reserved with at least some evidence of extrapyramidal symptoms or diencephalic disease. Caregivers should be counseled to communicate with patients in a way that adapts to the specific pattern of executive impairment.[13,37] For example, lack of intiative may be comnensated for by structure and cueing. Complex or multiple-step activities may be accomplished by simplifying the task or providing instructions matched to the patient's sequencing limitations. Recognizing that the behavior is stimulus bound can be used advantageously by maintaining patients in their homes and by including familar items in their new environment.

Conclusion

Apathy occurs as a symptom or syndrome in a variety of neuropsychiatric and medical conditions. Appropriate assessment, diagnosis and treatment of apathy may greatly improve patient quality of life. Treatment protocols are needed to examine systematically the effects of doaminergic drugs (agonist drugs or SSRIs) on apathy in neuropsychiatric disorders. Identifying the indications and risk factors for treating apathy in neurologic disease will likely depend the benefits of pharmacotherapy to clinical populations believed to be untreatable until recently. The advent of brain-imaging procedures, particularly functional imaging has opened many corridors for exploring the neurobiologic correlates of apathy.

References

1. Marin R.S Differential diagnosis and classification of apathy. AM J Psychiatry. 1990; 147: 22-30.
2. Marin RS. Apathy: a neuropsychiatric syndrom. J Neuropsychiatry Clin Neurosci. 1991; 3: 243-254.
3. Marin RS Apathy and related disorder of diminished motivation. In: Dickstein LJ, Riba MB, Olrham JM, eds. Review of Psychiatry. Vol 15. Washington, DC:
American Psychiatric Press; 1996.
4. American Psychiatric Association. Diognostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994: 771.
5. Marin RS. Biedrzycki RC, Firinciogullari S. Reliability and validity of the Apathy Evaluation Scale. Psychiatry Res. 1991; 38: 143-162.
6. Starkstein SE. Federoff JP, Price TR et al. Apathy following cerebrovascular lesions. Stroke. 1993; 24: 1625-1630.
7. Starkstein SE, Mayberg HS, Perziosi TJ, et al. Reliability validity, and clinical correlates of apathy in Parkinson's disease. J. Neuropsychiatry Clin Neurosci. 1992; 4: 134-139.
8. Marin RS. Firinciogullari MS, Biedrzycki RC, Group differences in the relationship between apathy and depression. J Nerv Ment Dis. 1994; 182: 235-239.
9. Beck AT, Weishaar M. Congnitive therapy In: Freeman A, Simon K, Beutler L, et al, eds. Comprehensive Handbook of Congntive Therapy. New York. NY : Plenum Press; 1989: 21-36.
10. Mega MS, Cummings JL. Frontal-subcortical circuts and neuropsychiatric disorders. J Neuropsychiatry Clin Neurosci. 1994; 6: 358-370.
11. Kalivas PW, Barnes CD, Limbic Motor Circuits and Neuropsychiatry. Boca Raton, Fla: CRC Press; 1993.
12. Morgenson GJ, Brudzynski SM, Wu M, et al. From
Motor Circuits and Neuropsychiatry. Boca Raton, Fla: CRC Press; 1993: 193-236.
13. Campbell JJ, Duffy JD, Salloway SP. Treatment strategies for patients with dysexecutive syndromes. J Neuropsychpatry Clin Neurosci. 1994; 6: 411-418.
14. Cummings J. Frontal-subcortical circuits and human behavior. Arch Neurol. 1993; 50: 873-880.
15. Hecaen H, Albert M. Disorder of mental functioning related to frontal love pathology In: Benson DF, Blumer D, eds. Psychiatric Aspects of Neuroligic Disease. New York, NY: Grune & Stratton; 1975: 137-149.
16. Green JG, Smith R, Gardinir M, Timbury GC. Measuring beharioral disturbances of elderly demended patients in the community and its effects on relatives : a factor analytic study. Age Aging. 1982; 11: 121-126.
17. Burns A, Folstein S, Brandt J, et al. Clinicla assessment of irritability, aggression and apathy in Huntington and Alzheimer diseases. J Nerv Ment Dis. 1990; 178: 20-26.
18. Petry S, Cummings JL, Hill Ma, et al. Personality alterations in dementia of Alzheimer's type: a three-year follow-up study. J Geriatr Psychiatry Neurol. 1989; 2: 203-207. patients. Brain. 1984; 107: 81-93.
19. Rubin EH, Morris JC, Storandt M, et al. The progression of personality . changes in semile dementia of the Alzheimer's type. J. Am Geriatr Soc. 1987; 35: 721-725
20. Craig AH, Cummings JL, Fairbanks L, Ltti L, Miller BL, Mena I. Cerebral blood flow correlates of apathy in Alzheimer disease. Arch Neurol. 1996; 1116-1120.
21. Stuss DT, Benson DF. The Frontal Lobes. New York, NY: Raven Press; 1975.
22. Marsden CD, Parkes JD, Success and problems of long-term levodopa therapy in Parkinson's disease. Lancet. 1997; 1: 345-349.
23. Albert M, Feldman R, Willis A. The "subcortical dementia" of progressive supranuclear pa;sy. J Neurol Neurosurg Psychiatry. 1974; 37: 121-130.24. Navia BA, Jordon DB, Price RW. AIDS dementia complex, clinical features. Ann Neurol. 1989; 19: 514-524.
25. Silva SG, Stern RA, Chaisson N, et al. Apathy and neurobehavioral functioning in asymptomatic HIV-seropositive gay men. J Neurophychiatry Clin Neurosci. 1994; 6: 311.
26. Robinson RG, Kubos KL, Starr LB, et al. Mood disorders in strok
27. Inamder SC, Simopoulos G, Osborn M, et al. Phenomenology associated with depressed moods in adolescents. Am J Psychiatry.1979; 136: 158-159.

28. Blazer DG, Depression in Life. St Louis, MO: <osby-Tear Book; 1982.
29. Raskin A, Sathananthan G. Depression in the elderly. Psycopharmacol Bull, 1979: 15 : 14-16.
30. Hoehn-Saric R, Lipsey JR, Mcleod DR. APathy and indifferences in patients of fluvoxamine and fluoxetine. J. Clin Psychopharmacol. 1990 : 32: 672-674.
31. Gelenberg A, ed. apathy and new antidepressants. Biological Therapies in Psychitry Newsletter. 1991 : 14 : 9-12.
32. Brenner I. Apathetic hyperthyrodis. J. Clin Psychiatry. 1978: 39: 479-480.
33. Bachman DL. ZAlbert ML. The dopaminergic syndromes of dementia. In. Pilleri G, Tagliavini F, eds. Cerebral again and Degenerative Dementias. Waldau-Berne, Switzerland : institute of Neurology, University of Berne; 1985: 91-118.
34. Willner P, Schee-Kruger J. Measolimbic Dopamine System : From Motivation to New York, NY John Wilery & Sons; 1991.
35. Marin RS, Fogel BS, Hawkings J, et al. apathu: a treatment syndrome. J Neuropsychiatry Clin Neurosci. 1995 : 7:23-30.
36. Chiarello RJ, Cole JO, The use of psychostimulants in general in psychiatry. Arch Gen Psychiatry. 1987 : 44: 286-295.
37. Royall DR, Mahurin RK, Neuroanatomy, meaaaasurement, and clinical significance of the executive cognitive functions , In : functions In : Dickstein LJ, Riba MB, Oldham JM, eds. Review of Psychiatry. Vol 15. Washingtom, DN : American Psychiatric Press : 1996 : 175-204.

Continued from page no. - 190

MSD NEWS

Tuesday, 12th February 2004 at department of Surgery, Rangpur Medical College Hospital where the eminent Professor Dr. M.A Sobhan, Principal & Head of the dept. of Surgery, Rangpur Medical College Hospital chaired the session.

Symposium on "Common Urological Problems in Bangladesh"

Venue: Auditorium of RDRS, Rangpur.

From left to right : Assoc. Prof. Dr. M. A. Salam, Prof. Dr. M. A. Sobhan, Dr. M. N. Nag, Prof. Azizul Islam, Mr. Quamrul Hassan, Vice-President, OLL, Mr. A. K. M. Sirajul Islam, Sales Manager OLL.

A symposium was sponsored by Orion Laboratories Ltd. on "Common Urological Problems in Bangladesh" on Wednesday, 24th March 2004 at auditorium of RDRS, Rangpur where Professor M. A. Sobhan, Principal & Head, dept. of Surgery, Rangpur Medical College Hospital chaired the session. Eminent Urologist Dr. M. A. Salam, Assoc. Prof. of Urology, BSMMU presented the scientific papers on" Common Urological Problems in Bangladesh" as a keynote speaker. Prof. Omor Ali, Prof. Nazmul Islam, Prof. Azizul Islam, Dr. M. N. Nag were also present as special guests.

Venue: Auditorium of Northway Motel, Bogra.

A symposium was sponsored by Orion Laboratories Ltd. on "Common Urological Problems in Bangladesh" on Thursday, 25th March 2004 at Auditorium of Northway Motel, Bogra where Dr. Abdus Shukur, Principal, SZMC, Bogra chaired the session and Dr. M H Alamgir, Project Director, SZMC, Bogra was also present as Co-Chairperson. Eminent Urologist Dr. M. A. Salam, Assoc. Prof. of Urology, BSMMU presented the scientific papers on " Common Urological Problems in Bangladesh" as a key-note speaker. Prof. Shahjahan Ali , Head of the dept. of Surgery & Dr. Gulshan Ara, Head of the dept. of Gynae were also present as panel of experts. Prof AKM Moyazzem Hossain, Civil Surgeon of Bogra, Dr. Shah Md. Shahjahan Ali, President of BMA, Bogra Dr. Azfarul Habib, Secretary, BMA, Bogra, Dr. Mainul Hasan sadik, Vice Prersident Central BMA were present as special guests.

Round Table Meeting on "Role of antibiotics in Wound healing"

Venue : Suruchi Food Court, Momtaz Plaza, Dhanmondi, Dhaka

Orion Laboratories Limited arranged a RTM on "Role of Antibiotics in wound healing" on 29th March 2004 at Suruchi Food Court, Momtaz Plaza, Dhanmondi, Dhaka. Dr. M.A Momen, R/S, Casualty, DMCH, chaired the occasion & Dr. Sarwar Mahabub, EMO, DMCH discussed on the topic

Round Table Meeting on "Stimulin-A Life Style Advance in Diabetes"

Venue : Conference Room of Wari NHN, Dhaka.

Orion Laboratories Limited arranged a Round table meeting with the doctors of Wari NHN on Stimulin - A life Style advance in diabetes on Wednesday 17th March 2004 at conference room of Wari NHN, Dhaka. Where Dr. Ataur Rahman, Incharge Wari NHN chaired the session.

Venue: Conference Room of Diabetic Room of Hospital, Khulna.

Orion Laboratories Limited arranged a RTM on "Stimulin - A life Style advance in diabetes" on 12th April 2004 at conference room of diabetic hospital khulna.

Scientific Seminar on "Management of Ischemic Heart Disease"

Venue: Seminar Room 6th Floor of, Johnson Road, DNMCH.

A Scientific Seminar was sponsored by Orion Laboratories Ltd. on "Management of Ischemic Heart Disease" on Thursday, 15th April 2004 at Seminar Room (6th Floor) of 53/1, Johnson Road, DNMCH where Professor Dr. M. A. Bashar, Head of the dept. of Cardiology, DNMCH chaired the session. Dr. Masudur Rahman, MO, dept. of Cardiology and Dr. Dipankar Chandra Nag, Asst. Professor, Cardiology, DNMCH, presented their scientific papers on "Management of IHD" respectively.

Scientific Seminar on"Nitrates in Cardiovascular Practice"

Venue: Yung king Chinese Restaurant, Mymensingh.

From left to right : Assoc. Prof. Dr. Md. Shamsul Haque, Asst. Prof. Dr. M. A. Bari

A Scientific Seminar was sponsored by Orion Laboratories Ltd. on "Nitrates in Cardiovascular practice" on Wednesday, 17th March 2004 at Yung King Chinese Restaurant. Where Assoc. Professor Dr. Md. Shamsul Haque, Head of the dept. of Cardiology, MMCH chaired the session. Dr. Ashutosh Dev Shorma, Internee Doctor, MMCH, presented the scientific paper on " Nitrates in Cardiovascular Practice". Dr. M. A. Bari, Assist. Professor of cardiology, MMCH was also present as special guest.

Trimetazidine : An innovative metabolic approach to ischemic heart disease

Patwary MSR[1]

The ORION 2004 ; 18 : 173-174

Introductioin

Patients with stable angina require risk factor modification, education, and pharmacological treatment with beta-blocker, calcium channel blockers and nitrates, together with cardioprotection with aspirin, lipid-lowering drugs and ACE inhibitors. Despite this treatment, about one-third of patients do not become free of angina. Various combinations of haemodynamic agents did not demonstrate significantly superior efficacy on exercise test parameters. Therefore, there is a strong rationale for using new combined therapeutic approaches including metabolic drugs such as trimetazidine[1]. But interventional treatment should be performed in higher risk cases those who have disabling angina despite pharmacological treatment.

Antianginal cardioprotective metabolic modulators

1. Inhibitors of fatty acid beta-oxidation
   Trimetazidine
   Ranolazine.
2. Inhibitors of carnitine palmitoyl transferase
   Perhexiline
   Etoxomir
   Oxfenicine
3. Inhibitors of lipolysis
   Nicotinic acid & it's derivatives

Trimetazidine

-Effective anti anginal agent.
-Cardiac Metabolism modulating drug.
-Without having direct hemodynamic effects.
-Cardioprotective.
-Favorable safety and excellent tolerability profile

Mechanism of action

Selectively inhibit mitochondrial long chain 3- Ketoacyl co-enzyme A thiolase, the last enzyme involved in beta-oxidation. Affects myocardial substrate utilization by inhibiting fatty acid oxidation and shifting ATP production with less O_2 consumption from FFA to glucose oxidation

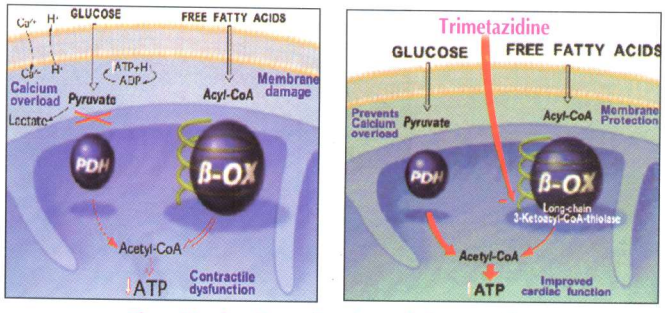


Fig : Mechanism of action of trimetazidine

1. **Dr. Md. Shafiqur Rahman Patwary,** MBBS, MCPS, FCPS, MD.
Department of Cardiology, NICVD.

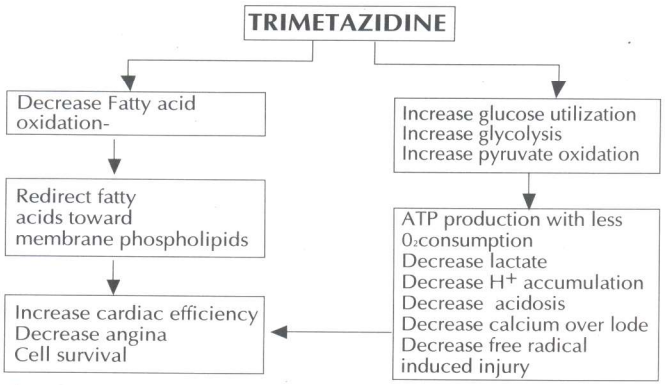


Fig: Pharmacological effects of trimetazidine

Effects of anti-anginal drugs on coronary blood flow, central hemodynamics, and myocardial contractility

Class of drug	Oxygen Supply	Oxygen Demand			
	Coronary blood flow	Heart rate	Arterial pressure (after load)	Venous return (preload)	Myocardial contractility
Beta-Blockers	No effect	↓↓	↓	No effect	↓
Ca^2+-antagonists Dihydropyridines	↑↑	↑ (Reflex)	↓↓	↓	↓
Ca^2+-antagonists Diltiazem	↑	↓	↓	↓	↓
Long-acting nitrates	↑	↑ (Reflex)	↓	↓↓	No effect
Trimetazidine	No effect	No effect	No effect	No effect	No effect

Indications

-Angina pectoris
-Vertigo and tinnitus
-Visual disorders of circulatory origin.

Possible field of application

-Chronic ischemic contractile dysfunction
-Cytoprotective agent during myocardial revascularization procedures.

Trimetazidine and stable angina

The efficacy of trimetazidine as an antianginal drug has been assessed in randomized, placebo-controlled studies, both as solo treatment and in combination with beta-blockers and calcium channel blockers. Several studies have tested the efficacy of trimetazidine and have demonstrated this agent to be at least as effective as and better tolerated than haemodynamic agents[2]. In stable angina it improves exercise tolerance[3,4] and elevates the ischaemic threshold to an extent comparable with beta-blockers and calcium channel blockers. The combination of trimetazidine and a beta- blocker appears more effective than the combination of nitrates and a beta- blocker, and the addition of trimetazidine improves symptoms in patients resistant to diltiazem or metoprolol[5,6,7]. It is ideal for combination therapy. Ideal target populations for trimetazidine are diabetic, not suitable for revascularization. It is beneficial for refractory symptoms in spite of maximal traditional therapy or following revascularization.

Trimetazidine and left ventricular ischemic dysfunction

Improves myocardial contractility and stroke volume

↓

Improves peripheral perfusion

↓

Decreases neurohumoral activation

↓

Improves prognosis and decreases arrhythmogenic risk.

Trimetazidine should be considered as a valuable therapeutic adjunct to be used on top of other more traditional available agents, especially in patients with severe, chronic ischaemic dysfunction, particularly if this is not amenable to revascularization[8]. The myocardial effects of trimetazidine has been assessed in three randomized, double -blind, placebo-controlled studies in patients with ischaemic cardiomyopathy, stable angina or hibernating myocardium showed improved LV function and improved contractile response to inotropic stimulation[9,10,11].

Trimetazidine in myocardial revascularization procedures

Myocardial injury during revascularization procedures is an important determinant of clinical outcome. Therefore, protection of the ischaemic myocardium during such procedures should be an important goal, both for cardiac surgeons and interventionists. In elective coronary angioplasty, primary coronary angioplasty and coronary surgery, patients who were pretreated with trimetazidine exhibited lesser release of markers of myocardial injury[12,13,14].

Conclusion

Clinical efficacy profile and favorable safety built a reputation as the ideal drug for chronic angina. Use of trimetazidine should not be restricted to angina, its indication might include left ventricular dysfunction due to severe ischemic cardiomyopathy to hibernating myocardium.

References

1. Klein W.Treatment patterns in stable angina :objectives and reality .Eur Heart J 2001; 3(Supplement 0):08-11.
2. Detry JM, Sellier P, Pennaforte S et al. Trimetazidine: a new concept in the treatment of angina. Comparison with propanolol in patients with stable angina. Br J Cli Pharmacol 1994;37:279-88.
3. Detry JM. Clinical features of an anti -anginal drug in angina pectoris. Eur Heart J 1993;14:18-24.
4. Sellier P ,Audouin P, Payen B et al. Acute effects of trimetazidine evaluated by exercise testing. Eur J Cli Pharmacol 1987; 33:205-7.
5. Marzilli M. Trimetazidine: a metabolic agent for the treatment of stable angina. Eur Heart J 2001; 3(Supplement 0): 12-15.
6. Szwed H, Sadowski Z, Elikowski W et al. Combination treatment of stable effort angina using trimetazidine and metoprolol: results of a randomized, double-blind, multicentre study (TRIMPOL II). Eur Heart J 2001(in press).
7. Levy S,and the group of South of France Investigators. Combination therapy of trimetazidine with diltiazem in patients with coronary artery disease. Am J Cardiol 1995; 76:12B-16B.
8. Chierchia SL. Trimetazidine and left ventricular ischaemic dysfunction: an overview of clinical evidence. Eur Heart J 2001; 3(Supplement 0): 16-20.
9. Brottier L, Barat JL, Combe C et al. Therapeutic value of a cardioprotective agent in patients with severe ischaemic cardiomyopathy. Eur Heart J 1990; 11:207-12.
10. Lu C, Dabrowsky P ,Fragasso G, Chierchia S. Effects of trimetazidine on ischemic left ventricular dysfunction in patients with coronary artery disease. Am J Cardiol 1998;82:898-901.
11. Belardinelli R ,Purcaro A. Effects of trimetazidine on the contractile response of chronically dysfunctional myocardium to low dose dobutamine in ischaemic cardiomyopathy. Eur Heart J 2001(in press).
12. Kober G, Buck T, Sievert H ,Vallbracht C . Myocardial protection during percutaneous transluminal coronary angioplasty: effects of trimetazidine. Eur Heart J 1992;13:1109-15.
13. Steg PG, Laperche T, Karila-Cohen D. Value of trimetazidine as adjuvant therapy for primary PTCA at the acute stage of myocardial infarction. Eur Heart J 1999;(suppl 0):019-23.
14. Fabiani JN, Ponzio O, Emerit I et al. Cardioprotective effects of trimetazidine during coronary artery graft surgery. J Cardiovasc Surg 1992; 33:486-91.

Non operative treatment modalities of clubfoot

Amin MR[1]

The ORION 2004 ; 18 : 175-176

Introduction

Clubfoot still remains an unsolved problem in the field of pediatric surgery. In spite of extensive research, Hippocrates first documented treatment of clubfoot, although Egyptians and Aztecs knew about clubfoot in ancient times. The treatment pattern has changed through centuries from repeated gentle manual correction to forcible correction by using splints and wrenches. Use of adhesive plast for the correction of clubfoot, has been succeeded by use of plast of paris cast. The surgical procedure included soft tissue surgery for early correction of the deformity and bony surgery in late cases where secondary bony change has occurred. Tendon transfer and correction of supra malleolar lateral tibial rotation in clubfoot by osteotomy have also been suggested by various authors. Slow and controlled distraction of soft tissues by various devises has been used in the twentieth century for correction of clubfoot.

In spite of various methods for the correction of clubfoot the main stages of treatment are correction of contracted soft tissues at early age and bony surgery for secondary deformities.The talipes equinovares or clubfoot is shape deformity of the foot including fore foot and hind foot. A typical equinovaras looks like a club, so the deformity is known as club foot(Fig-1). he abnormal relationship between the tarsal bones associated with soft tissues contractures is the main factors for the deformity. But the aetiology has not been elicited yet. So the non-operative treatment protocol for clubfoot has changing from time to time, which will be illustrated in the following lines.

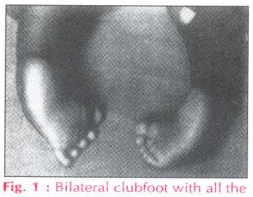


Fig. 1 : Bilateral clubfoot with all the components of the deformity.

Non-operative treatment protocol for clubfoot

A. Repeated seatle manual correction

The Egyptial tomb wall paintings showing clubfoot deformity, yet archeologic investigators in Mexico, who revealed that Aztecs knew about clubfoot and treated it with Cactus leaves, unearthed another early evidence of clubfoot. However, the first documentation on clubfoot was from the work of Hippocrates (300 BC), who described clubfoot deformity and caunciated two definite principles- i) most care were reducible and ii) the treatment should begin as early as possible, before the deformity of bones is established. He used to treat clubfoot since birth by repeated gentle manual correction with application of strength bandages during manipulation and also used special shoes to hold the correction. Arcaeus in France in 1658 describes in details about the Hippocrates gentle stretching maneuver in the treatment of clubfoot. In Thomas hospital london, Cheselden treated stretching using tape in the year 1733. He practised this technique for about forty years.

1. **Dr. Md. Ruhul Amin,** MBBS, MCPS, FCPS, MS
Post Fellowship training in padiatric surgery and urology (Japan)
Associate Professor, Dept. of Paediatric surgery, BSMMU, Dhaka.

B. Mechanical device for gradual correction

Clubfoot was treated by Fabricius Hildamus in Italy in 1646 using an apparatus shaped like a boot fitted with a plate on the lateral side hinged at the ankle connected with a turnbuckle for gradual correction. Similar use of a metal splint was advocated by Ambrose pare in france in 1665. Which corrected all or part of a defect. He used special shoes to maintain the correction in 1803 Scarpa described clubfoot deformity as a "Congenital dislocation of the astragalo calcaneus scaphoid complex". He used specially made shoe with spribgs to treated clubfoot.

C. Use of splint and wrench for forcible correction

In the late nineteenth century Bruckner used metal splints for the correction in 1796. Thomas in 1886 initially proposed the use of his own splint but ultimately rejected because splint itself causes deformity.

D. Use of Denis Browne splint after forcible correction

Denis Browne introduced his metal splint in 1934 with adhesive strapping for the maintaince of correction after forcible correction. The splint held the deformity forefoot in a over corrected position of abduction and eversion with plantigrade position at the ankle. The splint connected with both feet with an aluminium bar, which would stimulate the baby to kick the splint and thereby help in the development of calf muscles.

E. Application of adhesive strapping & repeated manipulation

In 1896 whitman in England use adhesive strapping for the correction of clubfoot. Jones and Lovett in 1929 and Brockman in 1930 presented fairly large series of paticats with clubfoot treated with strapping and repeated manipulation. They claim good results in half of their cases.

F. Manipulation and use of plaster of paris cast for holding the correction

Guerin was first use plaster of paris last in the treatment of clubfoot in 1838. Whitman in 1910 and Elmslic in 1920 emphasized the use plaster of paris cast for the correction of deformity and maintaince corrected position. Before the end of the nineteenth century the use of plaster of paris distinguised surgeon like Thomas, Jones and little kite practised cast for fixation after manipulation in 1930.

G. Gentle manipulative correction as the mainstay of treatment

Most author of the twentieth century are proponents of gentle manipulative correction. Shaw reviewed three different methods-

i) Gentle stretching and Jones strapping

ii) Manipulation and serial plastering

iii) The use of Denis Browne splints as a corrective measure.

H. A new forefoot abduction device

The special forefoot abduction device with a turnbuckle has been used by De Mazumdar which incorporated in a above knee plaster cast (Fig.-2, 3 & 4). The device produces good result in supple and moderately rised varieties of clubfoot.

I. Slow and controlled distraction of soft tissues by different devices

During the last decade of the twentieth century, the neglected and poorly treated clubfoot has been treated with a new approach of slow and control distraction of soft tissues of the deformed foot by applying either Ilizaror or Orgnasyan or Joshis apparatus with good (Fig-5).This device use frames with passing of pins through bones, the distraction rate being at the rate of 0.25 mm 6 hourly i.e.1 mm in 24 hours. This takes about 6 to 8 weeks for correction of the deformity, after which the frame removed & the limb is plastered. The plaster is maintained for 3 to 4 months when the child is allowed to walk with an overfoot on the plaster. No wasting or stiffness of the Joint is reported.The above description reveals different methods of non operative treatment for the correction of the clubfoot starting from gentle manual correction to slow & controlled distraction of soft tissue by different device. The methods have changed with time but mainstay of treatment is correction of contracted soft tissue at an early age and bony surgery when there are secondary deformities.

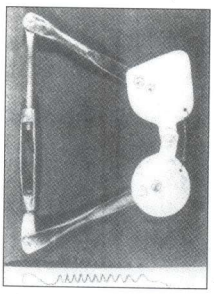


Fig 2 : Forefoot abduction device and a spring.

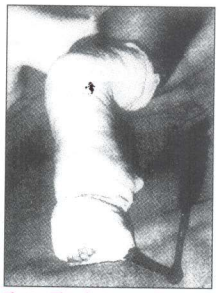


Fig 3 : The device applied with plaster.

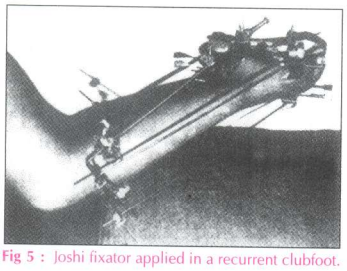


Fig 5 : Joshi fixator applied in a recurrent clubfoot.

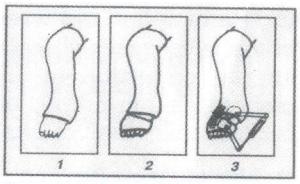


Fig 4 : Application of forefoot abduction device by plastering-(1) the forefoot part of plaster. (2) the forefoot and thehind part of plaster with a wedge-shaped space between them, (3) the device applied under the plaster, a spring is applied on the dorst-medial part by further plastering.

References

1. Fripp AT and Shaw NE. Clubfoot Edinburgh, E& S Livingstone, 1967, P-6-20.
2. B Mukhopadhaya, 1 diopathil congenital clubfoot. In Current Concepts in Orthopaedics, DK Tanej (ed) indore , Sat- Prachar press, 1966, P. 69-98.
3. Browne O: Talipes Equino- varus Lancet, 1934; 11: 969-974.
4. Jones R & Lovelt RW: Orthopaedic surgery: 2nd ed. London. Oxford University
5. Kite JH, Non-operative treatment of congenital clubfoot: A review of one hundred care. South Medical Journal, 1930; 23: 337.
6. De Mazumdar N, Mukherjcep. Evaluation of 73 Consecutive care of clubfoot treated in the clubfoot Clinic. J Vivekannda 1st Med. Sciences, 1978; 1:14-19.
7. Turco VJ. Clubfoot. Churchill Livingstone, New york: 1981; 118-119
8. Mckay DW. New Concept of and approach to clubfoot treatment. Section-1- Principles and Morbid anatomy J paediatr Orthopaed; 1982; 2: 347-356

Diagnosis of irritable bowel syndrome : A review

Alim A M[1], Ekram A R M S[2], Begum F A M A A[3]

The ORION 2004 ; 18 : 177-178

Definition

Irritable bowel syndrome (IBS) is the best recognized functional gastrointestinal disorder characterized by chronic or recurrent abdominal pain associated with disturbed defecation and often bloating for at least 3 months[1]. It is a highly prevalent disorder & reported prevalence rate varying from 17 to 22% in general population[2,3] to 52% in out patient population[4]. It is the commonest diagnosis in gastrointestinal clinic & accounted for 50-70 % work of gastroenterologist[5,6].

Diagnostic criteria

Functional bowel disorders have their basis in abnormal physiology or function and because of physiologic testing in gastrointestinal tract is less well-defined thus diagnosis of functional disorder primarily depend on clinical rather than laboratory data. IBS is considered as functional motility disorder and no endoscopic , radiographic & biochemical abnormality associated with its diagnosis[7]. So diagnosis is often made by exclusion of organic disease. Till date IBS has become a symptoms criteria based diagnosis , not a diagnosis of exclusion[8]. Incomplete understanding the patho-physiology has hampered a diagnostic precision and absence of specific treatment. So patients consult one physician after another and are subjected to costly investigations . Unnecessary investigations not only involve cost but also increase the diagnostic uncertainty and heightens patients anxiety, frustation and monitory loss[3]. Beginning in the late 1970s, investigators attempted to define irritable bowel syndrome using symptoms based criteria derived from epidemiological surveys. In an attempt at greater precision of diagnosis , Manning et al[9] reported the prevalence of 15 symptoms in IBS and compared these with symptoms in patients with organic disease.(Table-1). They concluded that six cardinal symptoms discriminated the IBS from organic bowel disease.

Presence of two or more Manning criteria has been detected to have a sensitivity of 94% and a specificity of 55%, three or more has a sensitivity of 84% and specificity of 76% [10]. Kruis et al[11] proposed another scoring systems for positive diagnosis of IBS. There have been three Rome working team reports on diagnostic criteria for IBS. The first report in 1988[8] was subsequently modified when a second Rome working team proposed a classification for all the functional gastrointestinal disorder[12]. A further update of Rome definition was published in1992[13]. Another consensus conference took place in Rome in June 1998 with aim to refine the current diagnostic criteria. The Rome 1 criteria (1992) recommend the diagnosis of IBS only in presence of main diagnostic criteria, that is, abdominal pain or discomfort associated with chronic altered bowel habit and two or more supportive criteria. In contrast Rome 11 working team (1998) recommend that diagnosis of IBS is based on the presence of two of the three main diagnostic criteria alone (Table-II). The supportive criteria may then be usedfor further classification of IBS into diarrhea-predominant for constipation predominant. A validation study of the Rome criteria, after excluding patients with warning features, showed sensitivity of 63%, a specificity of 100%, and more importantly, a positive predictive value of 100% and a negative predictive value of 76%[14].

Table-1: Discriminant value of symptoms in identifying the irritable bowel syndrome compared with organic bowel disease[9].

Manning criteria	Organic(%)	IBS(%)
Pain relieved after defecation	30	81
Looser stool at pain onset	27	81
More frequent stool at pain onset	30	74
Abdominal distension	21	53
Mucus per rectum	21	47
Feeling of incomplete emptying	33	59

Table-II: Rome II criteria for irritable bowel syndrome[15].

At least 12 weeks abdominal discomfort or pain (need not be consecutive) in the preceding 12months, with two of the following three features :

- Relieved by defecation
- Onset associated with stool frequency
- Onset associated with change in stool form

Symptoms supportive of irritable bowel syndrome

- Abnormal frequency (more than three bowel movements per day or less than three per week)
- Abnormal stool form (lumpy/ hard/ loose/ watery)
- Abnormal stool passage (straining/ urgency/ feeling of incomplete evacuation)
- Passage of mucus
- Bloating or sensation of abdominal distension

In clinical practice, diagnosis is based on positive symptoms known as the Rome criteria and limited diagnostic screening, taking into account warning features suggestive of organic disease. The sinister features are significant weight loss, fever, blood in stool, dehydration, abdominal lump and symptoms awakening patients from sleep. Presence of these features signifies that disease is more likely to be organic rather than functional. Minimal diagnostic tests are warranted to rule out structural lesion in a cost effective manner and to convince the patients of the diagnosis of IBS.

1. **Dr Md. Abdul Alim,** MBBS, FCPS (Med), MD (gastro)
Asstt. professor. Gastrointestinal and liver disease
Rajshahi medical college & hospital

2. **Dr A.R.M Saifuddin Ekram,** MBBS, FCPS (Med)
Associate professor, Medicine Rajshahi medical college & hospital

3. **Dr. F. A. M. Anjuman Ara Begum,** MBBS, MPH (PH)
Health officer, Rajshahi city corporation

There are several other factors to consider that can help in planning a diagnostic strategy

a) The duration and severity of symptoms : Recent onset of symptoms, particularly in older patient or more severe and disabling symptoms may require more extensive studies.

b) Demographic features : IBS is more common in women & younger age.

c) The referral status of patients : Patient seen in primary health care setting are less likely to require extensive investigation.

d) Previous diagnostic evaluation.

e) A history of colon cancer in the family.

f) The nature & extent of psychological difficulty.

Clinical presentation-

Abdominal pain

Abdominal pain and disturbed defecation are characteristics of IBS & required to make a diagnosis of IBS. The intensity and location of pain is highly variable. Pain is often precipitated by meal and relieved by defecation. Rarely does the pain awaken the patients from sleep. Only 2 to 20 percent of IBS patients with chronically altered bowel habit have painless diarrhea[16].

Altered bowel habit

A change in bowel habit is the key element of IBS. The disturbance of bowel function is gradually progressive, eventually developing a characteristic pattern, most commonly alternating constipation and diarrhea, with either predominating. In constipation predominant IBS stool are usually hard, often stool caliber is narrow, pencil- thin or ribbon-like due to colonic or rectal spasm. The diarrhea predominant IBS usually consist of small volume of loose stool, evacuation is often precipitated by extreme urgency, tenesmus typically in the morning or after meal. A sensation of incomplete fecal evacuation may lead the IBS patients to make the multiple attempt to stool passage over a short period of time.

Abdominal distension, belching, flatus

Bloating or perceived abdominal distension is a common complaints of IBS. Belching and excessive flatus is also commonly reported Quantitative measurement reveal that most patients who complaint of increased gas, bloating, flatulence generate a normal amount of intestinal gas[17].

Non colonic and extra intestinal symptoms

IBS is accompanied by numerous symptoms referable to other section of gastrointestinal tract or abdominal organs. Dyspepsia, heartburn, pyrosis, nausea and vomiting appear in 25 to 50 percent of patients[18]. Urinary symptoms have been reported in 33 to 50 percent patients and sexual dysfunction including dyspaerunia & inhibited sexual desire has also been shown to be 5 to 15 times more common in patients with IBS[18].

Physical examination

A physical examination should be performed on the first clinical visit and on subsequent visit as recorded. Although the presence of a palpable , tender sigmoid colon and discomfort with rectal examination has been proposed to aid diagnosis of IBS, the physical examination serves primarily to exclude other diagnosis. Importantly, the laying on of hands also provides reassurance to the patients.

Diagnostic screen

If the symptoms suggestive of organic disease and physical findings are absent, then few investigation should be undertaken. The hemoglobin, white cell counts, erythrocyte sedimentation rate, flexible sigmoidoscopy and serum albumin should be done to exclude organic disease. Among others, needed for limited screening test are stool for ova and parasites. If over 40 years of age, a barium enema preferably double contrast, is prudent[19]. Other tests will depend upon patients age, duration and nature of symptoms, unless indicated these should be avoided

Symptoms assessment
Rome criteria

↓

Limited screening for organic disease
Hematology, biochemistry, ESR, TSH
Stool for ova and parasites
Flexible sigmoidoscopy + barium -enema
or colonoscopy if > 50 years.

Fig. 1: Basic diagnosis of IBS[19]

Conclusion

The clinical diagnosis of IBS is based on identifying symptoms criteria with a "positive diagnosis" and excluding the organic disease with minimal diagnostic workup. Additional diagnostic studies are based on symptom predominance and presence of warning features.

References

1. Talley NJ. Functional gastrointestinal disorder. In: Grendall JH, Mc Quaid KR, Friedman SL , editrs. Current diagnosis and treatment in gastrenterology. 1st ed.. Stampford: appleton and Lange,1996:86-94.
2. Talley NJ, Zinsmeister AR, Van Dyke C, Melton LJ. Epidemiology of colonic symptoms and irritable bowel syndrome. Gastroenterology 1991; 101: 927-34.
3. Jones R, Lydeared S. Irritable bowel syndrome in general population. Br Med J 1992; 304: 87-90.
4. Fielding JF. A year in outpatients with irritable bowel syndrome. Ir J Med Sci 1977; 146: 162-5.
5. Harvey RF, Read AE, Salih Y. Organic and functional disorder in 2000 gastroenterology outpatients. Lancet 1983; 16: 632-34.
6. Everhart JE, Renault PF . Irritable bowel syndrome in office based practice in the united states. Gastroenterology 1991; 100:998-1005.
7. Wingate DL .The irrritable bowel syndrome. Gas Cli Nor Am 1991; 20: 351-61.
8. Thomson WG, Doleval G, Drossman DA, Heaton W. Irritable bowel syndrome; A guideline for diagnosis . Gastroenterol int, 1989; 2: 92-5.
9. Manning AP, Thompson WG, Heaton KW, Morris AF. Toward positive diagnosis of irritable bowel syndrome. Br Med J 1978; 2: 653-4.
10. Thompson WG. Gastrointestinal symptoms in irritable bowel compared with peptic ulcer and inflammatory bowel disease. Gut 1984; 25 : 1089-92.
11. Kruis W, Thieme C, Weinzieri H, Schussler P, Holt J, Paulus WA. Diagnostic score for irritable bowel syndrome: its value in the exclusion of organic disease. Gastroenterology 1984; 47: 1-7.
12. Drossman DA, Thomson WG, Talley NJ, Funch -Jansen P, Janssens J,Whitehead WE. Identification of subgroups of functional gastrointestinal disorder. Gastrenterol int 1990; 3:159-72.
13. Thompson wG, Creed F, Drossman DA, Heaton KW, Mazzacca G. Functional bowel disorder and functional abdominal pain. Gastroenterol Int 1992; 5: 75-91.
14. Vanner S, Glenn D, Paterson W. Diagnosing irritable bowel syndrome : predictive value of Rome criteria .Gastroenterology 1997; 112:A47. Abstract.
15. Mc Laughlin J . Irritable bowel syndrome. Medicine international The medicine publishing co. Ltd .2003 ; 2 :59-61.
16. Talley NJ, Weaver AL, Zinmeister AR. Psychosensory modulation of colonic sensation in human transverse and sigmoid colon. Gastroenterology 1995; 109: 1722.
17. Levtt MD, Furne J, Olsson S. The relation of passage of gas and abdominal bloating to colonic gas production. Ann Intern Med1996; 124: 422.
18. Schuster MM. Irritable bowel syndrome. In: Sleisenger MH, Fordtran JS, editors. Gastrointestinal disease . 5th ed. Phildelphia WB saunders Company 1993: 91
19. Drossman DA, Cmelleri M. Irritable bowel syndrome: a technical review for practice guideline development. Gastroenterology; 1997; 112 :2120-37

Plain radiography : Yet an important preliminary diagnostic modality

Akhand MI[1]

The ORION 2004 ; 18 : 179-181

Introduction

Now a days, there is tremendous advancements in the field of diagnostic imaging procedures. These include digital X-ray, USG (3D/4D), colour doppler, CT Scan, MRI, PET etc[1]. Most of the above investigations are avilable in big centers and expensive. Among these, plain rediography is the cheapest one and is available in everywhere even in the remotest places. This topic shows how a simple plain X-ray aids the clinician a lot to reach a diagnosis of different medical and surgical conditions.

Chest pain

In acute pain the radiography frequently will not be helpful in distinguishing the more serious causes, i.e. myocardial infarction, dissecting aneurysm and pulmonary embolism from each other or from diseases. History, ECG and physical examination will be more effective[6].

Chest wall and joint Pain

- Occult rib fracture will be disclosed on X-ray ribs. In certain cases on the initial examination rib may look normal but later on X-ray may show radiolucent line or subsequent callus formation on the follow-up studies.
- Vertebral fracture may be visible on lateral X-ray chest.
- Pain of rheumatic origin can be detected by atlerations about shoulders or costo-vertebral junction.
- Anterior costal chondritis (Tietze syndrome) usually reveals no particular readiological change. But soft tissue mass may be noted clinically.
- Pancoast tumour causes chest, shoulder and arm pain. These tumors may be quite small and not readily detected on preliminary X-ray despite significant pain[6].
- Upper chest pain may be due to cervical degenerative change.
- Cervical rib may cause pain radiating to arm.

Pain originating from the pleura

- Primary pleural inflammatory processes are usually not evident on the plain X-ray chest.
- In lateral decubitus films small pleural effusion may be seen. Large effusions generally are not painful.
- Pneumothorax may result in pain and may be detected easily. It is better to include inspiratory and expiratory films to clearly define the pneumothorax.

Mediastinal Pain

Pain originating from medastinal emphysema is easily detected on chest film.

Oesophageal pain

Oesophagitis may not always be detected on the barium swallow. Cardiospasm may not be observed unless the examination is done during pain.

Abdominal pain

Pain associated with suspected disease of gastrointestinal tract:

Perforation

An erect film will usually demonstrate free gas beneath the diaphragm[7].

- If the patient is unable to stand, a left decubitus film may show the free air between the liver and abdominal wall. Free air may be seen even on a supine film, specially in children.

Obstruction

- When mechanical obstruction is suspected plain films of the abdomen should be done. Supine and upright position helps in better evaluating the air distribution.
- If the patient is unable to lateral decubitus films may be substituted for upright film.
- The enema will demonstrate or exclude large bowel lesions.

Vascular occlusion

- Vascular insults to the bowel generally result in a nonspecific sign. Frequently contrast studies are also nonspecific

Pain associated with pancreatitis

- Plain film studies in classical case of acute pancreatitis may show localised small bowel distension in upper quadrant often associated with a pleural reaction and plate like atelectasis in left lower lung.
- Pancreatic calcification indicates chronic pancreatitis.

Pain associated with gall bladder

- Radio-opaque stones will be visualized in right upper quadrant while radiolucent stones not, unless and until cholecystography is being done.
- Air in the biliary tract in patient without cholecystectomy is strongly suggestive of recent gall stone perforation.

Pain associated with suspected intra-abdominal inflammatory diseases

- Inflammatory masses can often be detected on the plain flim of abdomen. Abscess may appear as homogeneous soft tissue or may have soap bubble appearance.
- If the plain film is not contributory one can try to demonstrate displacement of normal structures by this mass. This is best done by opacifying the gastro-intestinal tract and IVU

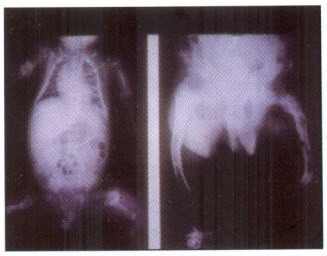
Pain associated with suspected disease of urinary tract

- The plain film will be able to detect radio-opaque stone or calcification in kidney, may be due to tuberculosis or nephrocalcinosis. Radio-lucent stones may not be visible at all.
- For confirmation of these shadows IVU is a must with the help of lateral X-ray of lumbar spine one can differentiate between gall bladder and kidney stones. Kidney stones will be posterior while gall stones will be anterior.

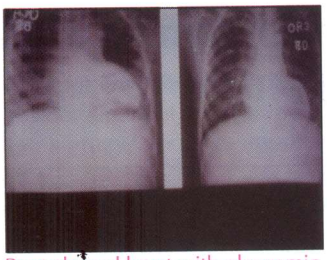
Pain in the back and neck

- Regardless of the presenting symptoms and signs, the first

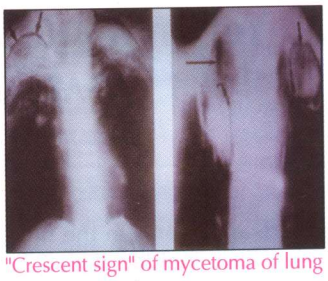
1. **Dr. Md. Ishaque Akhand** MBBS, MD
Associate Professor, Dept. of Radiology,
Moulana Bhasany Medical College Hospital, Dhaka.



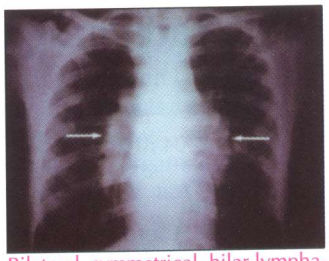
A csae of osteogenesis imperfecta



Boot-shaped heart with olaegemic lung field in fallot's tetrology



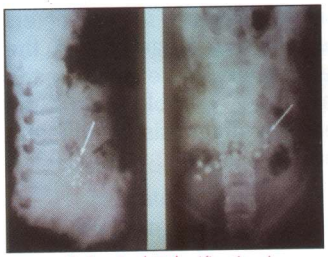
"Crescent sign" of mycetoma of lung



Bilateral, symmetrical, hilar lympha-denopathy-a case of sarcoidosis

Lytic lesions of different size on the skull-a case of multiple myeloma.

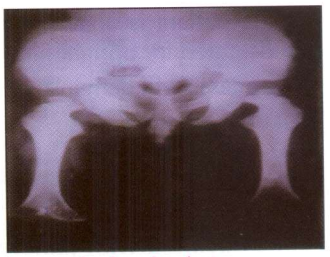
A case of T.B. of HIP



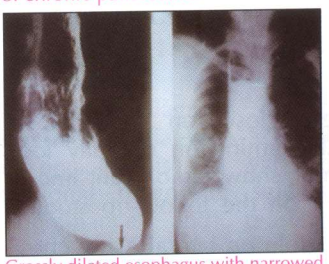
Upper Abdominal Calecification in case of chronic pancreatitis

A case of "scurvy" sharply margnated, sclerosed epiphysis with frankel's white line

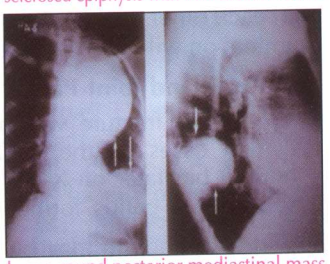
Destruction and disorganisation of PIP joints of hands arthritis



A case of achondroplasia

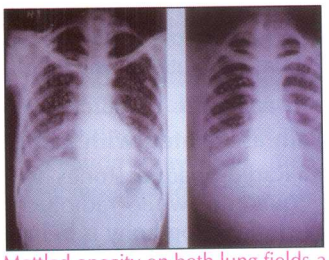


Grossly dilated esophagus with narrowed smooth distal end a feature of achalasia of oesophagas on ba-swallow x-ray

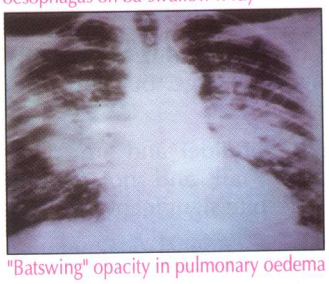


Lagge round posterior mediastinal mass -possibly a neurogenic tumour

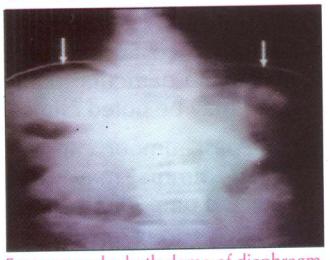
Tuberculous focuses on upper tibia



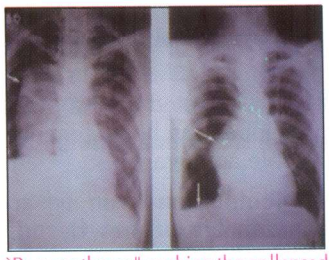
Mottled opacity on both lung fields-a case of miliary tuberculosis



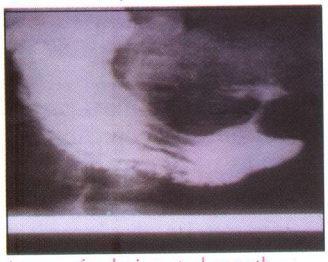
"Batswing" opacity in pulmonary oedema



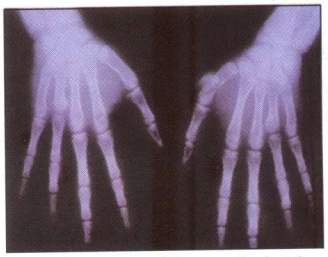
Free gas under both dome of diaphragm-a case of perforation of hollow viscus



`Pneumothorax" pushing the collapsed lung tow ards mediastinum

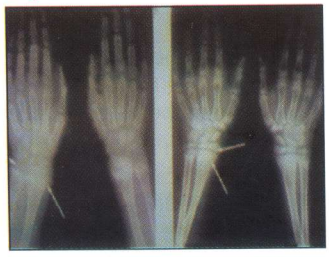


A case of pyloric antral growth-ca-stomach

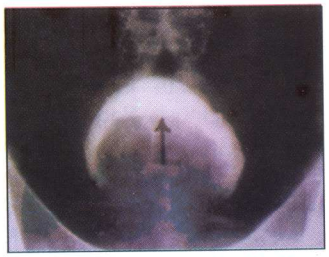


Short 4th metacarpal bone on both sides-case of pseudo-hypo parathyroidisum

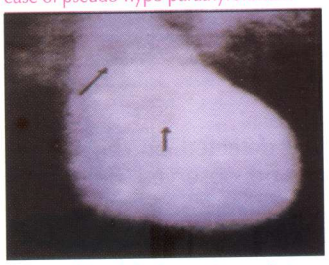
"Spina ventosa" a case of tuberculous dactilitis



Cupping, fraying metaphysis with widening of growth plate-a case of ricket



"Fish hook" deformity of U.bladder due to englarged prostate in IVU study



In OCG, filling defect by two large gall stones

Widening of deploic space with "hair on end" appearance-A case of " thalassaemia"

examination is plain X-ray of spine, may be AP/lateral and in cervical region oblique view may prove conclusive plain X-ray will help in diagnosing anomalies which may cause either abnormal position or instability and destructive lesions such as those due to neoplasm and inflammation.

- Special examination of sacroiliac or other appropriate joints may added to the routine examination if arthritic disease is suspected.
- It is true that trauma is the most frequent cause of low back pain, plain film is quite often unrewarding in this condition. Fractures are easily identified, but the soft tissue injury cannot be located[1].
- When pain in the lower back is accompanied by neurologic manitestation including nerve root involvement, myelography is indicated.
- Nack pain is extremely common after the age of 40 and most common cause is osteoarthritic changes. Sometimes large Osteoarthritic changes and spondylitic lesions are present. In oblique view any measurement below 12 mm of cervical canal should be regarded as abnormal because of encircling bony canal impact upon the spinal cord resulting in neurologic deficit.

Headache

- The patients with headache suggestive of migrain or muscular stress or with psychological causes may be followed for long periods of time without radiological assessment[2].
- In cases of frontal headache, X-ray of paranasal sinuses will be helpful to rule out sinusitis.
- The plain lateral view of skull gives assessment of the sellaturcica, which may be affected by increased intracranial pressure, increased. Sellar size, erosion of the dorsum sellae, or demineralisation of the sella floor may be present even in the absence of clinically evident papilloedema.
- Midline position of the calcified pineal gland on the frontal view of the skull suggests the absence of unilateral space occupying lesions.
- In those patients whose headache suggests subarachnoid heamorrhage whether from aneurysm, arteriovenous malformation or hypertensive vascular disease, the angiogram is the best method to make correct diagnosis.
- Isotope scanning is very useful to detect lesions such as malignant astrocytomas, meningiomas, and brain abscesses Many chronic subdural haematomas are also identified by this method, but vascular lesions are not as reliably diagnosed.
- The patients who have a clinical history consistent with posterior fossa abnormallity should undergo studies, e.g. ventriculography or pneumonencephlography. (But not practicing now a days)

Pain in extremities

X-ray evaluation is indicated for any patient with explained extremity pain having inflammatory disease involving bone. Trauma should be evaluated by plain AP and lateral films. Early osteomyelitis may not be evident in X-ray while follow-up studies may prove helpful. Lower extremity venography is useful in defining the origin of pulmonary emboli and degree of venous thrombosis. Lymphangiography may confirm lymphatic obstruction as a cause of swelling and pain.

Arteriography will be necessary in distinguishing among thrombosis, embolism and arterial sclerosis. The cause of neurotrophic pain from neuritis, ganglionitis or pressure on nerves may not be revealed. Early esteogenic sarcoma may not be seen in initial radiographs but follow-up examination may be helpful[4]. A small tumor can be extremely painful but quite obscure in early X-ray. In neoplastic lesions bone scan will show abnormalities earlier than conventional radiographs.

Conclusion

From the above discussion it is certain that how a simple plain radiography can give the clue of a severe and grave surgical or medical disorder. So, whatever may be the advancement of imaging modalities, yet now plain X-ray is the most important primary diagnostic tool for many medical and surgical conditions.

References

1. Grainger R.G & Allison D. J (2nd Edn.) 1991 Diagnostic Radiology- an Anglo American Textbook of Imaging, 2nd- Edinburgh Churchill Liyingstone.
2. Sutton D (1993) A Textbook of Radiology and Imaging, 5th edn Edinburgh: Churchill Living-stone.
3. Thompson W.m. (ed) (1994) Staging neoplasms. Radiol. Clin North Am..., 32(1)
4. Kirk D.R (1991) Practical pediatric Imaging, 2nd ectn. Edinburgh: Churchill Livingstone
5. Swischuk L.E (1984) Differential in Paedirtic Radiology. Baltimore : Williams & Wilkins.
6. Modic M. T. (ed) 1991 Imaging of the spine. Radiol. Clin. North Am, 29 (4).
7. Spranger J. W Langer L. O.. & W iedmann H. R. (1974) Bone Dysplasias. An Ailas of Constitutional Disorders of Skeletal Development. Philadelphia: saunders.
8. Felked B (1973) Chell Roenigenology. Philadelphlat: Sunders.
9. Feczko P J & Mezwa D. G, (eds) (1993) The alimentary teact. Radial. Clln. North Am, 31 (6).
10. Laufer I. & Levine M.S. (1992) Double Contrast Gastrointesil Radiology, 2nd edn. Philadelphia: Saunders. Sherwood. T (1980) Uroradiology. Oxford: Blackwell.

Publisher's Note

Contents of articles published in this journal are those of authors and do not neccessarily reflect those of its editors or of Orion Laboratories Ltd.

PUBLISHED BY
Chief Editor
The ORION
Orion Laboratories Ltd.
153-154 Tejgaon I/A, Dhaka-1208
Phone : 8822401, PABX : 9888494, 9888176
Fax ; 880-2-8826374, E-mail : orionmsd@dhaka.net
Web: www.orion-group.net, online : www.orion-group.net/journals

Disseminated intravascular coagulation in obstetrics

Tasnim S[1]

The ORION 2004 ; 18 : 182-184

Abstract

Disseminated Intravascular Coagulation (DIC) is an acute emergency characterized by inappropriate activation of coagulation and fibrinolytic system and manifested by severe bleeding. DIC is always a secondary phenomenon and often encountered in obstetric practice. Common condition predisposing to DIC include abruptio placentae, amniotic fluid embolism, sepsis, sever pre-eclampsia and eclampsia. Diagnosis is often made from clinical manifestation and estimation of coagulation profile though histological diagnosis of fibrin deposits is the definitive feature of DIC. Basic principles of management include understanding the pathophysiology, elimination of underlying cause and replacement of lost blood and specific components.

Key words

Disseminated Intravascular Coagulation, intrinsic and extrinsic system, replacement therapy, Fibrinolysis

Disseminated intravascular coagulation in obstetrics

Definition

Disseminated Intravascular Coagulation (DIC) is a pathologic condition associated with inappropriate activation of coagulation and fibrinolytic system that result in a tendency towards hypercoagulability but paradoxically result in sever bleeding[1]. Disseminated Intravascular Coagulation is always a secondary phenomenon and not a disease entity in its own rights[2].

Incidence

The incidence of DIC in obstetric patients is difficult to ascertain owing to the wide variation of precipitating events and the exceedingly complex range of clinical manifestations. Obstetric related DIC is encountered in 1 in 500 deliveries for the severe type of DIC and more commonly for milder forms[1].

Pathogenesis

The coagulation system is divided into intrinsic and extrinsic systems. The intrinsic system contains all the intravascular components required to activate thrombin by sequential activation of factors XII, XI, IX, X, V, and II (prothrombin). The extrinsic system is initially activated by tissue thromboplastin, leading to sequential activation of factors VII, X, V, and prothrombin[3]. Both the intrinsic and extrinsic pathways converge to activate factor X. Factor X subsequently reacts with activated factor V in the presence of calcium and converts prothrombin to thrombin.

Thrombin is a proteolytic enzyme responsible for splitting fibrinogen chains into fibrinopeptides, leading to the formation of fibrin monomer. This central enzyme is capable of activating factor XIII to stabilize the newly formed fibrin clot and will enhance the activity of factors V and VII[4]. DIC occurs when monocytes and endothelial cells are injured by toxic substances elaborated in the course of certain diseases that generate tissue factor activating the coagulation cascade. There is an unregulated explosive generation of thrombin that deplete clotting factor and platelets and activate the fibrinolytic systems[5]. Secondary to clot lysis an anticoagulant effect results in erythrocyte fragmentation, haemorrhage, tissue hypoxia and anemia[5]. It is the generation of free thrombin and plasmin in the circulation that is responsible for the thrombotic and haemorrhagic manifestation respectively. Functional healthy endothelium concentrates antithrombin molecule on its surface and express thrombomodulin molecules. If thrombin is generated next to healthy endothelium it is neutralized by antithrombin or bind to thrombomodulin which alters its property that it is no longer capable of converting fibrinogen to fibrin. Instead, thrombomodulin bound thrombin activate the natural anticoagulant protein C system[6]. DIC occurs when this antagonist systems of coagulation and anticoagulation are not balanced[7,8]. Figure-1 depicts the disease process of DIC[1].

Disseminated intravascular coagulation

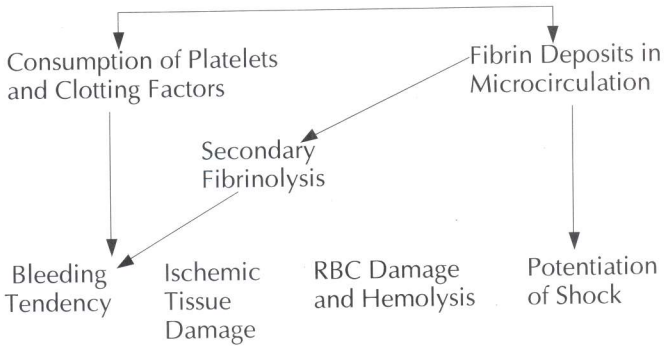


Fig.-1: The disease process of DIC

Most common obstetric conditions associated with DIC are

- Abruptio placentae
- Amniotic fluid embolism
- Septic abortion
- Intrauterine infection
- Retained dead fetus in utero
- Hydatidiform mole
- Placenta accreta
- Pre-eclampsia and eclampsia
- Prolonged shock from any cause

Mechanism of DIC in specific obstetric conditions

Placental Abruption

- Liberation of tissue thromboplastin and
- Intrauterine consumption of fibrinogen and clotting factors in retro placental clot - leads to activation of extrinsic system.

1. **Dr. Saria Tasnim,** MBBS, FCPS, M Med
Senior Consultant (Gynae)
Institute of Child and Mother Health

Retained dead fetus

- Liberation of tissue thromboplastin from non viable tissue

Amniotic fluid embolism

- liberation of tissue thromboplastin,
- intrinsic procoagulant property of fluid and
- associated hypotension, hypoxaemia and tissue acidosis encourage coagulation factors

Pre-eclampsia and eclampsia

- It is postulated that the abnormality may reflect platelet adherence to exposed collagen at the sites of damaged endothelium.
- This condition is associated with chronic coagulation abnormalities that lead to thrombocytopenia and elevation of Fibrin Degradation Product.

Septic abortion

- release of tissue thromboplastin
- release of bacterial endotoxin

Clinical findings

It relates primarily to haemorrhage, anaemia and ischaemia[8]. Patients generally have frank bleeding or a tendency to bleed from mucous membranes, intravenous line sites and surgical incisions. Abnormal bruising, purpura, petechiae and ecchymosis frequently are noted. There may be haematemesis, haematuria and vaginal bleeding. The quality and character of bleeding are directly related to severity of the disease process[10].

Essentials of diagnosis

- History of recent bleeding diathesis, especially concurrent with some obstetric condition.
- Clinical evidence of multiple bleeding points associated with purpura and petechiae on physical examination.
- Laboratory findings classically include thrombocytopenia, hypofibrinogenemia, and elevated prothrombin time[4].

Histologic diagnosis of fibrin deposits is the definitive feature of DIC. There are a host of indirect tests. Laboratory findings in DIC are described in Table1.

Table 1: Laboratory findings in DIC[10]

Test	Result
Partial thromboplastin time	prolonged in 40-50%
Prothrombin time	prolonged in 50-75%
Platelet count	decreased in 90%
Thrombin Time	prolonged in 80%
Fibrinogen	decreased in 70%
Fibrinogen	decreased in 70%
Fibrin degradation products	elevated in 85-100%
values greater than 40 microgram /ml suggestive of DIC	
Protamine procoagulant test	positive
Blood smear	Schistocytes in 40%

Clot observation test (Weiner)

It is an useful bed side test. It can be repeated at intervals. 5ml of venous blood is placed in a 15 ml dry test tube and kept at 37°C. Usually blood clot forms within 6-12 minutes. This test provides a rough idea of blood fibrinogen level. If the clotting time is less than 6 minutes, fibrinogen level is more than 150 mg percent. If no clot forms within 30 minutes, the fibrinogen level is probably less than 100 mg percent[12].

Newer tests

- D-dimer- This neoantigen is formed as a result of plasmin digestion of cross linked fibrin. This test is specific for FDP and abnormal in 90% cases.
- Antithrombin III level -abnormal in 89% cases.
- Fibrinopeptide A-abnormal in 75% cases[13]

Spectrum of severity of DIC[9]

DIC is an acute emergency and there is chances of rapid progression from stage 1 to stage 3 if appropriate measures are not taken[7]. There is a great spectrum of manifestation of ranging from a compensated state with no clinical feature but evidence of increased production and breakdown of coagulation factors to the condition of massive uncontrollable Haemorrhage[14].

Severity of DIC		Obstetric conditions commonly	In vitro finding associated
Stage-1	Low grade compensated	FDPs ↑ Soluble fibrin complexes ↑ Ratio VWF to factor VIII c ↓	Pre-eclampsia Retained dead fetus
Stage-2	Uncompensated but no haemostatical failure	As above plus fibrinogen ↓ Platelets ↓ Factor V and VIII ↓	Small abruptio placentae Severe Pre-eclampsia
Stage-3	Rampant with haemostatic failure	Platelets ↓ Gross depletion of coagulation factors fibrinogen ↑ FDPs ↑	Abruptio placentae Amniotic fluid embolism Particularly Eclampsia

Management of DIC

The clinical condition demands urgent management and there is no time to wait for the results of coagulation factor assays.

Basic principles of management[1]

- Understanding pathophysiology
- Eliminate underlying cause
- Use perinatal team approach for support of patient and family

Procedures

- Stabilize vital sings
- Maintain adequate urinary output
- Institute and maintain appropriate blood component therapy to replace consumable, blood clotting factors and platelets
- Conduct prudent fluid replacement
- Perform constant central venous pressure or Swan-Ganz monitoring
- Use anticoagulant therapy only in critical, individual situations[1]
- Obstetric DIC is usually associated with intrauterine pathology and when the uterus is emptied the DIC fades away[2].

Replacement therapy-

Plasma substitutes

There is much controversy to use plasma substitute to give to any bleeding patient. The choice lies between simple crystalloid such as Hartmann's solution and artificial colloids such as dextran or preparation of human albumin (albuminoids). If crystalloids are used two to three times the volume of estimated blood loss should be administered.

Problem with use of colloids are that dextran adversely alter platelet function, may cause pseudoagglutination and interfere with subsequent blood grouping and cross matching. It is also associated with anaphylactoid reactions and contraindicated in the pregnant women.

Use of whole blood and component

Whole fresh blood is advocated but it should be screened for Hepatitis and HIV[2]. Sometimes it may be waste of vitally needed components required for patients with isolated deficiency. The use of fresh frozen plasma (FFP) followed by bank red cells will provide all component except platelets. It is to mention that

-FFP Contains all the coagulation fractions present in plasma obtained from whole blood within 6 hours of donation.
-Plasma protein fraction (albumin) does not contain carry risk of transmitting infection .
-Cryoprecipitate is richer in fibrinogen than FFP but lacks antithrombin III which is consumed in obstetric hemorrhage. Concentrated platelets may be given in addition to FFP to achieve homeostasis[15].
-Red cell transfusion - stored bank blood is deficient in labile clotting factor (factor V, VIII and platelets). It is advisable to transfuse 2U of FFP for every 4-6 U of bank red cell administered. Administration of Heparin is controversial in acute DIC. It is beneficial in patients when progressive thrombin formation occurs or with large thrombosis. The recommended dose is 100 unit/kg subcutaneous every 4 to 6 hours[16].

Conclusion

As DIC is always a secondary phenomenon the mainstay of management is therefore to remove the initiating stimulus if possible. The mortality reported in patients with DIC range between 50-85 percent and the wide variation reflects the mortality of the underlying disorder. The major determinant of the survival is prompt identification of the underlying trigger, elimination of the cause and appropriate management.

References

1. Pamela G. B, James N M, Kenneth GP, High Risk Pregnancy: A Team approach 2nd edition chapter 28. 1993. W. B Saunders Company.
2. Ten Teachers obstetrics by chamberlain GVP ed. Sixteenth edition 1995.
3. Text Book of Medical Physiology. Guyton & Hall ed. Ninth edition 1996. W.B Saundress Company
4. Current Obstetric and Gynaecologic diagnosis and treatment. Decherney AH and Pernall ML ed. Ninth edition 1998. Appleton and Lange publication.
5. Harry L - M, William H. W. Disseminated intravascular coagulation Postgraduate Medicine. March' 2002
6. Ziegel EE. Disseminated intravascular Coagulation Obstetric Nursing 7th edition. New York. Macmillan 1979, P 638
7. William E. Disseminated intravascular coagulation Thrombosis and Hoemorrhage. 1994 : 921-944
8. Estonia CA. Possible involvements of cytokines in diffuse intravascular coagulation and thrombosis. Bandohrs clinical Haematology vol 7 : 3, 1994, 453-488
9. Pritchard JA, cunningham FG, Mason RA: Coagulation changes in eclampsia: Their frequency and pathogenesis Am J obstet Gynecol. 1976,124:855.
10. O'Brian BS, Woods S. The paradox of DIC. Am J. Nur' 1978:1878
11. Dewhurst's textbook of Obstetric and Gynaecology for Postgraduate. Sixth edition. Edmonds DK ed. 1999. Blackwell Science Ltd.
12. Datta DC. Text Book of obstetrics including Perinatology & Contraception. 3rd Edition 1997.
13. Carr J. Diagnosis of DIC: role of D-dimer. Am J Clin Pathol 1989, 91 : 280-287
14. Medical Disorders in Obstetric Practice. Michel de Swiet ed. Third edition 1995.
15. Elizabeth A. L. Coagulation defects in pregnancy and the puerperum. Turnbulls Obstetrics- 3rd edition. chapter 20. 2001 Churchill Livingstone
16. Agnes Aysola. Disseminated Intravascular Coagulation. Transfusion Medicine update. March' 1999.

Imaging hepatobiliary and pancreatic system by ERCP

Alam T[1], Khan ZR[2], Rabbi ANMA[3]

The ORION 2004 ; 18 : 185-186

Introduction

The development of fibroptic endoscopes which are designed specifically for duodenal observation and cannulation of the ampulla of vater with pancreatocholangiography has provided a new approach to the evaluation of duodenal, pancreatic, and biliary disorders[1]. Many reports attest to the effectiveness of these new instruments in visualizing duodenal pathology[2]. In this paper we will report our experience with cannulation of the ampulla of vater and cholangiopancreatography in 201 consecutive patients with symptoms suggestive of pancreatobiliary diseases.

Methods

The VIDEO fibroptic duodenoscope manufactured by pentax was used in the series. Premedication with inj. pethedine HCL 40-60 mg I/V is given just before the procedure. Pharyngeal anaesthesia with 10% Xylocaine spray is given immediately before duodenoscopy. In prone position of the patient, the fibroscope is inserted into the duodenum. The ampulla is brought into the field, and the orifice is identified. If hyperperistalsis or spasm of the sphincter of oddi are cannulated, additional I/V anticholinergics medication may be required. After insertion of the cannula into the ampulla of vater, under fluoroscopic control 60% iopemiro is injected untill the pancreatic duct or biliary tree is visualized. If only one system is visualized, the catheter is repositioned and a second injection is made. Generally 1 to 3 ml of iopemiro is required to visualize the pancreatic duct adequately, while 10-30 ml is usually needed for optimum radiographic visualization of the biliary tree. After injection radiographs are taken.

Results

A total of 201 patients with suspected pancreatic or biliary disease were evaluated by cannulation of the ampulla of vater with pancreatocholangiography, pancreatic pathology was suspected in 37 patients and the pancreatic duct was successfully visualized in 30 cases (81%). By contest, the biliary tract was successfully visualised in 119 cases (85%) of 139 patients with suspected biliary pathology. A satisfactory cannulation was obtained in 174 (86%) of 201 patients and is defined as adequate radiographic visualization of the clinically desired ductal system. For presentation of the data the 174 patients were divided into groups depending on the results on the radiographic evaluation of the pancreas and/or biliary tract (Table -1).

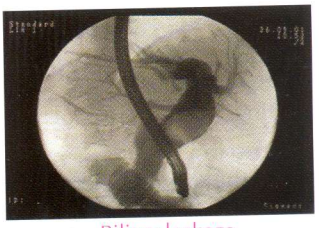
Table-1: ERCP in 174 Cases

Normal	12	Hepatolithiasis	4
Periampullary Ca.	40	Post Operative Stricture	3
Common duct stone	37	Choledochoal cyst	4
Cholangio Ca.	32	Pancreatic pseudocyst	2
Chr. Pancreatitis	16	External biliary fistula	6
Obs. at porta	16	Papillary stenosis	2

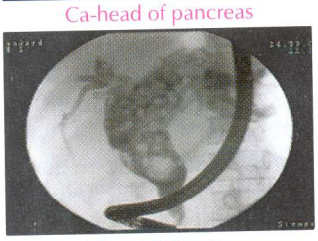
Normal cholangiopancreatography

Twelve patients had a normal ERCP (Fig-1). The normal pancreatic duct is smooth and tapering and is visualized from head to tail with only scanty branch ducts in the head and tail of the pancreas. In the absence of obstruction, the contrast media in the pancreatic duct is flushed into the duodenum within 20-30 sec. The mean maximum diameter of the pancreatic duct was around 3-4 mm in the head region of pancreas. The normal cholangiogram reveals an unobstructed common duct with smooth to tapering intrahepatic bile ducts. Frequently the cystic duct and gall-bladder can be seen. The mean maximum diameter of the common bile duct was 8-9 mm.

Ca-head of pancreas



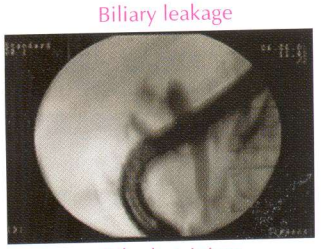
Biliary leakage



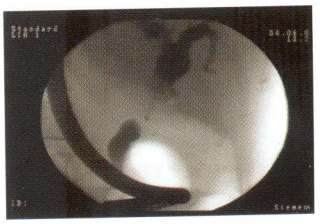
Hepatolithiasis

Biliary leakage

Choledochoal cyst



Bile duct injury



Cholangiocarcinoma

Bile duct injury

1. **Dr. Towhidul Alam,** MBBS, FCPS (Surgery)
Associate Prof. of Surgery, BSMMU

2. **Dr. Zulfiqur Rahman Khan,** MBBS, FCPS, FRCS
Asstt. Prof. of Hepatobiliary and Pancreatic Surgery, BSMMU

3. **Prof. A.N.M Atai Rabbi,** FCPS(S), FICS(USA), FCPS(Pak)
Prof. & Chairman, Department of Surgery, BSMMU

Periampullary Carcinoma
Forty cases of periampullary carcinoma have been diagnosed by ERCP. In cases have been confirmed by operation, 10 cases were managed by endoprosthesis and 20 cases have been lost to follow up.

Choledocholithiasis
Choledocholithiasis was diagnosed in 37 patients. This has been confirmed by surgery in 30 cases and by endoscopic stone extruction in 22 cases, stone in the intrahepatic biliary tree was also seen in four patients.

Cholangiocarcinoma
Thirty two cases of cholangiocarcinoma have been diagnosed by ERCP. In cholangiocarcinoma irregular stenosis or obstruction is readily seen by this method. In most cases the proximal bile duct and intrahepatic bile ducts are dilated and the contrast media clears very slowly from the biliary tree.

Obstruction at portahepatis
Sixteen cases of biliary obstruction at portahepatis was due to carcinoma of the Gall Bladder. In all these cases ultrasonographic findings was in favour of Gall Bladder mass. Six cases have been verified at surgery, remaining ten cases was beyond the scope of surgery.

Chronic pancreatitis
In 16 patients, stenosis and marked deformity of the main panctreatic duct was noted. These patients had well documented chronic pancreatitis confirmed by pancreatic calcification.

Miscellaneous lesions
Four cases of choledochoal cyst was diagnosed by ERCP. In 6 patients with post-operative complications ERCP helped to localize the nature and site of injury. In 27 cases ERCP findings was inconclusive and for which PTC was done.

Discussion
With the development of fiber-duodenoscopes specifically designed for duodenal observations and cannulation, the use of this procedure for the evaluation of pancreatic and biliary disorders has become a reality[3]. With experience, cannulation of the ampulla of vater with pancreatogram is easily performed in practically all cases and has proved to be useful in the evaluation of a variety of pancreatic abnormalities[4].

As with any test, false-positive and false-negative interpretations might be expected. The 12 "Normal ERCPrepresent the main source of false-negative exams. All patient in the group have had an extensive evaluation which included USG, Endoscopy, X-ray, Serum enzymes, test of liver and pancreatic function. They are currently being followed. To date no patient in this group has developed objective evidence of organic diseases. A longer follow-up period will help to resolve the question of false-negative ERCP.

Cannulation of the ampulla at vater with cholangiography can be performed in almost all cases. It has been most useful in the diagnose of common duct stone, carcinoma of bile duct, periampullary carcinoma and other lesion infiltrating the biliary tree[4]. The correct diagnosis of common duct stone was made in 37 cases, cholangiocarcinoma in 32 cases and periampullary carcinoma in 40 cases. Cholangiography was also helpful in the diagnosis of choledochoal cyst, and different types of post-operative complications. Transhepatic cholangiogram wasperformed in 27 cases where ERCP findings were inconclusive. Our data suggest that ERCP is the single mostimportant test in the diagnosis of biliary tract pathology.The application of pancreatogram to the evaluation of suspected chronic pancreatitis is less controversial. The severity and extent of ductal deformity can be evaluated and the cases of ductal stone should be easily recognized.

We have experienced no significant complication from ampullary cannulation with ERCP. Although serum amylase determinations were obtained on all patients who experienced pain, only one case of mild post ERCP pancreatitis was recognized. Both pancreatitis and cholangitis have been described after ERCP and must be anticipated, but careful attention to depth of cannula insertion, force of injection, and amount of contrast media injected should minimize any unwanted effects[5].

In conclusion, our data would indicate that cannulation of the ampulla of vater is a safe, diagnostic tool that may add significant new information in the evaluations of patients with pancreatic and biliary diseases.

References

1. Ogoshi K, Niwa M, Hara Y, et al; Endoscopic Pancreatocholangiography in the evaluation of pancreatic and biliary disease. Gastroenterology, 1973, 64:210-216.
2. Rahman SM, Rahman MA, Islam AFMS, Ultrasonography-A Method of diagnosis of obstructive jaundice and its practical aspects. Bangladesh journal of Radiology and Imaging 1994; 2(1)1-3.
3. Mohiuddin MG, Islam QT, Sadeque ASQM et al. ERCP Findings in patients with upper abdominal pain. Bangladesh Journal of Radiology and Imaging 1995, 3(1): 1-4.
4. Ruddell W.S.J, Lintott, Axon A.T.R. The diagnostic yield of ERCP in the investigation of unexplained abdominal pain. Br. J. Surgery 1983, 70; 74-75.
5. Stephen M, Kavic M.D, MarcD, et al. Complications of endoscopy. The American Journal of surgery 2001, 181: 319-332.

Successful surgical correction of total anomalous pulmonary venous connection (TAPVC Type - I) : A case report

Ahmed NU[1], Islam KS[2], Hossain A[3], Mohiuddin AK[4], Banu B[5], Razzaque SKA[6], Salam ABMA[7]

The ORION 2004 ; 18 : 187-188

Summary

A twelve years old female girl presented to us with the complaints of exertional dyspnoea and palpitation, occasional fever and cough since her early childhood. These symptoms were exaggerated for the last one year. Her parents gave history of bluish discolouration of lips and tongue during crying and exposure to cold in her early childhood. Echocardiography and cardiac catheterization was done. Initially it was diagnosed as a case of atrial septal defect (ASD) secundum variety. Before operation re-evaluation by echocardiography showed that it was a case of total anomalous pulmonary venous connection (TAPVC Type- 1). She was operated under cardiopulmonary bypass with hypothermia and low flow perfusion with antegrade intermittent cold blood cardioplegic arrest. Anastomosis between the common venous sinus with the left atrium, closure of ASD with pericardial patch and ligation of the vertical vein was done. Pre-operatively her arterial oxygen saturation (SPO_2) was 90% Post operatively just before discharge it was 100%. She un-eventfully recovered from operation. This cyanotic congenital heart disease is an uncommon anomaly which frequently confuses with ASD (Secundum). It bears a relatively favorable prognosis after surgical repair.

Key words

TAPVC, surgical correction, case report

Introduction

The term TAPVC describes the anomaly in which the pulmonary veins have no direct communication with the left atrium. Instead, they connect to the right atrium or to one of the systemic veins.

In 1957, Darling and associates divided the anomaly into four subtypes that describe the anatomic corrections of the pulmonary venous to the systemic venous circulation. Type I (supracardiac), type II (cardiac), type III (infracardiac), type IV (Mixed). Associated cardiac defects are : ASD, nearly in all cases, Patent ductus arteriosus in 25 to 50%, asplenia syndrome. Cooley and Ochsner (1957) reported the first open heart correction using cordiopulmonary by pass in a patient with a supracardiac anomaly[1].

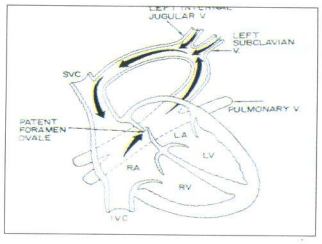


Figure : Type I-TAPVC

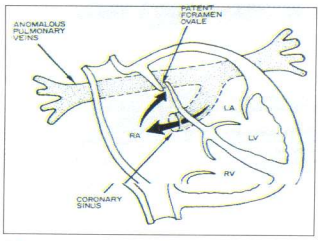


Figure : Type II-TAPVC

Case Report

A 12 years old female child presented with the history of exertional dyspnoea and palpitation, occasional cough with fever since her early childhood. These symptoms were exaggerated for the last one year. Her parents give history of bluish discolouration of her lips, tongue and whole body during crying and after exposure to cold. Other members of the family were healthy. She was ill loking cachectic, mildly cyanotic (central & peripheral), her height- 144 cm, body weight- 23 kg, with engorged neck vein, mild hepatomegaly. Left lower parasternal heave was present. There was a systolic murmur in the pulmonary area with loud second heart sound. Both the lung fields were clear on auscultation All routine investigations except electrocardiography (ECG) &X-ray chest postero-anterior (CXR-PA) view were within normal limit. Her blood group was B+ve. Her arterial saturation of oxygen (SAO_2) determined by oxymetry probe (SPO_2) was 90% pre-operatively. Pre-operative echocardiographic diagnosis was atrial septal defect (ASD), secundum variety by two cardiologist. Cardiac cathe terization was done which showed oxygen saturation at different chambers of the heart in favour of ASD (Secundum). ECG showed right ventricular hypertrophy (RVH) with right axis deviation. CXR P/A view showed heart was enlarged in transverse diameter with a supracardiac shadow merging with the cardiac shadow. Lung fields were plethoric. Echocardiography showed pulmonary hypertension. Suspicious x-ray and echo findings led us to re-evaluate the case by different cardiologist. This time the echocardiography report was different.

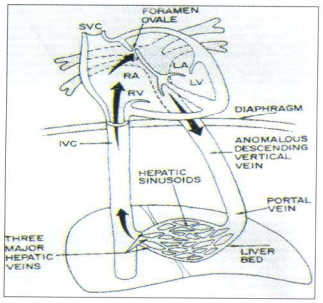


Figure : Type III-TAPVC

They diagnosed it as a case of TAPVC with ASD and PH. Four pulmonary veins had opened into the common venous sinus posterior to left atrium (LA), which had drained into left innominate vein via a vertical vein. There was an ASD secundum with right to left shunt. They could not find one pulmonary vein.

1. **Dr. Nasir Uddin Ahmed,** MS (CV & TS)
Professor, Cardiac Surgery, NICVD

2. **Dr. Kazi Shariful Islam,** MS (CV & TS)
Assistant Professor, Cardiac Surgery, NICVD

3. **Dr. Akter Hossain,** MS (CV & TS)
Assistant Professor, Cardiac Surgery, NICVD

4. **Dr. Abul Kalam Mohiuddin,** MS (CV&TS)
Resident, Final Part, NICVD

5. **Dr. Bilkis Banu,** MBBS
Chief Perfusionist, NICVD

6. **Dr. S.K.A. Razzaque,** FCPS (Paediatrics)
Assistant Professor, Paediatric Cardiology, NICVD

7. **Dr. ABM Abdus Salam,** FCPS (Paediatrics), MD (Cardiology)
Associate Professor,Cardiology, NICVD

With this echofindings we planned to operate her under hypothermic low flow cardiopulmonary bypass (CPB). Mid sternotomy was done. The superior vena cava (SVC) left innominate vein was found dilated. There was a thrill over the SVC. A common venous sinus was found posterior to the left atrium. CPB was established by selective SVC, inferior venacava (IVC)+Aortic cannulation. It was found that all four pulmonary veins opened into the common venous sinus and drained into the left innominate vein via a left vertical vein. There was an ASD secundum. So our per-operative diagnosis was total anomalous pulmonary venous connection (TAPVC) type-1 with ASD (secundum) with pulmonary hypertenstion (PH). Anastomosis between left atrium and common venous sinus was done with7/0 proline suture. Atrial septal defect was closed by pericardial patch with continuous proline suture. Left vertical vein was ligated by no - 2 silk. The whole operation was done under CPB with antegrade intermittent cold blood cardioplegic arrest of the heart.

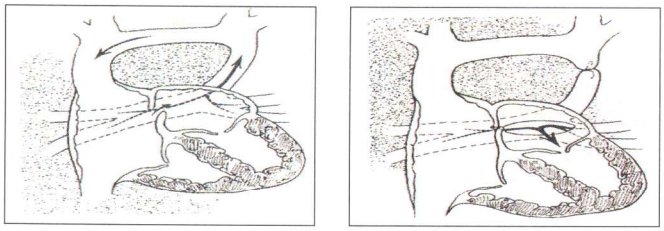


Figure : Supracardiac total anomalous pulmonary venous connection. A. The common pulmonary vein (CPV) connects with a vertical vein (VV) that drains into the innominate vein. B. The vertical vien is ligated, and an anastomosis is made between the CPV and the left atrium, the ASD is then closed.

In the intensive care unit (ICU) patient was ventilated overnight with dobutamine and glyceryl trinitrate support. Patient was weaned from ventilator and extubated in the following morning. She was discharged on 10th post operative day(POD) with an advice for further follow up 3 weeks later. On discharge her pulse rate was 96/min, BP 99/55 (69) mm Hg and SPO_2-100%.

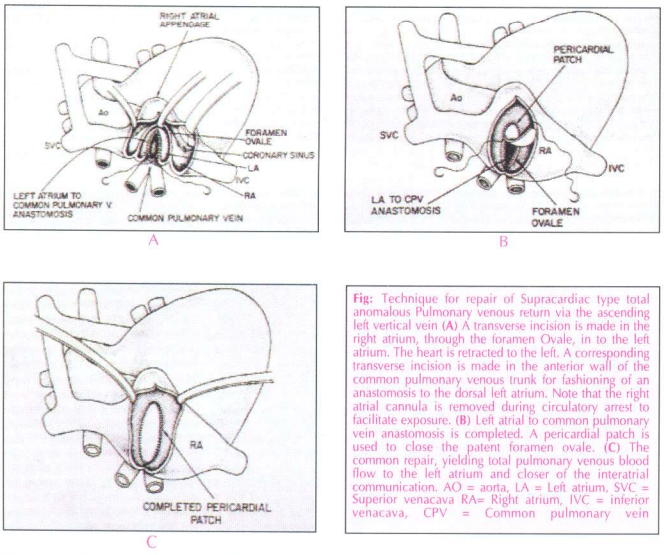


Fig: Technique for repair of Supracardiac type total anomalous Pulmonary venous return via the ascending left vertical vein **(A)** A transverse incision is made in the right atrium, through the foramen Ovale, in to the left atrium. The heart is retracted to the left. A corresponding transverse incision is made in the anterior wall of the common pulmonary venous trunk for fashioning of an anastomosis to the dorsal left atrium. Note that the right atrial cannula is removed during circulatory arrest to facilitate exposure. **(B)** Left atrial to common pulmonary vein anastomosis is completed. A pericardial patch is used to close the patent foramen ovale. **(C)** The common repair, yielding total pulmonary venous blood flow to the left atrium and closer of the interatrial communication. AO = aorta, LA = Left atrium, SVC = Superior venacava RA= Right atrium, IVC = inferior venacava, CPV = Common pulmonary vein

Figure : Operative procedure for TAPVC (Type -1)[3]

The Operative Procedure of supra-cardiac type of TAPVC is going on

Happy patients after the operative procedure.

Figure : Operative procedure for TAPVC supracardiac type[4]

Discussion

TAPVC is an uncommon congenital cardiac malformation, constituting <1% of all congenital heart disease. The majority of cases present at birth or in infancy, although survival into adulthood is reported. Uncorrected TAPVC carries a > 80% mortality in the first year of life from progressive cyanosis and congestive heart failure. However, recent improvements in surgical technique and peri-operative management of TAPVC have had a substantial impact on reducing the morbidity and mortality of even the most critically ill neonates[5]. Pre-operative perfect diagnosis is an important issue. In this case we are able to diagnose the case almost precisely. So we could plan our operation and we were able to come out successfully.

Conclusion

TAPVC is seldom found at National institute of cardio vascular diseases (NICVD) for operation. They are commonly confused with ASD (secundum) in inexperienced hand. Except this case twelve other TAPVC cases were operated at NICVD, Dhaka in the past. But all of them were misdiagnosed pre-operatively as ASD (secundum), they were diagnosed on the operation table by the cardiac surgeon.This is for the first time at the NICVD that a TAPVC was diagnosed preoperatively Simple closure of the ASD without surgical correction of the anomaly in a case of TAPVC is life threatening. Proper and meticulous pre-operative assessment of the patient can save us from misdiagnosis of this disease. So we must be very careful in diagnosing the case both pre-operatively and peroperatively to save the life of patients.

Acknowledgement

I am greatful to all the doctors & nurses who took part in the pre-operative preparation of the patient and actively participated in the operation theatre (OT), ICU and ward for the care of this patient. Thanks to the director of NICVD for allowing me to use the hospital documents of the patients to write this case report.

References

1. Hammon JW Border HW editors. Major anomalies of pulmonary and thoracic systemic veins. In: Sabistion DC, Spencer FC editors; Surgery of the chest. 6th ed. Philadelphia: WB Saunders company; 1995, P. 1409 - 1411.
2. Cope JT and kron IL : Anomalies of pulmonary venous return and cor triatriatum. in : Kaiser LR, Kron IL, Spray, TL editors; Mastery of the cardiothoracic surgery. 1st ed. Piladelphia, lippincot Raven; 1998. p. 869.
3. Synopsis of congenital heart disease. In: Bojar RM, Mathisen DJ, Warner KG, editiors; Manual of perioperative care in cardiac and thoracic surgery. 2nd ed. Oxford; Blackwell scientific publication; 1994. P. 361.
4. Cope JT and kron IL : Anomalies of pulmonary venous return and cor triatriatum. in : Kaiser LR editors; Kron IL, Spray, TL; Mastery of the cardiothoracic surgery. 1st ed. Piladelphia, lippincot Raven; 1998. p. 872.
5. Cope JT and kron IL : Anomalies of pulmonary venous return and cor triatriatum. in : Kaiser LR, Kron IL, Spray, TL; Mastery of the cardiothoracic surgery. 1st ed. Piladelphia, lippincot Raven; 1998. p. 867.

Launching of New Products

Orion Laboratories Limited has recently introduced the following five new products in the market

Clognil Plus

Clopidogrel INN 75mg & Aspirin USP 75mg

Two captains with one mission

Clognil Plus is a fixed dose combination containing Clopidogrel & Aspirin is an antiplatelet agent. It is indicated for the prevention of ischemic events, myocardial infarction, stroke and cardiovascular death in patients with acute coronary syndrome and PVD.The usual dosage is one tablet once daily after meal. Clognil-Plus is presented in form of tablet. MRP. Tk 11.00/tab.

Betacal

Atenolol BP 50mg & Amlodipine BP 5mg.

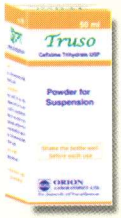
A logical combination for synergestic action

Betacal is a fixed dose combination of Atenolol and Amlodipine as recommended by world Health Organization - International Society of Hypertension (WHO-ISH). It is indicated for the treatment of Hypertension and chronic stable angina. Betacal is presented in the form of tablet. The usual dosage of Betacal is one tablet once daily. MRP. TK 3.00/tab.

Truso

Cefixime USP 100mg /5ml syrup.

3rd generation oral cephalosporin

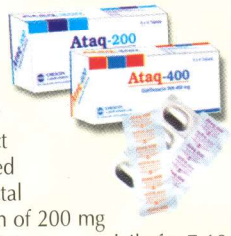


Truso 50 ml has been launched which is the line extension of Truso 37.5 ml. MRP. TK 190.0/phial.

Ataq

Gatifloxacin INN 200 mg & 400 mg tablet

The 4th generation weapon against bacteria



Ataq (Gatifloxacin) is a synthetic fluroquinolone anti-infectve agent. US FDA approved this drug covers the most causative pathogens of infections. Ataq is indicated for the treatment of acute bacterial exacerbation of chronic bronchitis, community acquired pneumonia, uncomplicated urinary tract infections (cystitis), complicated urinary tract infections, acute pyelonephritis, uncomplicated urethral gonorrhoea in men and endocervical rectal gonorrhoea in women. It is presented in the form of 200 mg & 400 mg tablet. The usual dosage is 200mg - 400 mg once daily for 7-10 days. MRP. Ataq 200: TK 6.00/tab. and Ataq 400: TK 10.00/tab.

Nitrocap

Nitroglycerin USP 2.6 mg SR pellets

Long acting nitrate therapy in angina

Nitrocap (Nitroglycerin) is a along acting antianginal product. It is indicated for the prophylaxis and treatment of angina pectoris, supplementary treatment of heart failure, refractory to Digitalis and Diurectic treatment. To decrease elevated filling pressure in acute myocardial infarction, Adjuvant therapy in emergency cases of left heart insufficiency and treatment of Pulmonary hypertension. Nitrocap is presented in the form of 2.6 mg capsule. The usual dosage of Nitrocap is one capsule 2-3 times daily before meal. MRP. TK 5.00/cap.

MSD NEWS

MSD personnel of ORION Laboratories Limited spent a bustling schedule in first quarter of the 2004, in organizing scientific seminars / Clinical meetings as a part of their Continued Medical Education (CME) Program.

Seminar on "Trimetazidine-the only cardiac metabolic enhancer, Role in Heart Failure"

Venue: Conference Room of NICVD, Dhaka.

From left to right : Mr. M. A. Mannan, Sales Manager OLL, Mr. Akter Hossain, RSM, OLL, Dr. Zakirul Karim, Manager, MDS, OLL, Dr. Azizul Haque, Assoc. Prof. NICVD, Prof. Abduz Zaher, NICVD, DR. AbdulKader Akond, Asst. Prof. NICVD, Dr. Rabani, Asst. Register, NICVD

A scientific seminar was sponsored by Orion Laboratories Ltd on "Trimetazidine - the only cardiac metabolic enhancer, Role in Heart Failure" on Sunday 28th December 2003 at Hospital Conference Room, NICVD, Dhaka. Where the eminent professor Abduz Zaher, Professor of cardiology, NICVD chaired the session. Dr. Syed Azizul Haque, Associate Professor of Cardiology, NICVD welcomed the participants. Dr. Md. Abdul Kader Akand, Asst. Professor of cardiology, NICVD presented the scientific paper on "Trimetazidine-the only cardiac metabolic enhancer, Role in Heart Failure."

Scientific Seminar on "Trimetazidine - Newer molecule in management of IHD"

Venue: Cardiology Conference Room of DMCH.

From left to right : Dr. Mr. Serajul Hoque, Assoc. Prof. of Cardiology, DMCH, Dr. H. I. Lutfor Rahman Khan Assoc. Prof. of Cardiology, DMCH, Prof. Dr. Razia Sultana Mahmud Prof. & Head of the Dept. of Cardiology, DMCH, Dr. Md. Shomsher Ali, Assoc. Prof. of Cardiology, DMCH.

A Scientific Seminar was sponsored by Orion Laboratories Ltd. on " Trimetazidine - Newer molecule in management of IHD" on Sunday, 25th January 2004 at cardiology conference room of DMCH, Dhaka. Where the eminent Professor Dr. Razia Sultana Mahmud, Professor & Head of the dept. of Cardiology, DMCH chaired the session. Dr. Ashok Kumer Dutta , Registrar , Cardiology , DMCH welcomed the participants and Dr. Md. Sirajul Hoque, Asst. Professor of cardiology , DMCH presented the scientific paper on" Trimetazidine - Newer molecule in management of IHD" as a key note speaker. Dr. H. I. Lutfor Rahman Khan, Assoc. Professor of cardiology, DMCH and Dr. Md. Shomsher Ali, Asst. Professor of cardiology, DMCH were also present as panel of experts.

Venue : Auditorium of Nuclear Medicine Center, SSMC & Mitford Hospital, Dhaka.

Sitting from left to right : Dr. Nazir Ahmed Chowdhury, Prof. A.K.M. Mohibullah, Dr. Md. Abu Zafar, Dr. Shahinur Rahman, Dr. Md. Zahirul Haque. Standing from left to right : Dr. Syed Aminul Islam, Dr. Monjurul Haque.

A Scientific Seminar was sponsored by Orion Laboratories Ltd. on " Trimetazidine - Newer Agent in Treatment of IHD" on Tuesday, 27th January 2004 at auditorium of nuclear medicine center, SSMC & Mitfort hospital, Dhaka. Where the eminent Professor Dr. A. K. M. Mohibullah, Professor & Head of the dept. of Cardiology, SSMCH chaired the session. Dr.Syed Aminul Islam, (MD, cardiology final) SSMCH, presented the scientific paper on " Trimetazidine - Newer Agent in Treatment of IHD" as a key note speaker. Dr. Nazir Ahmed Chowdhury, Assoc. Professor of cardiology, Dr. M. A. Hai, Assoc. Professor of neuromedicine, and Dr. Sk. Abu Zafer Asst. Professor of medicine were also present as panel of experts.

Venue: Seminar Room of Faridpur Medical College Hospital.

From left to right : Dr. Md. Badrul Alam, Dr. Md. Golam Kabir Mia, Dr. Md. Enamul Karim

A Scientific Seminar was sponsored by Orion Laboratories Ltd. on "Trimetazidine - A new molecule in the treatment of Ischemic Heart Disease" on Monday, 12th April 2004 at Seminar Room of Faridpur Medical College Hospital, Faridpur where Dr. Md. Enamul Karim, Principal, Faridpur Medical College, Faridpur chaired the session. Dr. Md. Golam Kabir Mia, Superintendent, FMCH was present as Chief Guest and Dr. Md. Badrul Alam, Asst. Prof. of FMCH was also present as Special Guest. Dr. Sk. Yunus Ali, Asst. Prof. of Cardiology and Dr. Md. Yusuf Ali, Asst Prof. of Medicine presented their scientific papers respectively.

Scientific Seminar on "Foot ulcer & Maximox, Linozid, Tamlosin & Ketorin"

Venue: Department of Surgery of Rangpur Medical College Hospital.

A Scientific Seminar was sponsored by Orion Laboratories Ltd. on "Foot ulcer & Maximox, Linozid, Tamlosin & Ketorin" on

The rest of the MSD NEWS is given on page no.-172

Medi News

No health without Zinc

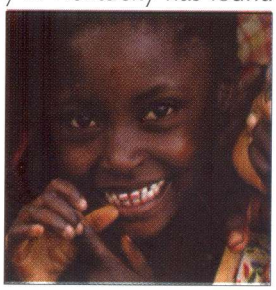
As one of nature's essential elements, zinc is required by men, women and children throughout the life cycle to grow and develop. Zinc occurs naturally throughout the earth, in plants and animals and in the foods we eat. Every cell in the body requires zinc to multiply. Zinc is required for smell and taste and helps regulate the body's immune system. It heals and protects the skin and boosts brain activity. Zinc is essential to life.

Men

Because this trace mineral is vital to the life-long good health of male reproductive organs, it is one of the key nutrients for sexual function. It has been called the "masculine mineral" because, outside of the eye, its highest concentration is found in the male prostate gland.Zinc also is concentrated in semen and is vital to fertility. Not getting enough of this important mineral may decrease seminal fluid and sperm count. In one study, men were given zinc sulfate (60 mg of elemental zinc) daily for 45 to 50 days. In the 22 patients with initially low testosterone levels, mean sperm count increased significantly from eight to 20 million. Testosterone levels also increased, and nine of the 22 wives became pregnant during the study. Despite its importance, zinc deficiency is fairly common among men due to improper diets, vegetarianism, nutrient-poor and depleted soils and nutrient loss during food processing or cooking.

Women

Zinc deficiency acts as a sustaining factor in abnormal eating behavior, found extensively among women. Dr. Laurie Humphries of the University of Kentucky has found that patients may develop eating disorders for psychological reasons, but certain patients then develop zinc deficiency, which perpetuates the altered food habits. It□s known that zinc activitates the areas of the brain that govern taste and smell, and without those, the desire to eat is vastly diminished. In a 1994 summary publication appearing in the Journal for Medical Research, Dr. Alex Schauss reports that studies from Stanford, University of Kentucky, and University of California at Davis found that most anorexics and many bulimics are zinc deficient. A five-year study showed an astounding 85 percent remission rate of anorexia nervosa in patients given a zinc supplementation. Using zinc supplements resulted in weight gain, better body function and improved mental outlook. Zinc may also help in the treatment of pre-menstrual syndrome (PMS), which affects 50 percent of all menstruating women. Although recent studies are far from conclusive, there is growing evidence that a deficiency of progresterone underlies PMS - and trace amounts of zinc regulate the secretion of hormones, including progesterone. Early research at Baylor College of Medicine in Houston found significantly lower levels of zinc among women with PMS during the luteal phase of menstruation, the 13 days preceding menstruation.



This reduction could lead to a decrease in secretions of progresterone and endorphines - the natural painkillers our bodies produce. The research is preliminary and if zinc deficiency does play a role, it might only affect a subgroup; nevertheless, studies continues to confirm zinc's importance to the regulation of hormones. Recent studies also have shown that zinc supplements could help certain women, especially those who are thin, deliver larger and healthier babies. Researches from the University of Alabama-Birmingham studied 580 women receiving prenatal care from local public clinics to study the impact of zinc on pregnancy. Results from their research found that babies born to the group receiving 25 milligrams of zinc daily weighed an average of 4.5 ounces more and had head circumferences averaging 0.4 inches greater than the other babies. One reason these babies were heavier is that only 3 percent were born more than two months premature.

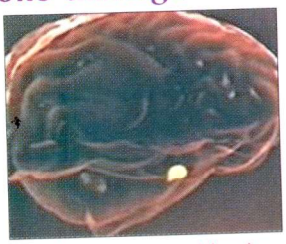
Children

Although zinc is absolutely essential for normal growth and brain development, it is significantly lacking in the diets of millions of children, according to a recent study by the Center on Hunger, Poverty and Nutrition at Tufts University School of Nutrition. More than 50 percent of poor children and 30 percent of non-poor U.S. children get less than 70 percent of the U.S. Recommended Dietary Allowance of zinc (10 milligrams per day for children). The study shows that of 16 key nutrients, more children were deficient in zinc than any other nutrient. Zinc is required for the metabolic activity of 200 of the bodys enzymes and is considered essential for cell division and the synthesis of DNA and protein. Clinical research has shown that zinc deficiency contributes to growth retardation and that even mild deficiency may limit growth in otherwise healthy children. A 1993 study published in Journal of Pediatrics found zinc supplementation effective for inducing growth and increasing caloric intake in short children with zinc deficiency. Stunting, which occurs when a child is shorter than normal at a given age, is a major health problem associated with zinc deficiency and affects 30 percent of the world's children. In the United States, the prevalence of stunting is about twice as high for poor children as non-poor children. The Pediatric Nutrition Surveillance System reports that 9 to 11 percent of the nation's low-income population is stunted. Zinc also is imperative for proper learning, and task behavioral performance among children. Found in vesicles of the mossy fiber system of the brain's hippocampus, zinc interacts with other chemicals to send messages to the sensory brain center, enhancing memory and thinking skills. Research has shown that zinc deprivation causes poor growth and maturation of the cerebellum and impairs the development of brain cells, which may contribute to learning disorders or emotional and behavior problems. Other studies have shown that zinc deprivation has a significant effect on cognitive function, resulting in learning impairments and deficits in working visual memory.

ZINC WORLD.org

Medi News

'Corkscrew' repairs stroke damage



The device removes blood clots from the brain

Scientists have developed a 'corkscrew' which can capture and remove blood clots in the brains of stroke patients. Doctors from the University of California were able to reverse the disabling effects of a stroke in patients using the device. It is inserted via an artery in the groin and guided through the body to the brain, where it 'remembers' to form into a corkscrew around the clot. The device is then removed, taking the clot with it and unblocking the artery. The researchers studied patients who had suffered ischemic stroke. These are caused by a blood clot that blocks the blood supply to the brain and are the most common kind of strokes. Doctors can give patients clot-busting drugs to dissolve the blockage - but these are only effective if they are given within three hours of a stroke. *bbc.com/health*

Watching TV 'is bad for children'

Children under two should not be allowed to watch any TV, experts say. Older children should watch no more than two hours a day, the researchers at the Children's Hospital and Regional Medical Centre in Seattle said. Each hour in front of the TV increased a child's chances of attention deficit disorder by 10%, their research in the Pediatrics journal showed. The study of 1,345 children showed three hours TV a day made children 30% more likely to have the disorder.Dr Dimitri Christakis at the children's hospital led the study. He said: "The newborn brain develops very rapidly during the first two to three years of life. It's really being wired." TV can cause the developing mind to experience unnatural levels of stimulation. Children who were exposed to the unrealistic levels of stimulation at a young age continued to expect this in later life, leading to difficulty dealing with the slower pace of school and homework. "TV can cause the developing mind to experience unnatural levels of stimulation." This was made worse by the rapid image change that television makers used to keep young children interested, Dr Christakis added. *bbc.com/health*

Some children watch too much TV

Penicillin warning to doctors

Doctors treating children with a throat infection caused by Streptococcus bacteria should use newer drugs, not penicillin, researchers say. Paediatricians at the US' University of Rochester Medical Centre said new antibiotics were three times better. But UK GPs said penicillin worked well and there was no immediate reason to switch over. "Strep throat" is passed by personal contact. School-age children seem particularly vulnerable. A new class of antibiotics, called cephalosporins, can be as cheap as penicillin and have a similar effect, the Rochester researchers said in the journal Pediatrics. Children who have strep throat will have a superior outcome if they receive cephalosporin rather than penicillin Dr Janet Casey previous studies, covering 7,000 children, to compare the effectiveness of the two drugs. Both penicillin and some first generation cephalosporins, such as Cephalexin and Cefadroxil, are "narrow spectrum", which means they are targeted enough to tackle the bacteria but not so strong that they cause resistance. Resistance can lead to the creation of a superbug and is one of the reasons penicillin has traditionally been used. However, the researchers said the newer drugs both met this requirement and were more effective in attacking the bacteria that cause strep throat. They examined a number of

Penicillin's role being questioned

cnn.com/health

Vitamin fights prostate cancer

Vitamin E can protect men from prostate cancer, according to researchers. Men with high levels of the alpha tocopherol form of vitamin E were 53 per cent less likely to develop prostate cancer. The researchers stressed it was better to take vitamin E from fresh food than supplements. The US National Cancer Institute study was presented at the American Association of Cancer Research annual meeting in Orlando. Scientists looked at 100 men who had prostate cancer and 200 who did not and compared amounts of vitamin E in the bloodstream before and after taking a supplement. The men who had the higher serum levels of vitamin E had a lower chance of getting prostate cancer The researchers then looked at the two main forms of vitamin E - alpha tocopherol and gamma tocopherol. Men with the highest natural levels of alpha tocopherol were 53 percent less likely to later develop prostate cancer. Men with the highest levels of gamma tocopherol, which only represents about 20 percent of the vitamin E in blood, had a 39 percent lower chance. The best absorbed form of alpha tocopherol is found in foods such as sunflower seeds, spinach, almonds and sweet peppers, not supplements. *bbc.com/health*

Peppers contain vitamin E

Smoking Speeds Up Memory Loss in Old Age

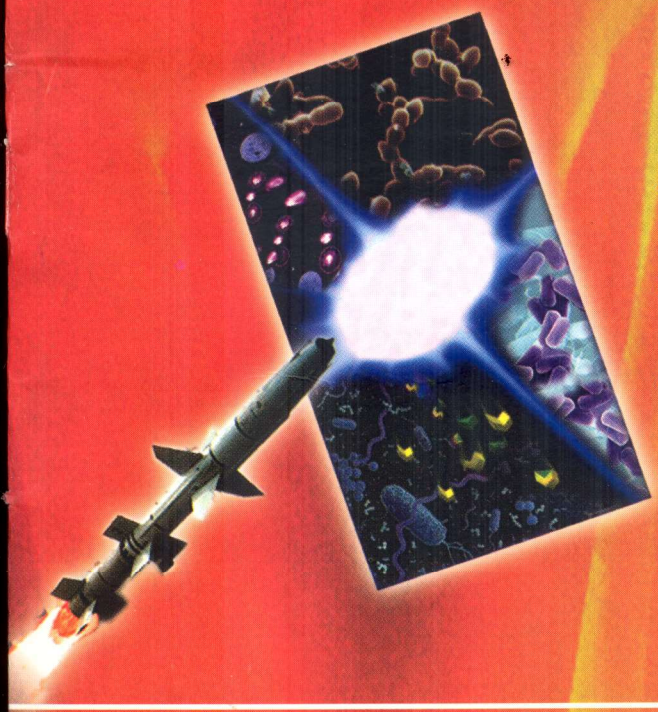
Elderly people who smoke show a five-fold faster rate of age-related mental decline than people who never smoked, according to new study findings. Among former smokers, mental decline occurred around twice as fast as in those who said they never smoked. And the more people smoked during their lifetimes, the quicker they appear to lose their mental faculties with age. These findings represent another reason why smokers should quit, and one that "may appeal to the people who didn't stop for other reasons," study author Dr. Lenore Launer of the National Institute on Aging in Maryland. This is not the first study to link smoking with mental decline. Previous research has shown that middle-aged smokers tend to show a faster rate of decline in old age, and may experience more cognitive changes than non-smokers even before they reach age 60. *Web Med/Health*

Ataq

Gatifloxacin INN 200 & 400 mg tablet

US FDA Approved

...the 4th generation Weapon against bacteria

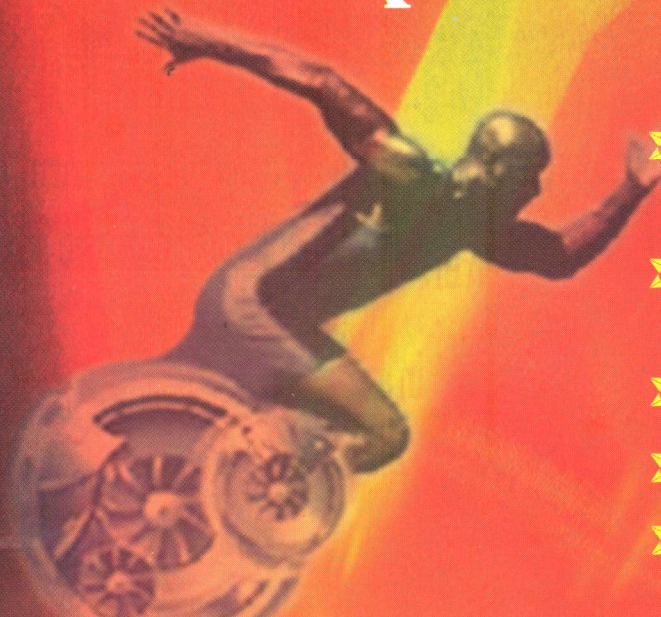


- Covers the most causative pathogens of infections
- Tremendous structural modification prevents resistance development
- Excellent tissue penetrating power than ciprofloxacin and levofloxacin
- Shows outstanding success rates in Community Acquired RTIs
- Better success rate than ciprofloxacin in Urinary Tract Infections (UTIs)

Moxifloxacin INN 400 mg

MAXIMOX

The 4th generation fluoroquinolone



- Ensures plasma and tissue concentrations well above MIC_{90} of key respiratory pathogens
- More potent than ciprofloxacin & levofloxacin considering MIC_{90} values
- Ensures better treatment success than ceftriaxone
- Ensures higher productivity
- Ensures cost effective and patient-compliance treatment

ORION
LABORATORIES LTD.
In Search of Excellence

URS UKAS QUALITY MANAGEMENT 043