

PRIMARY LIVER CANCER IN MALAYSIAN CHILDREN

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INTRODUCTION

THERE is a high incidence of primary hepatic cancer in the adult population in many parts of Africa and Asia. It is the most common malignancy among Malay males, the second most common cancer in Indian males and the third most common cancer among Chinese males in Singapore (Shanmugaratnam, 1973). Despite the high incidence of liver cancer in the adult population in these regions, there is a paucity of reported cases in children (Edmondson and Steiner, 1954). The International Union Against Cancer (U.I.C.C.) has drawn attention to the need for more epidemiological information from different countries regarding these tumours. In addition, the outlook for children with primary hepatic cancer seems to be improving with the introduction of multimodal therapy (Sinniah, *et al.*, 1973).

MATERIALS AND METHODS

For these reasons, a review was undertaken of 5 cases of liver cancer admitted to the Paediatric unit of the University Hospital, Kuala Lumpur from July 1967 to June 1979. The clinical records and autopsy reports were reviewed together with the histological sections of specimens obtained by biopsy and/or at post-mortem.

REPORT OF CASES

CASE 1:

L.Y.W., a 4 year old Chinese boy was admitted in 1969 with abdominal distension, oedema and jaundice. On examination, he was

pale and had enlarged supra-clavicular lymph nodes. The abdomen was distended; the liver was enlarged 5 cm and the spleen 4 cm. Investigations revealed haemoglobin 6.5 g/dl and ESR 40 mm/Hr. The serum albumin was 26, globulin 21 and total proteins 47 g/l respectively. Serum bilirubin was 20.5 μ mol/l, SGOT 31 iu/l, SGPT 80 iu/l and alkaline phosphatase 646 iu/l. A liver biopsy revealed congestion but no evidence of tumour. An intravenous pyelogram (IVP) showed extrinsic compression of the right ureter.

The patient died within three weeks and post-mortem, revealed a cholangiocarcinoma with intrahepatic metastases producing an umbilicated multi-nodular liver and extra-hepatic metastases involving the para-aortic and supra-clavicular lymph nodes.

CASE 2:

M.K., a 10 year old Malay boy was admitted in 1971 with epigastric pain for three days and guarding and rigidity in the right hypochondrium and epigastrium. Investigations revealed haemoglobin 9.8 g/dl, prothrombin time 24% and normal liver function tests. Liver scan disclosed a rounded cold zone in the inferior margin of the right lobe near the gall bladder. At operation a large tumour with multi-locular cystic degeneration was completely excised from the inferior margin of the right lobe of the liver. This was followed by a right hepatectomy one month later. Histology revealed a hepatoblastoma.

The patient later developed abdominal distension, hepatomegaly and anasarca and died 2 years later. Post mortem was not done.

CASE 3:

M.A., a 14 month old Malay girl was admitted in 1975 with constipation and anorexia. Palpation of the abdomen revealed a mobile mass measuring 12 x 10 cm in the right hypochondrium. Investigations revealed haemoglobin 6.3 g/dl, and ESR 5 mm/hr. The liver function tests were

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normal but serum fetoprotein was positive. Liver scan showed a normal liver and a cold mass situated outside the liver in the right hypochondrium.

At laparotomy, a 9 x 7 x 5 cm, well encapsulated hepatoblastoma with multi-nodular surface was found arising from the inferior edge of the right lobe of the liver and a right partial hepatectomy with complete excision of the tumour was performed. The patient was given several courses of vincristine and mitomycin - C and when last seen was alive and well 3 years later.

CASE 4:

C.M.C., a 2 month old Chinese female was admitted in 1976 with abdominal distension and fever for two weeks. On examination, the patient was anaemic and had generalised edema, and petechiae over the trunk and limbs. The abdomen was distended with ascites, a liver enlarged 8 cm and a hard 6 cm spleen. Investigations revealed haemoglobin 11 g/dl and blood urea 10.3 mmol/l. The patient died the day after admission and post-mortem revealed a hepatoblastoma completely infiltrating the liver and involving the pancreas.

CASE 5:

N.S.M., a 10 year old Chinese boy presented in 1979 with epigastric pain, anorexia and weight loss. On examination he was pale, the liver was enlarged 7 cm, hard and nodular and the spleen 5 cm. Investigations revealed haemoglobin 11.2 g/dl and ESR 5 mm/hr. Liver function tests were normal except for an alkaline phosphatase of 240 U/l (normal 82-192 I.U./l). Hepatitis B antigen was detected in the serum. Liver scan showed an enlarged liver with multiple cold areas in the right lobe and an almost completely cold left lobe. Liver biopsy disclosed a hepatocellular carcinoma.

The patient was started on chemotherapy but defaulted follow up.

DISCUSSION

With the progressive decline of infectious and nutritional disease, childhood cancer is fast becoming an important paediatric problem in many developing countries (Williams, 1975).

Geographical variations in the frequency of different types of neoplasms may be of importance in identifying possible oncogenic environmental agents. It is more feasible to test this aetiological hypothesis in childhood population groups who have had less exposure to oncogenic agents than adults.

We have studied the incidence of primary liver cancer in Malaysian children and found it to be comparable with that reported from several developed countries (see Table 1 and II). This does not correspond with the high prevalence observed in the adult population in this part of the world (Sumithran and MacSween, 1979). The commonest hepatic cancer in adult males is hepatocellular carcinoma which is relatively uncommon in childhood. Hepatoblastomas which constitute the commonest primary liver cancer in children, usually occur at a very young age and are probably of embryonal or congenital origin, while the hepatocellular carcinomas and cholangiomas are found in the older age groups. The relative frequency of hepatoblastoma and hepatocellular carcinoma in our series is similar to that reported in other countries (Ishak and Glunz, 1967; Kasai and Watanabe, 1970; Sinniah *et al.*, 1974) and helps support the embryonal or congenital aetiological theory.

The association between hepatocellular carcinoma, cirrhosis and hepatitis B antigen is now well established (Bagshawe, 1971; Sherlock, 1970). The hepatitis B antigen was positive in the serum of the one case of hepatocellular carcinoma studied by us.

The prognosis is generally worse for hepatocellular carcinoma and the only survivor in our series had a hepatoblastoma situated outside the liver and attached to it by a pedicle. This type of presentation has been seen previously by one of us and is associated with an excellent prognosis (Sinniah *et al.*, 1974).

The cholangiocarcinomas are rare tumours (Jones *et al.*, 1960) and little is known about its aetiology.

SUMMARY

The high incidence of primary liver cancer in Malaysian males is not observed in childhood,

Table 1 Frequency of primary hepatic cancer in relation to hospital admissions

Author[s]	Hospital	Period covered [Years]	No. of Admissions	No. of hepatic cancers	Frequency per 1000 admissions
Andersen	Babies Hosp. N.Y.	16	80,000	5	0.06
Neimann <i>et al</i>	Ped. Clin. Univ of Nancy	10	30,000	5	0.16
Hunerwadel	Basel Children's Hosp.	30	70,000	4	0.05
Silva Sosa & Silva Cuevas	Children's Hosp.	19	147,000	24	0.16
Sinniah <i>et al</i>	RCH Melbourne	22	252,306	20	0.08
Present study	UH, KL	12	30,963	5	0.16

RCH = Royal Children's Hospital; UH, KL = University Hospital, Kuala Lumpur.

Table II Frequency of primary hepatic cancer in relation to other malignant neoplasms [excluding leukaemia]

Author[s]	Hospital	Period covered [Years]	No. of Neoplasms	No. of hepatic cancers	Percent
Andersen	Babies Hosp. N.Y.	16	175	5	2.8
Claireaux and Williams	Hosp. for Sick children, London	15	1027	23	2.2
Neimann <i>et al</i>	Ped. Clin. Univ. of Nancy	10	86	5	5.8
Muir	Singapore Gen. Hosp.	11	75	2	2.7
Sinniah <i>et al</i>	RCH Melbourne	22	1062	20	2.0
Present study	UH, KL	12	154	5	3.2

where it constitutes 0.16 per 1000 paediatric hospital admissions and 3.2% of all childhood malignancies at the University Hospital, Kuala Lumpur. This frequency is comparable to that reported from several developed countries. The commonest liver tumour in children is the hepatoblastoma which is probably of embryonal origin and has a similar world wide incidence. The relative infrequency of hepatocellular carcinoma in childhood and its association with cirrhosis, the hepatitis B antigen and its prevalence in the older age group helps to substantiate an acquired environmental aetiology.

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