Special Communication

PRIMARY LIVER CANCER IN PAKISTAN

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Abstract

Primary liver cancer was diagnosed in 8.6 per cent of all malignant tumours. Biochemical parameters for liver function in these patients were non-specific. Multiple needle liver biopsy seemed to yield more positive results. Alpha-foeto proteins was detected in 24.7 per cent of the patients with hepato-cellular Carcinoma. A Cirrhosis occurred only in 2.7 per cent of these patients. The results of treatment with chemotherapeutic agents was poor (JPMA 29:99, 1979).

Introduction

Fifteen years ago the general impression was that primary liver cancer is relatively rare in Pakistan. However, this view was changed when the material of the Department of Pathology, Jinnah Postgraduate Medical Centre between 1963-68 was reviewed and it was found that primary liver cancer was 3.4% of all malignant tumours seen.

Epidemiology

As a result of this survey a study was started in 1969. All cases of liver malignancies diagnosed clinically were studied for 5-1/2 years (1969-1975). During this period 301 cases were seen, of which 127 were primary liver cancer (Zuberi et al., 1976).

In 1973 the Pakistan Medical Research Council initiated a multicentre study on the frequency of tumours in seven major centres of the country. This study lasted for 18 months (Jan. 1974 to Sept. 1975). A total of 9224 Malignant tumours were recorded, out of which 4842 were males and 4382 were females. Children under 15 years of age formed 4.6%. In this study liver cancer was 2.2% of all malignant tumours seen. The frequency of liver varied from centre to centre; the highest being 4.0% in Liaquat Medical College Hyderabad, the lowest being 1.8 % in King Edward Medical College, Lahore. In Jinnah Postgraduate Medical Centre it was 3.6%. Comparably the frequency of liver cancer in Bombay (India) is 0.9%, in Iran 1.6% and in Afghanistan 3.0%. To get a proper perspective of the frequency of primary liver cancer in Karachi area the data of 3 different sources namely the department of Radiotherapy, Jinnah Postgraduate Medical Centre, where most of the cases are referred, the department of Pathology, Jinnah Postgraduate Medical Centre where the histopathology of the majority of cases of the city is being carried out and the Pakistan Medical Research Council's Research Centre which is actively engaged in liver disease studies has been compiled. Over a period of 10 years (1968-1977) a total of 315 primary liver cancer cases have been recorded. Out of this 184 are males (58.4%) and 131 females (41.6). The yearly distribution is given in Table I. Histological confirmation of the tumour is available in 192 cases (61% of the 315 cases). The remaining 123 were diagnosed either on liver scan or on clinical grounds.

The presenting clinical features in all these cases were abdominal pain of varying severity, weakness, weight loss and abdominal mass.

Diagnostic Method

Liver function tests were impaired to a variable degree in all patients studied. However, none of the biochemical parameters was found to be specific for liver carcinoma.

Liver scans were done with Tc 99m in majority of cases and were positive as most of the cases had tumours large enough to be detected by this technique. Liver scans were also used to guide percutaneous needle biopsy done with Menghinc's's needle. In the study of 301 cases (Zuberi et al., 1977) liver biopsy was positive in 68.4% cases. In the same study an attempt was made to improve the positive yield of needle biopsy by doing the biopsy

Table I: Yearly Sex Distribution

Year	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	*Total*
Male	15	39	12	16	11	23	29	12	12	15	184
Female	19	43	10	4	7	9	16	7	6	10	131
Total	34	82	22	20	18	32	45	19	18	25	315

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from two different areas; one at the scan positive area or the palpable tumour and the other in the 8th or 9th intercostal space or the subcostal region or in the epigastrium. This procedure was used in 56 cases of which 48 showed a tumour. Out of 48 positive cases in 28 both the specimens showed a tumour. In the remaining 20 cases only one of the two specimens showed a tumour (Table II). Thus the extent of tumour can be better evaluated by doing biopsy at two different areas.

Table II: Results of Two Simultaneous Biopsies

Total No. of cases	*No. of cases positive for Malignancy*	
	Both sites	*One site*
48	28	20

In the same study both liver biopsy and cytology was done in 94 cases. The cytology was done by preparing a smear of the aspirate along the biopsy specimen and staining it with Papanicolaou method (Table III). Of these 94 cases, 3 had positive cytology with negative biopsy. Review of the slides confirmed that one out of these 3 cases was primary liver cancer. It is felt that simultaneous use of biopsy and cytology improves the diagnostic yield.

In a study of Alphaloeta protein in patients with primary liver cancer and other liver diseases Zuberi et al. (1977) studied sera of 45 healthy subjects and 194 patients with liver cancer and other liver diseases. The method used was counter Immunoelectrophoresis. Alphafoeta protein was detected in 24.7% cases

Table III: Cytology (94 Cases)

S. No.	*Groups*	*No. of cases*
1	Cytology+ve, Biopsy+ve	37
2	Cytology+ve, Biopsy+ve	5
3	Cytology+ve, Biopsy—ve	3*
4	Cytology—ve, Biopsy—ve	19
5	Cytology preparation unsatisfactory	12
6	Cytology inconclusive	18
	Total:	94

* One case on review of slide-Primary Carcinoma liver.

with hepatocellular carcinoma in 8% with metastatic liver cancer and 4.1% in cases of cirrhosis of liver, whereas it was absent in all the 45 healthy subjects (Table IV). Using Haemagglutination method 63.6% of 21 hepatocellular carcinoma cases showed alphafoeta protein, mean value of alphafoeta protein was 57.0 ug/ml.

Diagnostic laparotomy and biopsy was done in some cases of doubt.

The HBs Antigenemia in general population of Pakistan is high. According to Zuberi

Table IV: Alpha-Fetoprotein in Healthy Subjects and Patients with Primary Liver Cancer and other Liver Disorders.

(Countercurrent electrophoresis)

Diagnosis	*No studied*	*A. F. P. Positive No. of cases %*
Primary liver cancer	81	20 (24.7)
Hepatic Metastasis	25	2 (8.0)
Cirrhosis of liver	24	1 (4.1)
Hepatitis	50	0
Other liver disorders	14	0
Healthy subjects	45	0

et al. (1974) it is 3.4% in blood donors and 2.8% of healthy subjects have positive antigen by counter Immunoelectrophoresis method. Among the villagers around Lahore 4% had a positive antigen (Aziz et al., 1971). In a recent study by Qureshi et al. (1978) it has been reported that out of a total of 1200 healthy adult males, 3.6% had positive HBs Antigenemia. In this study 800 fresh recruits for Armed Forces and 400 in-service personnel have been studied. The mean age of fresh recruits is 19.5 years and of the inservice personnel it is 21 years. They were from all regions of the country and as such can be taken as a good representative segment of the population of Pakistan.

Zuberi and her associates (1978) have tested the sera of 81 patients of hepatocellular carcinoma by counter-Immunoelectrophoresis method and found 9.9% of patients positive for antigen which of course is much lower than reported by other workers who have used the more sensitive Radio-immunoassay method.

Association of cirrhosis with carcinoma liver has been reported from different countries. Tuyns and Obradovic from Geneva (1975) found cirrhosis in 56.3% of their liver cell carcinoma cases while Epstein (1964) from Texas found this association in 41.6% cases. Similarly Anthony (1976) reporting from England found the two conditions together in 77% of cases. Whereas in a study of liver biopsy specimens by Memon (1978) only 2.7% of hepatocellular carcinoma cases were shown to be associated with cirrhosis. This impression is also supported by the earlier observations of Zuberi (1976) when two simultaneous biopsies were done in 56 cases. Out of which 48 were diagnosed as hepatocellular carcinoma and only in 3 cases (6%) cirrhosis was found. This fact is further supported by the review of 2422 liver biopsies by Memon (1978) from Depart-

Table V: Histological Diagnosis of Needle Biopsies According to Sex

Histological diagnosis	*Male*	*Female*	*Total (% of total primary liver cancer)*	*Percentage of total 2422 biopsies*
Hepatocellular carcinoma	125	42	167 (78.77)	6.9
Cholangio carcinoma	2	10	12 (5.62)	0.4
Combined hepatocellular and cholangio carcinoma	6	3	9 (4.24)	0.3
Hepatoblastoma	2	1	3 (1.41)	0.1
Lymphosarcoma	2	—	2 (0.94)	0.08
Leukaemia	8	7	15 (7.07)	0.6
Hodgkin's disease	—	1	1 (0.47)	0.04
Neurofibrosarcoma	1	—	1 (0.47)	0.04
Fibrosarcoma	1	—	1 (0.47)	0.04
Liposarcoma	1	—	1 (0.47)	0.04
Total:	148	64	212 (100%)	

ment of Pathology, Jinnah Postgraduate Medical Centre, where cirrhosis was seen in only 85 cases i.e., 2.24%.

Contamination of food by aflatoxin has been described as an etiological factor of primary liver cancer. In a preliminary study (Nizami and Zuberi, 1977) found that 43% of food samples examined in Karachi were contaminated with aflatoxin.

Pathology

In the review by Memon (1978) the pathological pattern of liver malignancy has been described. Table V gives the pattern in 212 cases found in 2422 biopsies. Out of 212 primary liver cancers hepatocellular carcinoma was seen in 167 (78.77%), Cholangio carcinoma in 12 cases (5.62%).

The management of these cases always poses a serious problem. Surgical management has not been possible due to the extent of the disease. The poor general condition and severe impairment of liver function prevented chemotherapeutic management. Cases found suitable for chemotherapy were treated with 5 Fluorouracil with poor results.

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