EDITORIAL

Cancer Pain Management : Need for a Comprehensive Bio-Psycho-Social Approach

Pain is a frequent accompaniment of cancer. Much of our present rationale of pain control is based on the Cartesian idea that pain mostly originates from noxious stimuli of different kinds, internal or external, which are transmitted to and interpreted in the central nervous system[1]. Consequently, interventions at the level of cerebral awareness have been the prime target of pain management. It is only recently that the relationship between pain and other physical, psychological and social components of illness have been considered in the overall management plan for pain of any kind. Patients with cancer have symptoms of different kinds, they have impairments in physical and psychological functioning, and difficulties in other areas that can, in most of the cases, undermine their quality of life. If inadequately controlled, pain may have profound adverse impact on the patient and his or her family. The critical importance of pain management as a part of routine cancer care has been forcefully advanced by World Health Organization (WHO), different professional organizations and state agencies.

The prevalence of chronic pain is about 30 to 50% among patients with cancer who are undergoing active treatment for a solid tumour and 70 to 90% among those with advanced disease[2]. Most cancer pain is caused by direct tumour infiltration and approximately 20% cancer pain may be attributed to the effects of surgery, radiotherapy or chemotherapy. Cancer pain may be acute or chronic and chronic pain may cause psychological reactions that make effective treatment more challenging[3]. Cancer pain, particularly when it is chronic and related to an advancing condition, can interact significantly with many facets of daily living. A holistic model of quality of life in such patients should, therefore, include a modular or multidimensional assessment of these areas [1].

Pain in patients with cancer, at times difficult though, can be effectively managed. Comprehensive case assessment, specific anti-cancer therapy and systemic analgesics are pivotal in the management plan. However, management approach would not be complete if options for other non-invasive and invasive procedures are not kept alive. Different factors have been identified to be responsible for inadequate management of pain[2]:

- Lack of a comprehensive pain management plan, and inadequate attention to psychosocial aspect of pain and its aetiological entity;
- Insufficient knowledge of clinicians in pain assessment and therapy, and consequent under-treatment;
- Inappropriate concern about medication side-effects including addiction, specially of narcotic analgesics;
- Tendency to give lower priority to symptom control than to disease management;
- Under-reporting by the patients;
- Non-compliance with treatment; and
- Impediments to optimum analgesic therapy in existing health care system.

Effective pain management therefore requires a clear understanding of pain pathophysiology, the ability to identify and evaluate pain syndromes, and familiarity with

proven therapeutic strategies[4]. Recognition of the relevant pathophysiological process, and the psychological, emotional, social and spiritual components of suffering in both normal and psychologically dysfunctional cancer patients would provide the means for the treating physicians to rapidly choose the initial course of action, select the most appropriate therapies, and liaise effectively with other relevant health care professionals[5].

A comprehensive evaluation is mandatory in the treatment of pain from cancer. Pain has two basic components: perception of pain itself and psychological reaction to that perception. Pain is always a subjective experience and there is no precise method to quantify it. However, two approaches are usually followed to make a near accurate assessment of pain. The first is a psychophysical procedure to distinguish between patient characteristics for reporting of pain and the sensory experiences induced by noxious stimulus. The second is the use of tools to assess by the patient's description. Many kinds of rating scales are currently available to evaluate the intensity of clinical pain, but they cannot assess the quality of pain. Evaluation of pain is not complete without evaluation of mood and emotional symptoms. Attention should be paid to the specific nature of the pain complaints and attempts made to make accurate clinicopathological correlates for the pain. Assessment should be complete and ongoing.

In the first instance, the clinician should take all initiatives to assure the patient and to this end the clinician should always be willing to discuss the pain and to take active measures in suggesting remedies that might be helpful. The second principle of management is to assure the patient that the treatment will continue even if there is no immediate improvement. One of the fears expressed by many patients with cancer pain is of abandonment. Third, while not expecting a cure, it is important for the physician to be ever hopeful at least to reduce the discomfort. Treating physician should embark on developing strategies that help patients achieve specific goals while learning to tolerate the pain[6]. The use of single intervention in ultimate pain management is seldom successful in a progressive condition like cancer. Much of the success reported by contemporary pain management in such conditions can be attributed to the fact that several treatments are used in combination or in sequence. These include a wide range of biological, psychological, social and behavioural interventions. One mode of treatment should not be substituted by the other, rather they should be complementary to each other.

Systemic use of opioid or non-opioid medications is mainstay of biological treatment of cancer pain. Practical aspects of opioid pharmacology include drug selection, methods of analgesic administration, selection of the appropriate route, dose titration, and an understanding of the management of side-effects[7]. Psychotropic medications like phenothiazines and anti-depressants have an opiate-sparing effect in patients with pain from cancer. The above agents bind with opiate receptors and interact with encephalins. MAO inhibitors are claimed to have the similar pain relieving effects. Benzodiazepines appear to lower the pain thresholds. In addition to adjuvant non-narcotic analgesics, other agents recommended for intractable pain from cancer are carbamazepine, clonazepam, valproic acid, clonidine, propanolol, psychostimulants and steroids[8]. Psychotropic medications more often help alleviating features of depression and anxiety associated with pain and the attributing disease itself. Invasive methods of pain control in cancer include, among others, transcutaneous nerve stimulation, acupuncture, intraspinal analgesics, neural blockade, neuroablative techniques and intraoperative radiotherapy. Physiotherapy has also its own role[6].

One of the major components of a holistic management plan is to address the psychological aspect of pain itself and understanding the psychological aspect of pain management. It is important for several reasons. First, patients with pain have a significantly higher incidence of depression and anxiety. Chronic pain may be a depressive equivalent. Pain may itself cause psychiatric syndromes and it may coexist with psychopathology in vulnerable population. It has been suggested that treatment of one improve the other[9]. Second, the incidence of psychiatric complications is particularly high when the pain is underestimated or undermedicated by caretakers. Underestimation of pain and consequent undertreatment is a phenomenon more often than not displayed by the treating physicians also. Third, psychiatrists in this situation can reorient both the patients and caregivers to above responses in a supportive and nonjudgemental way by providing a sympathetic and respectful insight into the patient's psychological state, and also by educating them with management principles[10]. Cancer related pain and associated distress significantly challenge the physical and psychological wellbeing of patients with advanced cancer and their families. Patients frequently manifest symptoms and maladaptive behaviour that require specialized interventions to restore a sense of focus and control[11].

Modification of perception and tolerance of pain is largely aided by psychosocial and behavioural interventions. Cognitive behavioural interventions are uniquely suited to address the most common psychological and emotional problems. As an adjunct to medical care, cognitive behavioural interventions promote optimal functioning. Such interventions are necessary to dig out the psycho-socio-environmental, communicative, and operant aspects of pain[11]. However, these interventions are often difficult to implement initially owing to the resistance on the part of patients and their families to psychosocial and behavioural concept of pain management. It essentially needs contribution and cooperation of agencies and significant others[12]. Management of persisting pain needs clarity to the idea of pain and its management, and fear, myth and misconception attached to them. While the clinicians feel that their patients should be pain free, they still underestimate the effective dose, overestimate the duration of drug action and there is exaggerated notion of the danger of addiction. Education may contribute to make one acutely aware of the patient's suffering. Education to the patient and his family will help changing their attitude towards the multidimensional nature of the problem and need of a multidisciplinary approach to its management[13]. It would facilitate the treatment compliance and persistence to treatment programme.

Cognitive therapy in pain patients encourages various techniques by which the patients of early cancer with mild to moderate pain learn to distract or distance from their pain[12]. Psychotherapy as an individual measure is rarely prescribed for cancer pain management. However, when used in conjunction with other treatment modalities it might well produce significant benefit, particularly if insight can be given on the nature of the problem. It would facilitate acceptance of reality and help elevating mood and allaying anxiety. Psychotherapy has been shown to improve quality of life[14]. Hypnosis, for cancer pain, is seldom helpful alone, although the life enhancing attitude provided by hypnosis can provide a much needed experience of personal efficacy and strength, and physical comfort[15].

In a very advancing condition, the patients often feel helpless and shy off from seeking help. Their needs may be expressed in the guise of overt or covert hostility, deliberate self-harm and unrelated complaints. In such situations of learned helplessness, assertiveness training and role-playing may

help the patients express their needs more directly[16]. Muscular contraction or vascular dilatation, often incriminated as a worsening factor in cancer pain, may be helped by biofeedback and relaxation[17]. Relaxation, a less expensive and simpler treatment option, may also ease out the physical components of pain related anxiety. Family and relatives may have important contribution in mastering new skill and developing new adaptation by the patient to deal with a terminal condition like cancer and its associated pain. However, the family, often unknowingly, play a significant role in shaping the illness behaviour of the patient in response to his illness and its consequences. Family therapy is a powerful adjuvant to rehabilitative process of intractable diseases[18]. Group therapy and peer support groups are more practical treatment component to provide sustained positive attitude and behaviour to a specific problem in a homogeneous population. In this therapeutic method the emphasis is given on mutual sharing and problem solving, and seeking collective solutions to coping with pain[14]. A rehabilitative approach in many cases augments the healthy living in a terminally ill patient especially if the patient is bothered by a persisting symptom like pain. There is always a need to practice pain management in the natural environment and to plan the patient's reentry into social and occupational functioning[11]. Other psychosocial treatments recommended for cancer pain include, among others, autogenic training, operant conditioning, music or art therapy, and meditation.

Healing or successful intervention leads to partial or complete resolution of pain. However, in conditions like cancer, both biological and psychological propagating factors are usually progressive and often continue uninterrupted. Despite incurable nature of the condition, successful pain management can be accomplished in nearly all terminally ill patients. Pain must be assessed in terms of its biological, psychological and social components. An individualized treatment plan needs to be developed with incorporation of all available relevant therapeutic modalities. Improvement of cancer pain management largely depends on the availability of an up-to-date medical information for the treating clinicians and an appropriate pain education for the patients and their families.

This editorial is based on a plenary paper presented by the author elsewhere.

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Editor-in-Chief

(J Bangladesh Coll Phys Surg 2000; 18 : 92-96)

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ORIGINAL ARTICLES

Clinical Profile and Treatment Outcome of Diabetic Ketoacidosis in Adults

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Summary :

Sixty consecutive episodes of diabetic ketoacidosis (DKA) in 46 diabetic patients were studied at Gurayat General Hospital in Kingdom of Saudi Arabia (KSA). Thirty (65.22%) were type I and 16 (34.78%) type II diabetics. Mean age was 30.5 years and mean duration of diabetes 3.8 years. Infections were the most common precipitating factor accounting for 22 episodes (36.66%). Fifteen patients (32.60%) had hyperosmolality (serum osmolaliy > 320 mosmol/L). Mean serum sodium was 130.6 mmol/L and potassium 4.5 mmol/L. Sixteen (34.78%) were hyperkalaemic at presentation. Six patients (13.04%) were comatosed while 28 (60.86%) alert. Mean random blood glucose (RBG) was 615 mg/dl, mean pH 7.10, and osmolality 312 mosmol/L. Main complications identified were septicaemia in four cases, cerebral oedema in one case and adult respiratory distress syndrome in one case. A leukaemoid response was seen in 82.60% patients. Mortality rate was 8.69%.

(J Bangladesh Coll Phys Surg 2000; 18 : 97-101)

Introduction :

Diabetic Ketoacidosis (DKA) is an acute complication of diabetes mellitus which requires prompt assessment and treatment to avoid devastating consequences. DKA is characterized by hyperglycaemia, ketonaemia and acidosis due to increased glucose and ketone body formation with decreased peripheral utilization of glucose and ketone bodies[1]. This occurs due to a bi-hormonal disorder of insulin deficiency and glucagon excess[2].

The aim of the study was to describe the clinical and biochemical features of DKA as well as the final outcome in adult patients admitted to Gurayat General Hospital in northern region of Kingdom of Saudi Arabia.

Materials and method :

A prospective study of 60 consecutive episodes of DKA in 46 patients presenting to Gurayat General Hospital in Northern region of KSA between May 1997 to May 1999 was done. Criteria for inclusion in the study were random blood glucose (RBG) >200 mg/dl, pH <7.30 and ketonuria[3]. All patients were in-patients. A detailed history was taken and complete physical examination was done in each patient. All had RBG, blood urea nitrogen and creatinine, assayed by the Astra Autoanalyser, Hb% and WBC by Coulter counter an arterial blood pH analysed by Corning pH blood gas analyser. Serum osmolality was calculated by the formula : Na x 2 + K x 2 + G ÷ 18 + BUN ÷ 2.8. Ketones in urine were checked by multistix and essential specimen culture. Clinical features, precipitating factors and biochemical profile at presentation were recorded in every case. Patients were classified into type I and type II according to clinical criteria of age, body mass index, rapidity of weight loss and previous tendency for ketosis. Neurological state on admission was assessed and patients were divided into three groups; alert, stuporous/ drowsy and comatose. Survival, death and duration of hospitalization were used as markers of outcome.

Results :

There were 60 episodes in 46 patients : 24 males (52%) and 22 females (48%). Six patients (13.04%) had three or more episodes

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Received : 31 May 2000 Accepted : 12 August 2000

of DKA. The mean age was 30.5 years (range 13-72 years, 16 were above 40 years of age. Thirty (65.22%) patients had type-I diabetes and sixteen (34.78%) type-II. Twenty eight were on insulin, of which two were type-II diabetics requiring insulin, while eight were on oral hypoglycaemic agents. Ten patients (21.73%) had DKA as the first manifestation of diabetes. Mean duration of diabetes in this cohort was 3.8 years. Table-I shows the presenting features. Most common symptom was gastrointestinal disturbance (anorexia, nausea, abdominal pain, vomiting or diarrhoea), present in 34 patients (73.91%). Ten (21.73%) patients complained of overt polyuria and polydipsia. Only two patients (4.34%) were in shock at the time of presentation. Six (13.04%) patients were comatosed, 12 (26.08%) were drowsy or stuporous and rest 28 were (60.86%) alert.

Table-I

Presenting features of diabetic ketoacidosis (n=46)

Features	Number of patients	Percentage
Nausea, vomiting, anorexia, abdominal pain	34	73.90
Polyuria, thirst	10	21.73
Weight loss	08	17.39
Fever	07	15.21
Weakness	06	13.04
Leg cramps	03	06.52
Blurred vision	02	04.34
Dehydration	46	100.00
Air hunger (Kussmaul breathing)	16	34.78
Smell of acetone	14	30.42
Drowsiness	12	26.98
Coma	06	13.04
Hypotension, tachycardia	02	04.34
Hypothermia	01	02.71

Main precipitating factor (Table-II) was infection accounting for 22 episodes (36.66%) followed by noncompliance with treatment in 12 (20%) episodes. DKA was the first presentation in 10 (16.66%) episodes. Three (5%) had miscellaneous causes for DKA while in 13 (21.66%) episodes no cause for ketoacidosis could be identified.

Table-II

Precipitating factors of episods of diabetic ketoacidosis

Precipitating factor	Number of episodes	Percent
Infection	22	36.66
Non-compliance with treatment	12	20.00
New onset diabetes	10	16.66
Miscellaneous (trauma, surgery)	03	05.00
No cause	13	21.66

Biochemical profile at presentation are shown in Table-III. Mean RBG was 615 mg/dl (range: 320-1520 mg/dl). Fifteen patients (32.60%) had osmolality greater than 320 mosmol/L at presentation. Serum sodium level ranged from 110-148 mmol/L with four (8.69%) having hypernatraemia and 18 (39.13%) hyponatraemia at the time of admission. Rest had serum sodium in normal range. There was a trend of decreasing sodium with increase in blood glucose. Sixteen (34.78%) had hyperkalaemia while five (10.86%) had hypokalaemia.

Table-III

Biochemical profile of diabetes ketoacidosis

Parameters	Range	Mean
Random blood glucose (mg/dl)	320 – 1520	615
PH	6.89 – 7.29	7.10
Osmolality (mosmol/L)	278 – 360	312
Na^+ (mmol/L)	110 – 148	130.6
K^+ (mmol/L)	2.5 – 7.5	4.5

Only eight cases (17.39%) had normal WBC counts on admission, while 38 (82.60%) had leucocytosis with six (13.04%) having WBC count above 30 x 10^3/ml. A leukaemoid response was encountered in patients with

and without infections. Positive cultures identified urinary tract infection in eight patients, tonsillitis in two, chest infection in two, *Staphylococcus aureus* abscess in two and candidiasis in one patient.

Management of these patients followed standard guidelines[4-6]. Mean duration of hospitalization was 6.4 days. Mean length of stay in hospital in those patients having RBG level less than 800 mg/dl was 5.8 days while those with RBG more than 800 mg/dl was 7.6 days. Four patients died resulting in a mortality rate of 8.96%. Ages of patients who expired were 55, 58, 60 and 62 years. Mean pH, RBG, and osmolality of the two groups, survived vs expired was 7.10 vs 7.06, 610 vs 665 mg/dl, 312 vs 334 mosmol/L respectively. Mean length of stay in patients who expired was 3.4 days. One patients had cerebral oedema, while four had septicaemia and one had adult respiratory distress syndrome complicating DKA.

Discussion :

Diabetic ketoacidosis (DKA) may occur at any age in diabetics and may either be the first manifestation or may be precipitated after many years of stable diabetes, as shown in this study. Nearly 35% patients were thought to be type-II diabetics. There are no data on the prevalence of diabetic ketoacidosis in non-insulin dependent diabetic patients but non-caucasian populations with new onset diabetes or infections may present, not infrequently, with ketoacidosis[6]. The clinical presentation is often dramatic. An antecedent history of polyuria and polydipsia for one to several days is typical, and nausea, vomiting and anorexia are frequent accompanying symptoms. The onset of vomiting is always a threatening symptom and is particularly useful as an warning in those already known to be diabetic[7]. Nonspecific abdominal pain is a recognised feature of DKA and a surgical cause of abdominal pain may be misdiagnosed in these patients[3]. The state of consciousness is very variable in patient with diabetic ketoacidosis; coma is uncommon[8]. In their study, Fulop et al concluded that the depth of coma did parallel with hyperglycaemia and more closely with hyperosmolality but not acidaemia[9]. Other less common symptoms include visual disturbance and leg cramps. In addition to the physical signs of dehydration, ketone bodies may be detected in breath (acetone breath). Although most patients have air hunger and respiration may be depressed when the systemic acidosis is severe. Pyrexia may not present initially because of vasodilatation secondary to acidosis. The acidaemia induced peripheral vasodilatation may aggravate the tendency to hypotension caused by volume depletion.

Wahtel et al found that infections were the most common precipitating factor of DKA (30%)[10]. Other causes were non-compliance with therapy (20%) and newly diagnosed diabetics (24%). These findings were comparable with patients in this study and those reported by Matoo et al from India[11]. Any form of stress, particularly that produced by infection, may precipitate severe ketoacidosis, even in patients with type-II diabetes. No obvious precipitating cause can be found in many cases[8]. In DKA, infections may be present even if body temperature is normal or subnormal, but an elevated temperature strongly suggests presence of infection[12].

Although the diagnosis of DKA can be strongly suspected clinically, confirmation is based on laboratory analysis. The cardinal biochemical features of diabetic ketoacidosis are hyperglycaemia and hyperketonaemia in the presence of metabolic aciodosis. Plasma glucose levels in patients with DKA range from nearly normal to extreme concentrations that are characteristic of hyperosmolar state. The plasma glucose level are very high primarily when extracellular volume has decreased to a point where urine flow (and therefore ability to excrete glucose) is impaired[3]. During evolution of DKA, losses of water are

disproportionately greater than losses of sodium and this would precipitate dehydration of brain tissue. The mean plasma level of sodium in patients with DKA tends to be low, despite an increase in osmolar concentration. This is because glucose draws water into the extracellutar compartment thereby decreasing Na^+ concentration. A very low serum sodium level is usually due to hypertriglyceridaemia but may be due to vomiting and water intake[4]. Patients with DKA tend to have elevated serum potassium (K^+) concentration despite decreased body K^+ content. This is due to decreased potassium excretion by the kidney once volume depletion reduces GFR and also due to the corresponding acidosis and insulin deficiency resulting in shift of K^+ from intracellular to exteracellular compartment. Therapy of diabetic ketoacidosis shifts potassium from the extracellular to the intracellular compartment by correcion of acidosis, repletion with sodium, and insulin effects on glycogen synthesis and potassium transport into the cell. The continuing renal loss of potassium and the shift of potassium into cell can lead to profound hypokalaemia and death, if not treated prospectively[6]. The metabolic acidosis is primarily due to accumulation of betahydroxybutyric and acetoacetic acids in plasma, although free fatty acids and lactic acidosis also contribute towards acidosis[4]. Wahtel et al in their study of 613 patients with DKA found that 33% were hyperosmolar (serum osmolality > 320 mosmoles/L)[10]. The frequent occurrence of mixed acidotic and hyperosmolar state were observed in this study also. A leucocytosis occurs commonly in DKA[13]. A leukaemoid response does not necessarily indicate the presence of infection. The mortality rate from DKA ranges from 2% to 5% in developed countries[14] and 6% to 24% in developing countries[6,11]. In developed countries, mortality and morbidity from diabetic ketoacidosis result mainly from sepsis or pulmonary and cardiovascular complications especially in individuals over 65 years of age in whom mortality rate exceeds 20% compared to about 2% in younger adults[15,16]. Children and young adults (≤28 years age) are uniquely susceptible to the development of severe and often fatal cerebral oedema during treatment of DKA[17]. This complication is estimated to occur in 0.7% to 1% of ketoacidotic episodes[18]. The pathogenesis of cerebral oedema is unknown; though it is often associated with osmotic disequilibrium secondary to a fall in blood glucose. Excessive rehydration and use of hypertonic fluids such as 8.4% bicarbonate may be sometimes responsible.

Due to significant mortality and morbidity, prevention should remain the main focus in diabetic patients, but good critical care management is required when the condition arises.

Acknowledgement :

The author is grateful to Dr. Adnan Sahlab, Medical Director and Chief of Physicians of Gurayat General Hospital KSA for allowing collection of data for this study. The author would also like to thank Dr. Shethardi and all laboratory staffs of Biochemistry and Microbiology department of Gurayat General Hospital for their cordial help during the study.

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Journal of Bangladesh College of Physicians and Surgeons
Vol. 18, No. 3, September 2000

Comparison Between Fine Needle Aspiration Cytology (FNAC) and Fiberoptic Bronchoscopy (FOB) in the Diagnosis of Peripheral Pulmonary Lesions

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Summary :

Fine needle aspiration cytology (FNAC) was performed in 105 cases. There was 78 (74.29%) malignant cases, 21 (20%) non malignant cases and in six (5.71%) cases no diagnosis could be possible. The results of FNAC were compared with fiberoptic bronchoscopy (FOB). No endobronchial lesion was seen in 84 (80%) cases 21 (20%) cases revealed evidence of malignancy, which was proved histologically. Diagnosis could be possible in two more cases by FOB which were undiagnosed by FNAC. Sensitivity of FNAC was 94%, which conforms to the previous studies. FNAC is a much better procedure to obtain a tissue diagnosis in peripheral pulmonary lesions ($p=<0.001$). Complications were minimum and the procedure is cost-effective.

(J Bangladesh Coll Phys Surg 2000; 18 : 102-107)

Introduction :

Specific diagnosis of pulmonary lesions, which persists even after three weeks broad spectrum antibiotic therapy, is essential. Available non-invasive and minimally invasive procedures include, among others, sputum examination, transtracheal aspiration, scan of the chest, chest MRI, fiberoptic bronchoscopy (FOB) and endobronchial biopsy, transbronchial biopsy, transbronchial needles aspiration and CT guided fine needle aspiration cytology (FNAC). Of them, CT scan and MRI scan is costly, nonavailable everywhere, moreover, tissue diagnosis is not possible with these investigaions. FOB is also a costly procedure, not readily available, experienced hand is required, more over only endobronchial lesions could be visualised by it. Transbronchial biopsy can be done in peripheral lesions but it requires screening either by C-arm or by CT. In the improvised techniques, FNAC is a less costly and safe procedure; results can be obtained within hours to days. Moreover, CT guided FNAC can be done in difficult cases. So, if it could be established that FNAC is superior to FOB in the diagnosis of peripheral pulmonary lesions, then it could be an immense help to both the physicians and the patients. Percutaneous needle aspiration biopsy under screening is a useful method of cytological diagnosis of peripheral lung lesion[1]. Fine needle aspiration cytology of suspicious lung masses is a widely accepted and simple diagnostic method of relatively low cost, with negligible mortality and limited morbidity[2]. In patients with lung cancer that is inoperable owing to local factors or the patients general condition, FNAC confirms the diagnosis and reveals the tumour type. This is useful in deciding the therapeutic

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Received : 17 Feb. 2000 Accepted : 06 August 2000

approach in patients in whom results of bornchoscopy and sputum cytological study are not diagnostic[3]. In candidates for surgery with indeterminate solitary pulmonary nodule i.e., without clear radiological signs of malignancy or benignity[4], for whom results of routine cytological studies are normal, findings from FNAC may be diagnostic[5]. The presnet study is done with an attempt to find the efficacy of FNAC in the diagnosis of peripheral pulmonary lesions and to find the efficacy of FOB and endobronchial biopsy in the diagnosis of peripheral pulmonary lesion, and to compare the efficacy of both modalities in the diagnosis of peripheral pulmonary lesion.

Materials and method :

The study was done in the Institute of Diseases of Chest and Hospital (IDCH) Mohakhali, Dhaka during the period from January '97 to September '98. It was a prospective study and patients were selected from indoor of IDCH. A total of 105 patients having a suspecious radiological shadow in the chest x-ray and fulfilling the inclusion criterion was the study population. Persistent or gradually increasing peripheral radiological shadow measuring atleast 3 cm or more in diameter inspite of two weeks broad sprectrum antibiotic therapy with or without chest pain, cough, hemoptysis, weight loss and clubbing were the inclusion criteria for the study. Here peripheral lesions were arbitrarily defined as lesions situated in the peripheral of the lung and medial margin of the lesion situated atleast 2cm from the hilum. Patients having sputum positive for acid fast bacilli (AFB), strongly positive tuberculin test, bleeding diathesis, x-ray shadow less than 3 cm in diameter were excluded from the study. Proper history of the patients was taken and physical examination was done. FNAC was done in all patients as per standard procedure. The slides were immediately sent to the laboratory. The results were collected from the laboratory and compiled in the data sheet. A second check was done for any report, which seemed to contradict the clinical and radiological findings. Complications during or after the procedure were noted on the data sheet. Fiberoptic bronchoscopy was done in all cases. The results were entered in the data sheet. All the collected data were compiled and tabulated in a master sheet. These data were analysed statistically by *chi-square* test to arrive at a definite conclusion in respect to objectives of the study.

Results :

A total of 105 cases were included in the study of which 98 were male and seven female. Their age ranged from 16 to 95 years. The mean age was 54.22 (±16.24) years (Table-I).

Lymph node biopsy was done in 23.81% of patients. Of them 7.62% revealed squamous cell carcinoma, 4.76% small cell carcinoma, 8.57% adenocarcinoma, and 2.86% large cell carcinoma (Table-II).

Results of FNAC is shown in Table-III. More than 74% patients had malignant lesions, 20% non-malignant lesions and in 5.71% patients, the results of FNAC was inconclusive even after repetition. On an average, one to three passess were necessary to obtain adequate samples. In four cases repeat FNAC revealed conclusive results. Among the malignant cases. squamous cell carcinoma was on the top of the list (44.76%), 13.33% cases had adenocarcinoma, 9.52% small cell carcinoma and 5.71% had large cell carcinoma. Among the non-malignant lesions, 8.57% were diagnosed as lung abscess, 7.62% had features of tuberculosis, and one case each had pneumonia and empyema.

Fiberoptic bronchoscopy was done in all patients to confirm the diagnosis and to compare the results of FNAC (Table-IV). No endobronchial lesion was found in 80%, 20% cases revealed evidence of malignancy endoscopically.

Final diagnoses are shown in Table-V. Squamous cell carcinoma was on the top of

the list (46.67%), 13.33% had adenocarcinoma, 9.52% small cell carcinoma and 5.71% metastatic renal cell carcinoma; lung abscess was found in 8.57% and 7.52% had tuberculosis. FNAC was done in 105 patients with peripheral pulmonary lesions. Definite histological diagnosis was possible in 94.28% cases. Diagnosis could not be made in 5.71% cases. So, sensitivity of FNAC in the diagnosis of peripheral pulmonary lesion is 94%. FOB was done in all cases to compare the efficacy of FNAC in relation to FOB. Surprisingly, the diagnosis could be possible in 20% cases only. In 80% cases tissue diagnosis could not be possible. The sensitivity of FOB in the diagnosis of peripheral pulmonary lesion is 20% only. Finally, it was evident that FNAC is a superior and more reliable method than FOB in the diagnosis of peripheral pulmonary lesions ($p<.001$).

Table-I

Age of the patients in years

Age in years	Number of cases	Percent	Malignancy	Percent	p value
≤ 25	07	06.67	01	00.95	
26-35	10	09.52	05	04.76	
36-45	15	14.28	11	10.47	
46-55	20	19.04	16	15.23	.00255
56-65	24	22.85	19	18.09	
> 65	29	27.61	28	26.66	
Total	105	100.00	80	76.19	

Table-II

Results of lymph node biopsy

Type of lesion		Number of cases	Percentage
Not done		80	76.19
Malignant		25	23.81
Type of malignancy	Squamous cell carcinoma	08	07.62
	Small cell carcinoma	05	04.76
	Adenocarcinoma	09	08.57
	Large cell carcinoma	03	02.86

Table-III

Results of FNAC

Type of lesion		Number of cases	Percentage
Malignant	Sqeamous cell carcinoma	47	44.76
	Small cell carcinoma	10	09.52
	Adenocarcinoma	14	13.33
	Large cell carcinoma	06	05.71
	Metastatic renal cell carcinoma	01	00.95
	Total	78	74.29
Non-malignant	Lung abscess	09	08.57
	Tuberculosis	08	07.62
	Pneumonia	01	00.95
	Empyema	01	00.95
	Mycosis	01	00.95
	Cyst	01	00.95
	Total	21	20.00
Non-specific		06	05.71

Table-IV

Results of fiberoptic bronchoscopy

Type of lesion		Number of patients	Percentage
No endobronchial lesion seen		84	80.00
Malignant lesion	Squamous cell carcinoma	12	11.43
	Small cell carcinoma	07	06.67
	Adenocarcinoma	01	00.95
	Large cell carcinoma	01	00.95
	Total	21	20.00

Table – V

Final diagnosis of the patients

Diagnosis		Number of cases	Percentage
Malignant lesions	Squamous cell carcinoma	49	46.67
	Adenocarcinoma	14	13.33
	Small cell carcinoma	10	09.52
	Large cell carcinoma	06	05.71
	Metastatic renal cell carcinoma	01	00.95
Non-malignant lesions	Lung abscess	09	08.57
	Tuberculosis	08	07.62
	Empyema	01	00.95
	Pleural effusion	01	00.95
	Mycosis	01	00.95
	Cyst	01	00.95
Inconclusive		04	03.81

Discussion :

Since the first report of percutaneous transthoracic fine needle aspiration biopsy (FNAC) in 1983, this procedure gradually has become an efficient and safe diagnostic technique for malignant and benign thoracic lesions[6].

Total number of cases were 105 in this series, of them 98 (93.33%) were male and seven (6.67%) were female. Female cases are less because malignant pulmonary lesions are rare in females in our population. Male-female ratio was 14:1, this is very much similar with the findings of Samir[1], the first published report of pulmonary FNAC in Bangladesh. In his series the male to female ratio was 10:1. Most of the patients in present series belongs to more than 55 years age group (50.46%). Of them 47 (44.75%) were proved to have malignancy. This finding is similar to those of others.

Lymph node biopsy was done in all cases presented with lymphadenopathy. Malignancy was found in all cases. Eight patients had sequamous cell carcinoma, five had small cell carcinoma nine had adenocarcinoma and three had large cell carcinoma. FNAC showed 78 (74.29%) malignant cases, nonmalignant cases were 21 (20%), in six (5.71%) cases no definite diagnosis could be obtained. In four cases diagnosis could be obtained after repetition of the procedure. Among the malignant cases, squamous cell carcinoma was predominating (44.76%), next was adenocarcinoma (13.33%), 9.52% had small cell carcinoma and 5.71% had large cell carcinoma and only one patient had metastatic renal cell carcinoma. In Samir's series, malignancy was found in 41% cases, 48% cases revealed no malignancy and other remained undiagnosed[1]. In his series also squamous cell carcinoma was predominanting (50%), small cell carcinoma was 33%, adenocarcinoma was 2% and no large cell carcinoma was found.

Fiberoptic bornchoscopy was done in all patients in order to identify the superiority of the procedure over FNAC. As the lesions were peripheral, most of the FOB results showed that there was no endobronchial lesions in 80% cases and in only 20% cases malignancy was found. Of them 11.43% were squamouse cell carcinoma, 6.67% small cell carcinoma, one adenocarcinoma and one large cellcarcinoma. This revealed that FNAC is far superior to FOB in the diagnosis of peripheral pulmonary lesion ($p<.001$).

Final diagnosis, after compiling all the modalites of investigation revealed that squamous cell carcinoma was present in 44.76%, adenocarcinima in 13.33%, small cell carcinoma in 9.52%, large cell carcinoma in 5.71% and metastatic renal ell carcinoma in 0.95%. Of the non-malignancy lesions, nearly 9% cases revealed lung abscess. In this cases FNAC was done in suspicion of activity malignancy eight cases revealed tuberculosis. With all efforts diagnosis could not be made in four cases.

Complications were very minimum and only two cases had evidence of pneumothorax. In Samir's series there was no complications[1]. In Jack's series minor haemoptysis was found in 8% cases, which required no treatment; 27% cases developed pneumothorax but only 10% cases required treatment[7]. In his series, the complication rate is more than the present series. This may be due to that they used a relatively large-bore needle (20G), where as needle used in this series was 23G. Moreover, his target was to diagnose hilar and mediastinal lesions, in contrast to peripheral lesions in this series. FNAC offers several advantages over other diagnostic procedures used in the evaluation of patients with pulmonary lesions.

Biopsy of a peripheral lesion using direct needle aspiration is much easier than fiberoptic bronchoscopy. It is important to recognise which patients should not undergo biopsy; patients with endobionchial lesions, atelectasis or lobar consolidation should have bronchoscopy rather than needle biopsy as

the initial diagnostic procedure. Obviously, needle biopsy may result in a false negative finding if one samples from an area of obstructive pneumonitis or collapse distal to an endobronchial lesion[7]. Several large studies have confirmed that transthoracic aspiration with fine needles is safe and can achieve high accuracy (upto 90% sensitivity), especially for the diagnosis of cancer[8,9,10]. In this series, sensitivity of FNAC was 94%. However, there are still some drawbacks for fine needle aspiration. Because tumour heterogeneity is a common phenomenon and some of the tumours may have pleomorphic morphological characterisics. Small samples obtained by fine needle aspiration are good only for cytological study and are not adequate for histological diagnosis. Moreover, it is difficult to use fine needle aspiration cytological findings to confirm the diagnosis for a benign lesion or a tumour with pleomorphic pathological characteristics such as lymphoma and thymoma. A large bore cutting biopsy is necessary is such a cases.

From the above study it can be concluded that FNAC is a much better procedure to obtain a tissue diagnosis in peripheral pulmonary lesions. Complication rate is minimum and the procedure is cost effective. So, in case of peripheral pulmonary lesions, FNAC is the first procedure of choice to reach a tissue diagnosis. The sensitivity of FNAC in the diagnosis of peripheral pulmonary lesions was 94%. The sensitivity of FOB in the diagnosis of peripheral pulmonary lesion was only 20%. So it is evident that FNAC is superior over FOB in the diagnosis of peripheral pulmonary lesions.

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Journal of Bangladesh College of Physicians and Surgeons
Vol. 18, No. 3, September 2000

Relationship Between I^{131} Therapy and Extent of Thyroid Surgery in Well-differentiated Thyroid Carcinoma

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Summary :

This is a systematic five-year compilation of 492 patients treated with radioactive iodine after thyroid surgery for well differentiated thyroid carcinoma. The objective was to see whether there was any relationship between the extent of surgery done and the number of I^{131} doses required within the subsequent five years follow-up of these patients. Group-I patients had small remnant size of the thyroid gland after surgery, ranging from 0.8 x 1 cm to 1.2 x 3 cm, and Group-II had partial and/or subtotal thyroidectomy with size of remnant ranging from 3.0 cm x 2.0 cm to 3.2 cm x 5.0 cm. In Group-I, the first ablation dose by itself was effective in controlling the further recurrence of disease in nearly 16 % cases. Second dose was required in 62.64% and multiple doses in 8.06% cases to make them disease free. Five-year follow-up in 86.45% of these patients showed no recurrence and/or metastasis. In Group-II patients, the first dose was ineffective in ablating the large thyroid remnant. Second and multiple doses were required to render only 6% patients free of the disease. Five-year follow-up showed progressive disease in almost 75% cases as evidenced by recurrent local and distant metastasis. Death occurred in 0.9% patients and more than 18% patients were lost to follow-up. The importance of total thyroidectomy is therefore emphasised so that ablation of residual functional tissue can be done successfully. If a partial thyroidectomy has been performed, leaving significant amount of tissue in the neck, it may be best to consider a more extensive surgical extirpation.

(J Bangladesh Coll Phys Surg 2000; 18 : 108-112)

Introduction :

Surgery is the definite and potentially curative treatment for differentiated thyroid cancer. The extent of the operative procedure should involve a near-total thyroidectomy with excision of all macroscopic disease including resection of adjacent muscle should this be involved. In many practical situations, however, total thyroidectomy is not always warranted at a first or second operation due to increased morbidity. Consequently, there are patients with thyroid cancer who undergo sub-total or hemi-thyroidectomy. The cases are then referred for radioactive iodine (I^{131}) ablation and follow-up treatment.

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The aim of the present study was to determine the outcome of I^{131}. therapy in patients with well-differentiated thyroid carcinoma and relate this to the extent of surgery undertaken to remove the thyroid gland.

Materials and method :

Four hundred and ninety two patients treated with I^{131} at the Institute of Nuclear Medicine, Dhaka during 1984 to 1991 for papillary, mixed and follicular thyroid carcinoma were included in this study. The following factors were considered for analysis :

a) amount of functioning thyroid tissue left in the neck after surgery;

b) initial I^{131} dose given to ablate this thyroid remnant;

c) number of I^{131} doses given within the successive five year follow-up; and

d) progress of the disease during this period.

The amount of functioning thyroid tissue after surgery was assessed from the scan done on the rectilinear scanner by direct measurement of the visually identifiable concentration of

radiotracer in the thyroid bed. In some cases, ultrasonographic correlation was also available. Radioactive iodine uptake (RAIU) at 24 hours was done on every patient. The dose administered for the scan and uptake was between 50 and 60 mCi of I^{131}.

Based on history and the post-operative RAIU and scan findings, patients were divided into two groups as follows:

Group I: patients who had total or near total thyroidectomy either at a first or second surgery with RAIU ranging from 0.2 % to 5%.

Group II: patients who had partial thyroidectomy and in whom the second surgery was not possible for various reasons. In these patients, the RAIU ranged from 2 % to 15 %.

Histopathology report was reviewed to determine the type of the tumour and the presence of regional metastasis. Thyroid hormone status and TSH level before radio-iodine therapy in all the patients, and baseline thyroglobulin (Tg) level done in more recent patients were also available for review. The initial dose given to ablate the functioning thyroid tissue together with the successive therapeutic doses required within the five-year follow-up period was noted. Difference in the prognosis of the disease in these two groups of patients was correlated with the extent of thyroid surgery.

Though all patients receiving I^{131} therapy remain on a life long follow-up at the institute, only the five years period following initial treatment was included in the study for the sake of uniformity and also because patient turnover was found to be more consistent during this period of follow-up. Regular check-up after initial therapy included periodic whole body survey for metastasis using I^{131} and monitoring of serum Tg level in patients treated more recently. These records and also records of physical examination, haematological investigations, chest X-rays etc. were reviewed to assess the prognostic status of the patients.

Results :

The age range of the patients treated was from 11 to 80 years. Among them, nearly 60% were females in a female to male ratio of 1.5 : 1. The highest incidence of cancer, about 34% in this series, was found in the third decade of life in both sexes (Table-I). Histopathological differentiation of the cases showed that almost 68% of the patients were suffering from papillary carcinoma, nearly 24% had follicular carcinoma and 8.54% percent of the patients had a mixed papillary-follicular variety of cancer (Table-II).

Table -I

Age- and sexwise distribution of the patients (n -492)

Age range in years	Male	Female	Total (%)
11-20	06	09	15 (03.05)
21-30	42	97	138 (28.05)
31-40	72	94	166 (33.74)
41-50	52	47	99 (20.12)
51-60	16	42	5 8 (11.79)
61-70	06	05	11 (02.25)
71-80	04	00	04 (00.82)
Total	198 (40.24%)	294 (59.76%)	492 (100%)

Female to male ratio 1.5:1

Table-II

Histopathological types of thyroid cancer (n -492)

Papillary	Follicular	Mixed	Total
332 (67.48%)	118 (23.98%)	42 (08.54%)	492 (100.00%)

Based on the RAIU and scan findings the patients were divided into two groups (Table-III). The size of the post-surgery residual thyroid activity in Group-I ranged from 0.8 cm x 1 cm to 1.2 cm x 3 cm and the 24 hours uptake was between 0.2 and 5%. The size of thyroid remnant in Group-II ringed from 3.0 cm x 2.0 cm to 3.2 x 5.0 cm and the 24 hours uptake was from 2 to 15 %.

The outcome of the patients in these two groups in a five-year follow-up is shown in Table-IV and Table-V. In Group-I, there were 273 patients and they had total or near total thyroidectomy and nearly 16% of these cases were effectively controlled by a single dose of radioiodine, 62.64% required a second dose while more then 8% cases required more than two doses to control the disease. Thirty seven patients (13.56%) in this group came irregularly for check-ups and no records of their follow-up were found within the five year period after initial therapy. These patients were therefore considered lost to follow-up.

In Group-II, there were 219 patients. All of them received the first ablation dose ranging between 60 and 75 mCi. Among them, two patients did not have any further records of follow- up while all the rest presented with local recurrence. A second dose of 100 mCi was successful in controlling only 4.11% of these patients while 49.32% again showed local recurrence and nearly 42% patients had distant metastasis. Ninty one percent patents in this group received more than two doses ranging from 150 to 200 mCi. These multiple doses could control the disease in only 2.28% patients. In 75% cases, the disease was progressive with almost 33% cases showing persistent local recurrence in and around the neck and 41.55% showing distant metastasis to the lungs and skeletal system. Death occurred in two patients in this group.

Table-III

Distribution of patients according to RAIU and post-surgery scan findings (n-492)

Group	Remnant size	RAIU	Total number of patients
Group-I	0.8 x I cm to 1.2 x 3 cm	0.2 to 5 %	273 (55.49%)
Group-II	1.5 x3.2 cm to 3.3 x 5 cm	2 to 15 %	219 (44.51%)

RAIU = Radioactive iodine uptake

Table-IV

Number of dose received and the outcome of Group-I patients in a five year follow-up

I^{131} dose in mCi	Total number of patients (%)	Disease free (%)	Local recurrence (%)	Distant metastasis (%)	Death (%)	Lost to follow-up (%)
First 75 to 100	273 (100.00)	43 (15.75)	177 (64.84)	25 (09.16)	00 (00.00)	28 (10.26)
Second 100 to 150	202 (73.99)	171 (62.64)	10 (03.66)	17 (06.23)	00 (00.00)	04 (01.47)
Multiple 150 to 200	27 (09.89)	22 (08.06)	00 (00.00)	00 (00.00)	00 (00.00)	05 (01.83)

Table - V

Number of dose received and the outcome of Group-II patients in alive year follow-up

I^{131} dose in mCi	Total number of patients (%)	Disease free (%)	Local recurrence (%)	Distant metastasis (%)	Death (%)	Lost to follow-up (%)
First 60 to 75	219 (100.00)	00 (00.00)	216 (98.63)	00 (00.00)	00 (00.00)	03 (01.36)
Second 75 to 100 1	216 (98.63)	09 (04.11)	108 (49.32)	91 (41.55)	00 (00.00)	08 (03.65)
Multiple 100 to 200	199 (90.87)	05 (02.28)	72 (32.88)	91 (41.55)	02 (00.91)	29 (13.24)

Discussion :

Ablation is used primarily to denote the removal of tissue remnants that might obscure or render sub-optimal the subsequent radiotherapeutic measures. The goal of the ablative procedure is to prepare the patients for more definitive treatment by[3]:

- elevating TSH levels sufficiently to expose neoplastic tissue to thyrotropin so as to facilitate radioiodine uptake into metastasis for localization and therapy; and
- removing normal tissue so as to eliminate extraneous thyroglobulin sources and ultimately decreasing the rate of the recurrence of thyroid cancer.

A true total thyroidectomy is in reality an impossible task and residual thyroid tissue will always be present in the neck. Therefore, routine ablation of the remnant thyroid tissue is an absolute requirement if the patient is to be further treated by radioiodine. So far, there is no standard regimen as to the amount of I^{131} prescribed. A fixed activity of radioiodine is usually prescribed based on clinical experience and likely side effects[4].

In the patients studied here, Group-I received ablation doses ranging from 75 to 100 mCi and this was effective in controlling the further recurrence of disease in nearly 16% cases, while none of the patients in Group -II were ablated with the first dose of radioiodine. The activity of I^{131} administered in this group however was small ranging from 60 to 70 mCi. The reason for using a smaller hose in this group was to avoid the risk and consequent immediate complication of radiation thyroiditis in the relatively large thyroid remnant. The patients in Group-II thus ended up with repetitive administration of doses in an attempt to ablate the large remnant of thyroid tissue. There is a possibility that the sub-optimal radiation doses given may decrease the biological half-life and effective half-life of subsequent radiation doses making it ineffective to ablate the functioning tissue and thus leading to prolongation of treatment and/or treatment failure.

With regards to long time morbidity and mortality, a significant difference is observed between the two groups of patients. Follow-up of nearly 82% cases in Group-II shows that almost 75% of the patients were still suffering from the disease after five years while more than 86 % patients that came for follow-up in Group-I appeared disease free. This difference in prognosis appears to be directly related to the presence of the amount of thyroid tissue in the neck. Total removal of the thyroid gland facilitating a subsequent optimal I^{131} dose is therefore a significant

prognostic factor. In Bangladesh, there are innumerable constraints to a standard mode of treatment and often therapy must be given in less than an ideal situation. As seen in about 45% of the cases studied here, I^{131} had to be given in presence of significant thyroid tissue because a second surgery could not be done due to various reasons. It is reported that, although the incidence of immediate post-surgical complication is higher after total thyroidectomy at a first or second operation, many post-operative complications can be avoided when these procedures are performed by surgeons skilled in thyroidectomy[5]. Proponents of total or near-total thyroidectomy suggest that the increased morbidity associated with extensive surgery is justified perhaps by decreased recurrence of the malignant condition at extended intervals. Moreover, in one of the studies, 27.40% recurrent papillary cancers were found in residual thyroid tissue, suggesting the importance of total or nearly total thyroidectomy to eradicate potential sites of recurrence[6].

The female to male ratio of thyroid cancer in the 492 patients studied was found to be 1.5:1. This appears slightly higher than the reported female to male ratio of 1.4:1[4]. It has been reported that papillary tumours occur more frequently in iodine rich areas while follicular ones appear to be more common in low-iodine endemic goitre areas. This is quite contrary to the findings here where inspite of 69% reported prevalence of iodine deficiency in Bangladesh[8], the ratio of papillary to follicular carcinoma appears high. This observation may not be statistically valid since the present study is not an epidemiological survey. Nevertheless, the cases were collected from one of the largest thyroid referral centres in the country, and the findings regarding the prevalence of the histopathological type of tumour appears remarkable. It therefore merits further extensive evaluation on an epidemiological scale to fully validate this observation.

In conclusion, the importance of total thyroidectomy should be considered as the first line of treatment so that ablation of residual functional tissue can be done successfully. Moreover, surgical removal of the bulk of thyroid tissue would decrease the administration of repeated multiple I^{131} doses and thereby avoid unnecessary whole body irradiation. If a partial thyroidectomy has been performed, leaving significant amounts of tissue in the neck, it may be best to consider a more extensive surgical extirpation before further treatment with radioactive iodine.

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Journal of Bangladesh College of Physicians and Surgeons
Vol. 18, No. 3, September 2000

Electrocardiographic Analysis and Arrhythmia Pattern in Mitral Valve Prolapse : A Review of 188 Cases

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Summary :

Mitral valve prolapse (MVP) has been described as an important cause of abnormal elctrocardiogram and varities of cardiac arrhythmias. Evaluation of electrocardiograms (ECG) and arrhythmia pattern of 188 patients with documented primary mitral valve prolapse was done. T-wave inversion mimicking coronary artery disease was noted in 117 (62.23%) patients. T-inversion in inferior leads was the commonest ECG abnormality and was present in 96 (51.06%) patients. T-wave inversion in anterolateral leads were seen in 11 (5.85%) patients, V1-V3 in six (3.19%) patients and diffuse T wave changes in both anterior and inferior leads in four (2.13%) patients. Premature ventricular and atrial ectopics were noted in 21 (11.17%) cases, non-specific ST depression in anterolateral leads in 16 (8.51%) patients and ECGs were normal in the remaining 34 (18.09%) patients. Twenty one patients with arrhythmia in resting 12 lead ECG were further evaluated by 24 hour Holter monitoring. Holter study revealed non-sustained ventricular tachycardia in three (1.60%) patients, supraventricular tachycardia in three (1.60%), atrial fibrillation in two (1.06%), frequent ventricular ectopics in four (2.13%), and combination of ventricular and atrial ectopics in the remaining five (2.66%) patients.

(J Bangladesh Coll Phys Surg 2000; 18 : 113-116)

Introduction :

Mitral valve prolapse is a disorder with prevalence estimates generally ranging from five to 15 percent[1]. The primary mitral valve prolapse is frequently associated with electrocardiographic abnormalities and various cardiac arrhythmias. Atrial and ventricular arrhythmias have been reported with variable incidence in patients with MVP[2,3,4]. The aim of this study was to analyse the electrocardiographic abnormalities and rhythm disturbances in 188 patients with primary mitral valve prolapse.

Materials and method :

A total of 188 cases were diagnosed to have primary mitral valve prolapse in Combined Military Hospital, Dhaka during the period from March 1997 to December 1997. Cases were consecutively enrolled from the Non-Invasive Cardiac Laboratory of the hospital. Age of the patients ranged from eight years to 65 years with mean age 32.3 years (SD±12.6). All subjects underwent standard Echo-Doppler study with a commercially available Hewlett Packard Sonos 2000 cardiac ultrasound system. Current two-dimensional echocardiographic criteria was used to diagnose mitral valve prolapse according to the maximal superior displacement of the mitral leaflets during systole relative to the line connecting the annular-hinge points[5,6]. Subjects were diagnosed to have MVP if displacement exceeded 2 mm and maximal thickness was at least 5 mm. The degree of mitral regurgitation was assessed according to the standard criteria[7].

Resting 12 lead electrocardiograms of all the patients with documented MVP were analysed. Stress test was done in 67 (35.64%) cases. On the basis of clinical symptoms and stress test result, coronary angiogram was done in 21 patients and out of them eight (4.26%) cases were documented to have significant coronary artery disease and hence excluded from the study. Holter monitoring was done in selected 21 patients and arrhythmia patterns were analysed.

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Received : 28 Feb. 2000 Accepted : 06 August 2000

Results :

Evaluation of the ECGs revealed various types of abnormalities including repolarization defect, nonspecific ST wave changes and arrhythmia in resting 12 lead ECGs (Table-I). Most common ECG abnormality was T wave inversions One hundred and seventeen (62.23%) patients had T wave changes mimicking coronary artery disease. T wave inversion in LII, LIII and aVF was present in 96 (51.06%) patients, anteroseptal leads in four (2.13%) patients. ECGs of 34 (18.09%) subjects were normal. Frequent premature ventricular and atrial ectopics were documented to be the most common arrhythmia in this series and were present in 13 (6.91%) cases. Alarming arrhythmia like non-sustained VT was noted in three (1.60%) patients, SVT in three (1.60%) patients and AF in two (1.06%) cases (Table-II).

Table-I

ECG changes in mitral valve prolapse

ECG change	Number	Percent
T wave inversion in inferior leads	96	51.06%
T wave inversion in anterolateral leads	11	05.85%
T wave inversion in anteroseptal leads	06	03.19%
T wave inversion in both anterior and inferior leads	04	02.13%
Premature ventricular and aterial ectopics	21	11.17%
Nonspecific ST depression	16	08.51%
Normal ECG	34	18.09%

Table-II

Pattern of arrhythmia in mitral valve prolapse

Arrhythmia	Number	Percentage
Premature ventricular complex	04	02.13%
Premature atrial complex	04	02.13%
Both atrial and ventricular premature complex	05	02.66%
Non sustained VT	03	01.60%
SVT	03	01.60%
AF	02	01.06%

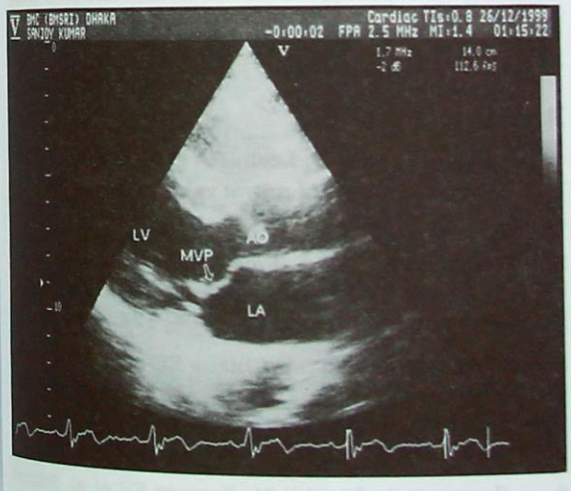

Fig.-1 : *Two-dimensional long-axis echocardiogram of a patient with mitral valve prolapse (MVP). Anterior mitral leaflet (arrow) curves in to the left atrium (LA).*

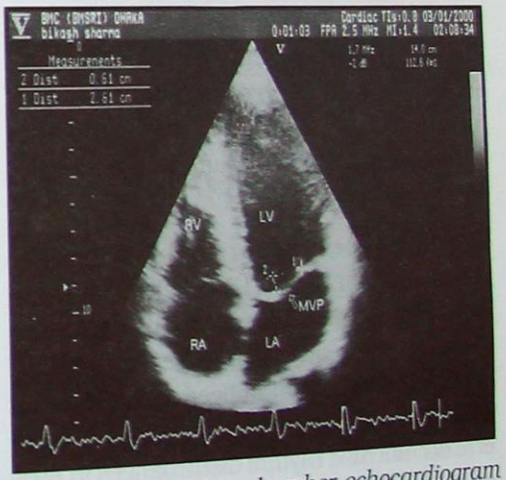

Fig.-2 : *Apical four-chamber echocardiogram of a patient with mitral valve prolapse demonstrating a curved anterior mitral leaflet that extends 6 mm beyond the plane of the mitral annulus (dotted line).*

Discussion :

MVP may be symptomatic or asymptomatic and the condition may remain undiagnosed for an indefinite period. When the patients become symptomatic, it may be misdiagnosed as coronary artery disease (CAD) as 12 lead ECGs are frequently abnormal. In most of the cases ECG mimics CAD. In this series, T wave inversion simulating CAD was present in more than 62% of patients. Repolarization defect was documented in 67% of patient with MVP in a recently published series[8]. In the present study, T wave inversion in inferior leads were the most frequent ECG abnormality documented and was present in 51.06% of cases. With the increasing use of ECG as a standard investigation there is an understandable increase of abnormal electrocardiographs. Even in a developing country such as Bangladesh, ECG is being used not only for cardiac complaints but also as a routine procedure in many situations. To the enlightened patients as well as non-specialist physicians, an abnormal ECG with T wave inversion along with nonspecific ST depression is often attributed to CAD. MVP is not an uncommon condition and it is frequently associated with abnormal ECG and erroneous diagnosis of CAD is possible if careful attention is not paid during ECG interpretation and clinical examination[9]. In patients not susceptible to CAD, an echocardiogram may confirm the diagnosis. In other situations, stress test and sometimes coronary angiogram is required to exclude the possibility of CAD.

Various types of arrhythmias were documented in 21 (11.17%) patients in this study. The incidence of arrhythmia was noted to be more frequent in other published data[8,10]. Rokicki et al noticed arrhythmia in 22% of patients in their series[8] and Calleja et al documented rhythm disturbances in 89% of patients with MVP[10]. Incidence of arrhythmia is probably underestimated in this series as selected sub-group of patients with MVP were sent for Holter monitoring. In this study, alarming arrhythmia like VT and SVT were documented in six (3.19%) patients. Whatever the incidence of arrhythmia may be, prognosis of such arrhythmia with MVP remains substantially benign, as is true for most cases of VT[11]. Possible risk of neurological ischaemia and arrhythmic sudden death is very low in patients with MVP. The cumulative risk of all forms of complications like progressive mitral regurgitation, infective endocarditis, syncope, ischaemic stroke and sudden death of MVP by age 75 is from 5% to 10% for affected men and 2% to 5% for affected women[12]. In a recently published series, the authors failed to demonstrate an association between MVP and ischaemic neurological events. So, patients with MVP requires thorough assurance regarding the natural history of the disease.

Abnormal ECG is quite frequent in MVP. Erroneous diagnosis of coronary artery disease is possible in this condition. But careful history taking, clinical examination and appropriate ECG interpretation are likely to avoid false diagnosis of CAD and premature invalidism. Clinicians must remember this condition during ECG interpretation particularly in young patients, so that correct diagnosis, management and assurance may be accorded to the every increasing number of cardiac diagnosis.

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REVIEW ARTICLE

(J Bangladesh Coll Phys Surg 2000; 18 : 117-121)

Genetic Predisposition to Cancer : A Review

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Introduction :

The biological nature of tumour in childhood is clinically, histopathologically, and biologically distinct from adult onset malignancies. The vast majority of typical childhod cancers are confined to the first two decades of life[1]. Childhood cancers tend to have short latency poeriod, are often rapidly growing and aggressively invasive, and rarely associated with exposure to carcinogens[1]. In developed countries, approximatly one in 600 children develop cancer before they are 15 years old. Half of all childhood malignancies are diagnosed during the first five years of life. About 33% of cases are leukaemia, 25% brain tumours and 10-12% lymphomas. The remaining cases are mainly embryonal tumours including neuroblastoma, Wilm's embryonal rhabdomyosarcoma, retinoblastoma and hepatoblastoma[2].

Most childhood tumours occur sporadically in families. In approximately 10% to 15% of cases, however, a strong familial association is recognized or the child is affected with a congenital or genetic disorder that is known to impart a higher likelihood of specific cancer types[1]. Example of genetic disorder which render a child a increased risk of tumour development include xeroderma pigmentosa, Blooms syndrome or ataxia telengiectasia which predispose to skin cancers, leukaemias or lymphoid malignancies respectively. In all three cases, the constitutional gene alterations that disrupt normal mechanisms of genomic DNA repair are blamed for the propensity to cell transformation[1]. Some cancer predisposition syndromes are recognized only by their malignant manifestations with non-malignant characteristics virtually absent. These include hereditary retinoblastoma, the Li Fraumani syndrome (LFS), familial Wilm's tumour and familial adenomatous polyposis coli. Each of these present with distinct cancer phenotypes and for each the identified molecular defect is unique[1].

The study of paediatric cancer, and rare hereditary cancer syndromes and associations have led to the identification of numerous cancer genes including dominant oncogenes and tumour suppressor genes which have proven to be important not only in hereditary predisposition but also in the normal growth, differentiation and proliferation of all cells. The study of these factors in paediatric cancers offer a clear genetic model to work with. The better understanding of the nature of the genetic events leading to these cancers will also augment understanding of normal embnryogenesis.

The study of the nature of the genetic events of cancer has a multipotential effect in general. Apart from the understanding of the tumour behaviour which will ultimately fortell the course and prognosis, it will also help in the screening for the common causes due to inherited susceptibility. Specifically, who and

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Received : 20 August 2000 Accepted : 27 August 2000

at what age somebody is to be screened[3] or how often the screening should go on or at what sites screening is to be done could be determined more easily and clearly.

Inherited cancer syndromes :

Inherited cancer syndromes includes several well-defined cancers in which inheritance of a single mutant gene greatly influence the risk of developing a tumour. These syndromes are characterized by a high incidence of specific cancer within an affected family[2]. Usually there are no associated non-neoplastic phenotypic markers of gene carrier status. The genetic hypothesis of cancer implies that a tumour mass results from the clonal expansion of a single progenitor cell that has incurred the genetic damage[4]. It is said that three classes of normal regulartory genes : the growth promoting protoncogene, growth inhibiting cancer suppressor gene and genes that regulate programmed cell death or apoptosis are the principal targets of genetic diseases. While protoncogenes encode proteins that promote cell growth, the products of tumour suppressor genes apply brakes to cell proliferation. Best example of these is in retinoblastima, a rare paediatric eye tumour in which a small region of the long arm of chromosome 13 is frequently missing[1].

Retinoblastoma and the Rb1 gene :

Retinoblastoma affects approximately one in 20,000 live-born children and occurs in hereditary and sporadic form[2]. Approximately 40% of retinoblastoma are familial[4] and carriers of this gene have 10,000 fold increased risk of developing retinoblastoma and is usually bilateral. The also have a greatly increased risk of developing a second cancer particularly osteosarcoma[4]. Hereditary retinoblastoma is often diagnosed during the first year of life. Multiple tumours within a single eye are common.

Rb gene : Much is known about the Rb gene because this was the first tumour suppressor gene discovered[4]. PRb the product of Rb gene is a nuclear phosphoprotein that plays a key role regulating a cell cycle. It is expressed in every cell type examined where it exists in an active under-phosporylated and inactive hyperphosporylated state. In its active state, PRb serves as a brake on the advancement of cell from the G1 to S phase of the cell cycle.

Germ line mutation of the Rb gene predisposes to occurrence of retinoblastomas and to a lesser extent osteosarcoma. Further more, somatically acquired mutations have been described in glioblastoma, small cell carcinoma of lung, breast cancers and bladder cancers[1].

Neurofibromatoses :

Neurofibromatosis refers to genetic disorders that give rise to tumours of the nerve sheath, glia, and meninges. This describes two similar disorders NF1 and NF2[1]. NF1 is an autosomal dominant disorder affecting about one in 3,500 people. Individuals who harbour mutant NF1 are predisposed to a variety of tumours including optic nerve glioma, neurofibroma and neurofibrosarcoma, malignant schwanoma, astrocytoma and pheochromocytoma. Occuring with less frequent are leukaemias, osteosarcoma, rhabdomyosarcoma and Wilm's tumour[1].

The NF1 gene on chromosome 17q11 spans over 300 kb of genomic DNA. An intersting feature of this gene is that three other genes EV1 2 A, EV1 2 B and OMGP are embedded within it. It is not clear whether these play any role in the expression of NF1[1].

Neurofibromatosis type 2, NF2, is seen much less frequently than NF1 occurring in only one in 50,000 to 100,000 individuals. The hallmark of NF2 is bilateral accoustic neuroma, which may result in deafness, tinnitus, headache, facial paresis, and mental state changes[1]. NF2 is inherited in an autosomal dominant fashion with over 95% penetrance. The NF2 gene is mapped in chromosome 22q12.

Li Fraumeni syndrome and the Tp53 gene :

In 1969, Li Fraumeni observed that the close relatives of children with soft tissue sarcomas had a high frequency of cancer, particularly other soft tissue sarcomas and breast cancer. They concluded that this represent a new familial cancer syndrome with a genetic origin[1]. The Rb1 gene was the first tumour suppressor gene to be cloned and the second was the Tp53 gene. Germ line mutations to Tp53 gives rise to familial clusters of cancers consistent with Li fraumeni syndrome (LFS)[2]. LFS is characterized by bone and soft tissue sarcoma, breast cancer, brain tumour, leukaemia and adrenocortical carcinoma with onset during childhood or early adult life[5]. At least 70% of families with clinical features of LFS carry germ line Tp53 mutations[6]. The pattern of cancers and penetrance vary according to type of mutations.

Historically, childhood onset tumours associated with LFS conferred a poor prognosis. Most gene carriers therefore would not have survived to representative age. Recognition of individuals with Tp53 mutations could be important clinically because the presence of such a mutation may influence response to cytotoxic treatment. Furthermore, as with Rb1 mutation, the risk of developing second and subsequent malignancies is greatly increased in patients with Tp53 mutation[7,8].

Autosomal recessive syndromes of defective DNA repair :

Besides the dominantly inherited pre-cancerous conditions, a small group of autosomal recessive disorders is collectively characterized by chromosomal or DNA instability[4]. This is true for Fancon's anaemia (FA) and Bloom's syndrome both of which show lymphocytic defects in chromatid gaps, breaks and interchanges[1]. It is mostly acute leukaemias that are found in patients with Bloom's syndromes.

Ataxia telengiectasia (AT) is a chromosomal instability disorder whose phenotype also includes an increased susceptibility to cancer. It occurs with a frequency of one in 300,000. Approximately 10% of patients with AT develop malignancies specially leukaemias and lymphomas. Non-lymphoid tumours, mainly carcinoma, also represents about 13% to 22% of all malignancies in patients with AT.

Congenital malformation syndromes associated with childhood cancers :

The presence of cancer and a congenital anomaly in the same child may be explained in certain cases by an underlying genetic abnormality[9]. The study of these associations may lead to the identification of genes that are important in both processes. So, certain malformations and childhood cancers can arise therefore as a result of the same aberrant developmental process[1].

Wilm's tumour, Wagr syndrome, Deny-Drash syndrome and the WT1 gene :

Wilm's tumour is an embryonal tumour arising in the developing kidney, affecting approximtely one in 10,000 live birth. Children with Wilm's tumour experience an excess of various congenital anomalies including bilateral congenital aniridia. Children with anirdia often also display genito-urinary abnormalities and mental retardation. The association of Wilm's tumour with these abnormalities is known as Wagr syndrome[2]. As with retinoblastoma, familial cases occur in younger age group (mean age 30 months) and are more frequently bilateral. The Deny-Drash syndrome (DDS) is also consists of Wilm's tumour, severe genito-urinary malformation and glomerulo-nephropathy. Finally, Wilm's tumour can be found along with hemihypertrophy and malformation like Beckwith Weidemann syndrome (BWS).

A gene, designated WT1, which is important in kidney development was isolated from the short arm of chromosome[11]. Whereas deletions involving WT1 gives rise to Wagr syndrome, specific constitutional point

mutations within WT1 give rise to Denys-Drans syndrome (DDS)[2].

Congenital overgrowth syndromes and embryonal tumours :

Several overgrowth syndromes are associated with increased risk of embryonal tumours[2]. The best known is Beckwith Weidemann syndrome (BWS). The genetics of BWS have implicated a gene that maps to chromosome 11p15 and is paternally imprinted[10]. The principal characteistics of BWS are prenatal and postnatal gigantism, macroglossia, abdominal wall defects, visceromegaly, muscular hypertrophy, advanced bone age, craniofacial and ear abnormalities, and neonatal hypoglycaemia. The overgrowth may affect only part of the body (hemihypertrophy). More recently, other overgrowth syndromes which appear to predispose to embryonal tumours have been recognized including Simpson–Golabi–Behmel syndrome (SGBS) and Pelmen's syndrome[7]. SGBS shares many features with BWS but in children with SGBS, cleft lip and palate, cardiac and skeletal anomalies, and developmental delay are common features. SGBS is X-linked and the gene responsible which maps chromosome Xq26 is a glypican gene designated as GPC3. In Pelmen's syndrome, there is high association with neonatal mortality and mental retardation.

Interaction of genetic and environmental factors in childhood cancer aetiology :

Various ways exist in which individual susceptibility to carcinogenic effects of environmental agents may depend on genetically determined factors.

Transplacental carcinogenesis and genetic variation in susceptibility : Epidemiological studies have indicated an increased risk of certain childhood cancers in the offspring of individuals in occupations associated with exposure to potentially mutagenic chemicals during child's prenatal life. Additionally, some studies appear to show an association between maternal diet during pregnancy and risk of cancer in offspring[11]. Of particular interest is maternal diet and infant leukaemia. It is speculated that maternal exposure during a pregnancy to environmental agent that inhibit DNA topoisomerase II may be associated with development of leukaemia in infancy[11]. DNA topoisomerase II inhibitors have been found in specific fruits and vegetables and in soya, coffee, wine, tea, coca as well as in certain pesticides, solvent and medications. There is also implications that transplacental carcinogens may have a role in the aetiology of some childhood leukaemia[2].

Childhood leukaemia, infections and HLA genotype : Epidemiological evidence has suggested that some paediatric leukaemias may be initiated in utero and for some pairs of identical twins with concordant leukaemia. This possibility has been strongly endorsed by molecular studies of clonality[12]. There are many epidemiological evidence to suggest that childhood leukaemia arises as a rare outcome of a common infection. Infection has long been suspected as a possible factor in the aetiology of leukaemia and lymphoma[13]. Birch et al showed supporing evidence of an infectious aetiology for common acute lymphoblastic leukaemia (C-ALL) and Hodkin's diseases (HD). The association of HLA genotype and leukaemia is another much talked about topic now-a-days. Such an association would provide an example of genetically determined susceptibility to an environmental risk factor. Dearden et a had shown that HLA associated susceptibility may be determined independently by at least two loci, HLA DQB 105 and DQB 1050[14]. Also GSTM 1 mu and Cyp 1A1-2A genotypes were both found to be significant predictors of ALL risk[15].

Predictive testing for germline mutation and childhood cancers :

Important issues have arisen as a result of the identification of germline mutation of tumour suppressor genes in cancer prone individuals and families. These include ethical questions of predictive testing in such families

and in unaffected relatives, and selection of patients to be tested as well as the development of practical and accurate laboratory techniques, development of pilot testing programmes, and the role of clinical intervention based on test results[1]. The ethical principles of predictive testing for a germline mutation in tumour suppressor genes include respect for the autonomy for the patient and freedom from coercion to participate in screening programmes, benefit to the patients in addition to prevention of any perceived harmful effects, accessibility to the test for all and freedom from discrimination based on the test results and confidentiality results, and particular avoidance of inadvertent disclosure of test results to a third party.

Conclusion :

Genetic susceptibility is important in childhood cancer aetiology. At least 5% to 10% of childhood cancers are known to have their origin in high risk genes. About the predictive testing, despite many drawbacks, the potential to reduce marked loss of human potential resulting from the deaths of a child or young adult from cancer makes pilot research effort for early intervention in carriers of mutant germline tumour suppressor genes may be worthwhile. The understanding of genetic susceptibility to childhood cancer is important scientifically and clinically, and may eventually lead to intervention and preventive measures.

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CASE REPORTS

Metaplastic Spindle Cell Carcinoma of Breast with Monophasic Morphological Pattern : A Case Report

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Summary :

This report describes the histological and immunohistological features of metaplastic spindle cell carcinoma that developed in the breast of a 58 year old woman. Two firm and well-circumscribed lumps, the larger one measuring 3.5x3.1 x 1.8 cm. were located on the upper outer quadrant of the left breast. Histologically, the tumours were largely composed of sheets of malignant spindle shaped cells. No glandular or ductal differentiation could be identified. The immunohistochemical expression of epithelial markers like cytokeratin and EMA was recognized in the spindle cells. Moreover, the expression of vimentin and S-100 protein was also observed. These findings thus suggested an epithelial origin and myoepithelial participation in the genesis of the tumour.

The present tumour is interpreted as an unusual spindle cell variant of breast carcinoma showing monophasic morphological pattern. The histogenesis and metamorphosis of the tumour is reviewed from the literature in the context of its rare occurrence.

(J Bangladesh Coll Phys Surg 2000; 18 : 122-126)

Introduction :

Metaplastic breast carcinoma refers to a heterogeneous group of neoplasms in which the typical glandular growth pattern of the tumour undergoes metaplasia, either epithelial or stromal[1]. Sarcomatoid or metaplastic spindle cell carcinoma is one rare variety of this group. This tumour initially appear to be sarcoma and most frequently has a spindle cell pattern resembling fibrosarcoma[2]. Caution therefore must be exercised in the diagnosis of sarcomas of the breast in which the predominant component comprises spindle cells. In most of the cases, examination of multiple sections reveal transition from epithelial to mesenchymal elements. In the spindle cell lesions, the carcinomatous elements often show squamous metaplasia. Wide sampling of these tumours is essential because they must be distinguished from true sarcomas for reasons of difference in their biological behavior. In cases where multiple sampling fail to produce any conclusion about the nature of the tumour, immunohistochemistry helps a lot in the differential diagnosis. The pseudosarcomatous elements stain positively with vimentin and sometimes with other mesenchymal markers, but it is also nearly always possible to demonstrate epithelial markers in at least occasional cells. Reticulin stain may also be helpful in showing the characteristic "maze - like" pattern of carcinoma[3]. Ultrastructural examination may also identify the true epithelial nature of the

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Received : 30 January 2000 Accepted 15 May 2000

cells[4]. In addition to the features of adenocarcinoma, myoepithelial differentiation can be confirmed in the spindle cells. Oestrogen receptor expression and lymph node metastasis tend to be low in this tumour[5]. Despite multiple case reports[6,7] and a few series[8,9] little is known about the clinical behavior of these neoplasms. According to some authors[5], relatively favourable prognosis is expected in spindle cell carcinoma of the breast compared to common breast carcinoma.

Case report :

A 58 year old woman presented with a few months history of a lump in her left breast. On examination, a firm nontender nodular lump was felt in the upper outer quadrant of the breast. Mammographically, it appeared as a well-circumscribed mass. Ultrasonographically, it was a homogeneously hyperechoic nodule. Fine needle aspiration cytology was performed which revealed few scattered spindle cells and absence of recognizable tissue architectural pattern. A simple lumpectomy under general anesthesia was done and the specimen was sent for histopathological examination. The lesion was suggested to be an unclassified sarcoma. Few weeks later, the patient had undergone radical mastectomy operation. The resected breast revealed another nodule with similar histological features. Immunohistochemistry was performed and the diagnosis was revised as metaplastic spindle cell carcinoma.

Gross and light microscopic findings :

The excised lump consisted of a firm gray-white nodule with attached fatty tissue measuring 3.5 cm at greatest dimension. On sectioning, the cut surface was homogenous and whitish in color.

Serial sections were prepared from multiple blocks embedding the tumour tissues. The routine H and E stained sections revealed a malignant tumour dominated by interlacing bundles of spindle shaped cells containing plump oval nuclei with irregular chromatin pattern. These areas superficially resembled well differentiated fibrosarcoma or stromal sarcoma. On more careful examination, a great variation in the histological pattern was noted. Centrally the spindle cells were closely packed and often showed prominent nuclear atypia and plemorphism (Fig.-1). Peripherally, the tumour tended to be less cellular and was composed of spindle cells and interspersed bands of hyalinized collagen (Fig.-2). In these regions the cells appeared more uniform and bland. The number of mitotic figures ranged from less than one in the peripheral region to 10 per high power field in the densely cellular areas. An inflammatory cellular infiltrate was both present at the periphery and scattered among the cellular elements. Predominant

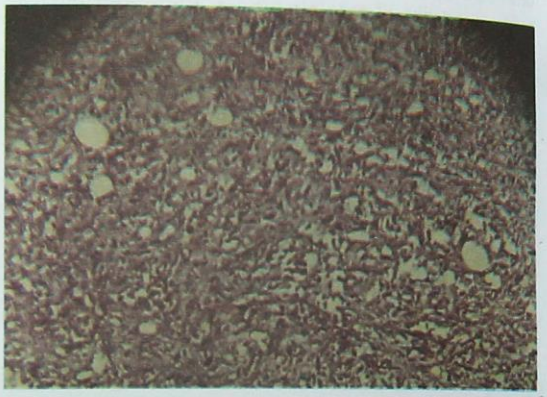

Fig.-1 : *Closely packed tumour cells with prominant nuclear atypia and pleomorphism.*

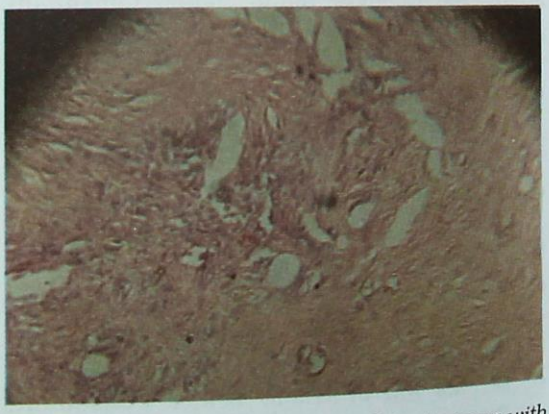

Fig.-2 : *Less cellular area of the tumour with bland appearing spindle cells separated by abundent collagen.*

cells were lymphocytes and plasma cells. No epithelial component could be seen in any of the fields examined. The tumour has invaded the fatty tissue and no breast parenchyma was seen. Considering the above microscopic findings, the neoplasm was suggested to be an unclassified sarcoma.

After radical mastectomy operation, the resected breast revealed another nodule (1.5 cm in maximum dimension) in its upper outer quadrant which was missed by the mammographic screening. The uninvolved breast was unremarkable. On microscopic examination, the second nodule presented the features similar to those seen in the previous one. Sections from the incision and the breast tissue beneath showed no residual tumour. The resected lymph nodes (six in number), adipose tissue and the interpectoral tissue was free of tumour.

Immunohistochemical findings :

The Immunohistochemical study was done at Tata Memorial Centre, Mumbai, India.

The findings were as follows :

Cytokeratin : Focally positive

EMA (Epithelial membrane antigen): Focally positive

Vimentin : Positive

S-100 protein : Positive

Estrogen receptor : Negative

Progesteron receptor : Negative

Co-expression of cytokeratin and vimentin was also reported within the sheets of spindle cells. On the basis of the above findings the diagnosis was in favour of a metaplastic spindle cell carcinoma. Ultrastructural study was not performed due to lack of facility.

Discussion :

Spindle cell carcinoma is an unusual neoplasm, which has been reported most frequently in the lip, oral mucosa and larynx[10,11]. Other sites such as oesophagus and skin are infrequently involved[1,12].

Although rare, spindle cell carcinoma do occur in the breast. A review of the literature indicated that spindle cell carcinomas of breast are very rare neoplasms presenting primarily in elderly patients. Their characteristic histological features have been described in scattered case reports, in which they have been identified as squamous cell carcinoma with a stroma often described as "pseudosarcomatous" or "fibrosarcoma like"[13,14]. Recently, these neoplasms have been included under the broad category of "metaplastic carcinoma"[9]. This term encompasses not only tumours with spindle and squamous differentiation but also a group of neoplasm of uncertain histogenesis that contain bone and cartilage.

In most of the cases of metaplastic spindle cell carcinoma, transitions between the epithelial cells and spindle cells have been identified[15,16,17]. The present tumour is interpreted as an unusual spindle cell variant of breast carcinoma showing monophasic morphological pattern. In this particular case, no epithelial element could be seen after meticulous search. As it is suggested by many authors[5,8,14,17] that a metaplastic breast carcinoma have better prognosis than the sarcomatous lesions, immunohistocemistry and/or electron microscopy are very much indicated for proper diagnosis of these unusual cases. In this particular case, immunohistochemistry revealed focally positive cytokeratin and epithelial membrane antigen (EMA) staining (which indicates epithelial origin) as well as diffusely positive vimentin and S-100 protein which suggested the diagnosis of metaplastic spindle cell carcinoma. Co-expression of epithelial and mesenchymal markers were observed within the spindle cells which was also reported by other authors[18,19]. Others who failed to find coexpression, reported vimentin reactivity in epithelial and spindle cells with cytokeratin expression only in the epithelial elements[9]. Focal EMA immunoreactivity as noticed in

this case was also observed in the spindle cells of 21 percent of 48 lesions studied[9]. The lesion showed nonreactivity to oestrogen and progesterone receptors which confirms the absence of any glandular activity. With few exceptions, metaplastic mammary carcinomas are found to be estrogen and progesteron receptor negative[19,20]. The real importance of the immunohistochemistry here is to recognize spindle cell carcinoma as an epithelial tumour rather than a sarcoma, since the prognosis and treatment will differ depending on the diagnosis. To the best of our knowledge, this case is a unique one of a monophasic form of metaplastic spindle cell carcinoma producing yet another variation in the theme of traditional metaplastic carcinomas of breast. It is therefore emphasized the need for immunohisto-chemistry in diagnosing any undifferentiated malignancy of breast.

Despite the sarcomatous features, spindle cells are likely to be derived from myoepithelial cells of mammary glands[5]. The possibility that the spindle growth pattern

might denote myoepithelial differentiation was first considered by Willis[21] and Jones[14] because of the light microscopic resemblance of the neoplasms to myoepithelial spindle cell tumours in the dog. Moreover, several authors, using electron microscopy, have suggested that myoepithelial cells play an important role in the formation of other benign and malignant tumours in the breast[22,23]. Pure malignant myoepithelioma shows morphological and clinical features similar to those of monophasic sarcomatoid carcinoma[24]. Most studies report cells with ultrastructural features intermediate between the epithelial and metaplastic elements. Myoepithelial cells are detectable to a variable extent occasionally constituting a significant part of the lesion[20] and they may be the cellular component that undergoes metaplastic change. Therefore it is possible that this particular case is linked histogenetically to malignant myoepithelioma. Here, however, no ultrastructural study was done to confirm myoepithelial differentiation in the spindle cells which could have supported this hypothesis.

This particular case had absence of lymph node metastasis. Absence of hormone receptor expression (oestrogen and progesterone) and absence of lymph node metastasis, as seen in this case, was also observed by Maemura and his colleagues[5]. They have suggested that relatively favorable prognosis is expected in spindle cell carcinoma of the breast compared to common breast carcinoma. The relationship between the type of metaplasia and prognosis is however uncertain because it has been difficult to assemble enough of these uncommon lesions to stratify them by stage[19,20]. Another study revealed direct correlation of tumour size to outcome as patients with tumours smaller than 4 cm had a relatively favourable prognosis[9,15].

This report highlights that metaplastic spindle cell carcinoma might present in a monophasic morphological pattern consisting entirely of spindle shaped cells. These lesions might mimic true sarcomatous lesions and thus require careful and accurate pathological study of adequate histological tissue. Diagnostic confirmation by immuno-histochemistry and / or ultrastruc-tural study are also recommended for these unusual cases which is of particular importance for therapeutic and prognostic purpose.

Acknowledgment :

We thank Dr. R.F. Chinoy MD, DCP, Pathologist, Tata Memorial Centre, Mumbai, India who had performed immunohis-tochemical stainings and interpretations.

We also thank Dr. A.S.M. Shawkat Ali, MBBS, Medical Executive of Square Pharmaceuticals Ltd. for providing necessary literature support.

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Journal of Bangladesh College of Physicians and Surgeons
Vol. 18, No. 3, September 2000

Accessory Liver – An Incidental Finding During Cholescystectomy Operation : A Case Report

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Summary :

A case of accessory liver, attached to the gallbladder is presented. The structure discovered incidentally. The patient was a 38 years old female who was operated for calculas cholecystitis. The accessory liver was found healthy, It may be pointed out that this rare abnormality usually has no clinical significance but it may harbor the same pathological process present in anatomically normal liver.

(J Bangladesh Coll Phys Surg 2000; 18 : 127-128)

Introduction :

The occurrence of accessory liver is extremely rare and usually it does not cause any symptoms[1]. Lacconi and Masoni reported two cases of accessory liver which was diagnosed incidentally at an elective cholecystectomy operation for calculas cholecystitis where the liver tissue was found healthy[2]. Castro-Viera et al described a case which was also diagnosed incidentally at cholecystectomy where the liver tissue showed signs of cholangitis and congestion secondary to gallbladder pathology[3]. In the literature, most of the cases are referred as an uncommon cause of abdominal pain.

Case report :

KB, a 38 years old woman was admitted in Shaheed Suhrawardy Hospital, Dhaka on sixth November 1998 with the complain of recurrent colicky upper abdominal pain for six months. On examination, everything was found normal except mild tenderness in right hypochondrium. On ultrasonography, there was multiple stones in the gallbladder with normal liver and common bile duct (CBD). The case was diagnosed as cholelithiasis and decision was made for open cholecystctomy. On laparotomy, it was found that there was a quadrangular piece of accessory liver tissue measuring 3" x 3" x 2" attached to the fundus of the gallbladder, which was completely detached from liver. There was multiple stones in the gallbladder. No stone could be palpated in CBD and it was not dilated. After cholecystectomy, gallbladder was opened up and it was found that there were multiple pitting in the area where accessory liver was attached resembling the opening of bile canaliculi.

Histopathology of the quadrangular piece of tissue revealed normal liver tissue and histopathology of gallbladder revealed chronic cholecystitis.

Discussion :

Betge reported a case of torsion of accessory liver in a 35 years old woman presenting with acute abdomen[4]. Another case of torsion of accessory liver in an infant was described by Sanguesa et al[5]. Accessory liver may be associated with other congenital abnormalities of hepatobiliary system. Ikoma

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Received : 19 June 2000 Accepted : 06 August 2000

et al described an accessory liver attached to a left sided gallbladder and it was recognized incidentally during an operation of intrahepatic cholangiocarcinoma[6]. An unusual case of primary liver cancer in an accessory liver was also reported by Basile et al[1]. Some authors suggested that accessory liver are more prone to develop hepatocarcinoma as it is functionally handicapped because it does not have a complete vascular and ductal system of normal liver[7]. In a patients who had alcoholic cirrhosis, the accessory liver was found to have the same histological changes as in the mother liver.

From above discussion it may be concluded that although the accessory liver is a rare congenital abnormality, it can be affected by any disease that can affect the normal anatomical liver. In addition, it can undergo torsion and may cause diagnostic dilemma.

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