Med. J. Malaysia Vol. XXXI No. 4, June, 1977

Primary carcinoma of liver

by *N. Islam*
MB(Cal)., TDD(Wales)., FCPS(Pk)., FCCP(USA)., FRCP(Edin)., FRCP(Lond).,

M. Hasan
MBBS(Dac)., FCPS(Dac).,

Institute of Postgraduate Medicine & Research, Dacca, Bangladesh

and

S. M. Ali
MBBS(Dac)., M.Phil(Kar)., DCP(Lond)., D.Path(Eng)., MRC Path(Lond).,
Consultant Histopathologist,
Central Middlesex Hospital, London.

PRIMARY CARCINOMA OF LIVER has a world wide distribution. The incidence in Africa and certain parts of Asia varies from 13 to 53% of all malignancies (Berman, 59; Sung et al, 1967; Tull, 1932; Ying et al, 1963).

A variety of carcinogens have been incriminated to be responsible for variation of the incidence in different parts of the world (Alpert and Davidson 1969; Higginson 1963; Lin, 1970).

Recent observations indicate an etiological relationship between hepatitis B virus and hepatoma (Ruoslahti and Seppala, 1973).

Various etiological factors for primary carcinoma of liver namely cirrhosis, malnutrition, aflatoxins, hepatitis B virus are prevalent in Bangladesh.

As has already been pointed out there is a wide range of variation in the incidence of cirrhosis in primary carcinoma liver. This varies from 16 – 80%. Macronodular variety is the predominant type. An incidence of 13.1 – 24% has been reported in macronodular cirrhosis (Purtilo and Gottlieb, 1973; Reed et al, 1973.)

Cirrhosis is one of the commonest gastro-intestinal disorders in Bangladesh and macronodular is the commonest type we have encountered (Islam, Chowdhury and Ali, 1976). It is therefore estimable that Bangladesh is one of the areas in which primary carcinoma liver is likely to have a very high incidence. The purpose of this article is to analyse the clinical details of 30 cases proved to be primary carcinoma of liver.

Materials and Methods

Thirty cases of primary carcinoma liver diagnosed histologically have been included in this study.

Initial diagnosis in most of the cases were based on clinical grounds. Investigations included plain X-ray liver and chest, various liver function tests, routine laboratory investigations and demonstration of alpha-fetoprotein. Scanning was done in a limited number of cases, barium and endoscopic examinations were performed to exclude extra-hepatic primary malignancy.

Results

A total of 30 cases could finally be accepted as primary carcinoma liver.

Table 1 shows the age distribution of 30 cases reported here.

Table 1

Age distribution in 30 cases of primary carcinoma of liver

Age	Number of Patients	Percentage
12 – 20 years	1	3.33
21 – 30 years	1	3.33
31 – 40 years	5	16.66
41 – 50 years	10	33.33
51 – 60 years	6	20
Above 60 years	7	23.33

Maximum number of cases namely 10 out of 30 (33.33%) were in the age group 41 – 50 years. Below 30 years it was rare. Only one case could be found in the age group 12 – 20 and there were five cases in the age group 31 – 40 years. Above 50 the incidence was higher than below 30 years. Twenty six cases were male (86.66%) and only four cases (13.33%) were female.

Table II shows the distribution of symptoms in 30 cases.

Table II

Symptoms in 30 cases of primary carcinoma of liver

Symptom	Number of Patients	Percentage
Mass in abdomen	23	76.66
Pain in abdomen	16	53.33
Anorexia	17	56.66
Fever	13	43.33
Loss of weight	14	46.66
Jaundice	5	16.66
Oedema of legs	6	20
Swelling of abdomen	6	20
Melaena	2	6.66

Commonest symptoms with which the patients presented was a mass in the epigastrium or right hypochondrium. Twenty three out of 30 cases (76.66) presented with this complaint.

Upper abdominal pain and loss of appetite were the next frequent symptoms. Sixteen cases (53.33%) had upper abdominal pain and 17 (56.66%) complained of loss of appetite.

Loss of weight and fever were present in 14 (46.66%) and 13 (43.33%) cases respectively. Jaundice was relatively infrequent and five out of 30 cases (16.66%) had jaundice.

Physical signs of the cases are shown in Table III.

Enlarged liver with or without tenderness was present in all 30 cases (100%).

Next in frequency was anaemia. Twenty out of 30 cases (66.66%) had anaemia. In 11 cases (36.66%) spleen was palpable and a similar number had ascites.

Table III

Physical signs in 30 cases of primary carcinoma of liver

Sign	Number of Patients	Percentage
Anaemia	20	66.66
Jaundice	6	20
Finger clubbing	3	10
Oedema of legs	7	23.33
Enlarged lymph nodes	2	6.66
Palmar erythema	4	13.33
Spider angioma	2	6.66
Flapping tremor	1	3.33
Enlarged liver	30	100
Bruit over liver	7	23.33
Palpable spleen	11	36.66
Engorged abdominal veins	3	10
Ascites	11	36.66

A bruit over the liver could be heard in seven cases (23.33%) whereas palmar erythema was present in four (13.33%) cases.

Laboratory investigations and the findings are shown in Table IV.

Table IV

Investigation findings in 30 cases of primary carcinoma of liver

Investigation findings	Number of Patients	Percentage
Polymorphonuclear leucocytosis	13	43.33
Elevated S. alk. Phosphatase	19	63.33
Elevated S. transaminase	9	30
Elevated S. bilirubin	6	20

Polymorphonuclear leucocytosis was present in 13 cases (43.33%) and serum alkaline phosphatase was elevated in 19 (63.33%) cases.

Alpha-fetoprotein was done in 17 cases and 10 were positive. For some technical difficulties scanning could not be done in all cases. All the four cases which had scanning done, showed abnormalities consistent with space occupying lesion in the liver. Liver biopsy was done in 21 cases of which 18

(85.7%) showed evidence of hepatocellular carcinoma.

Discussion

Incidence of primary carcinoma of the liver varies from country to country. This is partly contributed by the etiological factors responsible which constitute a wide range from chemicals namely azo compounds to malnutrition. Conceivably the age range shows variations in the eastern countries from that in the west. In the Chinese and the Bantu the disease usually occurs below 40 years whereas in the present series the highest incidence was above 40. Ten out of 30 (33.33%) cases were in the age group 41 – 50.

Male to female ratio shows wide variations from 2:1 to 9:1 (Ruoslahti and Seppala, 1973). The cases were predominantly males in the present series.

Vast majority of our cases presented with swelling in the epigastrium and right hypochondrium and enlargement of the liver was present in all the cases.

Anorexia (56.66%) pyrexia (43.33%), pain in the abdomen (53.33%) and loss of weight (46.66%) were the next frequent complaints by the patients. Spleen could be palpated in one third of the cases, and a similar number had detectable ascites. Oedema legs was present in a quarter of the cases and a similar number had jaundice. A bruit over the liver may be heard in cases of primary carcinoma liver due to increased vascularity, tortuosity, variations in the calibre of hepatic artery and relative stenosis of their larger branches (Sherlock 1975). This author stresses that in the absence of alcololic hepatitis presence of murmur is diagnostic of hepatocellular carcinoma. In the present series a quarter of the cases had bruit over the liver and friction rub could not be detected in any of the cases. All cases where bruit could be detected were ultimately found to be primary carcinoma liver.

It has not been possible for us to follow up the cases and as such relative frequency of metastases in the distant organs could not be axcertained. In one case however we had the unique observation of secondary involvement of the skin which was histologically proved. This particular patient had also widespread metastases in the lungs. We are not aware of any report on primary carcinoma liver involving the skin.

Polymorphonuclear leukocytosis (43.33%), elevated serum alkaline phosphatase (63.33%), and serum transaminase (30%) were helpful laboratory evidences. Of these a raised serum alkaline phosphatase was found in the majority of the cases (63.33%). In primary hepatocellular carcinoma a raised serum alkaline phosphatase is due to increased production and obstruction.

Alpha-fetoprotein was positive in 10 out of 17 cases. Serum alpha-fetoprotein has been found to be positive in 40 – 90% cases of hepatocellular carcinoma. This is however not a specific test and may be positive in other conditions namely carcinoma of the testis, stomach, pancreas and lungs, acute viral hepatitis, Indian childhood cirrhosis, and a wide range of other liver diseases (Bloomer et al, 1973; Davidson, 1973; Nayak et al, 1972). Inspite of recent advances in the diagnosis of hepatocellular carcinoma including liver scan with gallium 67, liver biopsy remains the most definite method for the diagnosis.

Summary and Conclusion

Clinical featues of 30 cases of primary carcinoma liver have been analysed and compared with the findings of other authors.

An epigastric mass has been found to be the most common finding.

Secondary metastases in the skin in one case has been recorded. This has not so far been reported in the literature.

A bruit over the liver has been taken as clinical diagnostic evidence for hepatocellular carcinoma whereas friction rub has not been recorded in any case.

Liver biopsy has been found to be the only definite evidence for diagnosis. Limitations of other evidences have been pointed out.

Acknowledgement

Thanks are due to Dr. S.M. Ali, Consultant Histopathologist, Central Middlesex Hospital, London for his assistance.

Professors A.M.S. Huda, M. Kasimuddin and K.M. Rahman have been responsible for various laboratory investigations. We recommend our appreciation for them.

References

1. Alpert M.E. and Davidson, C.S.: Mycotoxins, Am. J. Med. 46: 325, 1969.
2. Berman, C.: Primary carcinoma of the liver. Bull. N.Y. Acad. Med., 35: 275, 1959.
3. Bloomer, J.R., Waldmann, T.A., Mclntire, K.R. et al: Serum alpha-fetoprotein levels in patients with non-neoplastic liver diseases. Gastroenterology 65: A6/530, 1973.

4. Davidson, C.S.: Working conference on liver cell carcinoma. Summary of proceedings, National Cancer Institute and Fogarty International Center, June 15, 1973.
5. Higginscn, J.: The geographic pathology of primary liver cancer res, 23: 1624, 1963.
6. Lin, T.Y.: Primary cancer of the liver: Quadrennial Review, Scand. J. Gastroenterol, 5 (Suppl., 6): 223, 1970.
7. Nayak, N.C., Malaviya, A.N., Chawla, V., et al: Alpha-fetoprotein in Indian childhood cirrhosis. Lancet, 1: 68, 1972.
8. Purtilo, D.T. and Gottlieb, L.S.: Cirrhosis and hepatoma occurring at Boston City Hospital (1917 – 1968). Cancer, 32: 458, 1973.
9. Reed, W.D., Eddleston, A.L.W.F., Stern, R.B., et al: Detection of hepatitis B antigen by radioimmunoassay in chronic liver disease and hepatocellular carcinoma in Great Britain. Lancet, 2: 690, 1973.
10. Ruoslahti, E. and Seppala, M.: Alpha-fetoprotein in antenatal diagnosis, Lancet, 1: 155, 1973.
11. Seppala, M. and Ruoslahti, E.: A-fetoprotein in normal and pregnancy sera. Lancet, 1: 375, 1972.
12. Sung, J.L., Wang, T.H., and Yu, J.Y.: Clinical study on primary carcinoma of the liver in Taiwan. Am. J. Dig. Dis. 12: 1036, 1967.
13. Tull, J.C.: Primary carcinoma of the liver: A study of one hundred and thirty-four cases. J. Path. Bact., 35: 557, 1932.
14. Ying, Y.Y., Ma, C.C., Hsu, Y.T., et al: Primary carcinoma of the liver. Chinese Med. J., 82: 279, 1963.