most sure method of controlling haemorrhage from a ruptured hepatocellular carcinoma is to ligate the hepatic artery.

PROGNOSIS

The prognosis of primary hepatoma is extremely bad. Ong and Leong (1969) reported only 22 resections of liver in 76 cases of hepatocellular carcinoma. Balasegaram (1968) reported 10 cases of ruptured hepatocellular carcinoma, and of those that underwent resection none survived more than six months.

The prognosis of the disease may rest on whether the liver is cirrhotic or not. If the liver is markedly cirrhotic then survival, either immediately after resection or on a long-term basis, is poor. It is possible that because of the cirrhotic liver the tumour may be multicentric in origin, and despite adequate resection it may recur in the hepatic remnant.

So far as the control of haemorrhage is concerned, the longest period of survival in the present series was 148 days. This was contrary to what Berman (1951) had written, and in his small series of six cases none survived more than 40 days.

The outcome of hepatocellular carcinoma is usually fatal. From the time of diagnosis to death the period of life is on average six months. Of the 20 cases originally reported by Ong et al. in 1965, one was alive and well at the time of writing after having had a left hemihepatectomy done in 1962. Of the present series of 42 cases one was well after 54 years. There is no evidence of recurrence of the disease or metastases.

These cases show that long-term survival, even with rupture, does occur. Provided resection can be done on average of eight months to a year of a good life is possible.

References


PRELIMINARY COMMUNICATIONS

Primary Hepatoma and Hepatitis-associated Antigen in a Young White Woman

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Summary

A young woman whose serum was positive for hepatitis-associated antigen (H.A.A.) and alpha-fetoprotein developed a malignant hepatoma. Though the light-microscopical appearances of the surrounding liver tissue were normal, electronmicroscope examination of the tumour tissue disclosed both C-virus-like particles and H.A.A. particles. Possibly there was a causal connexion between one of these particles and the hepatoma.

Introduction

An association between hepatitis-associated antigen (H.A.A.) and chronic liver disease has been documented (Fox et al., 1969; Wright et al., 1969). It has also been suggested that hepatocellular carcinoma might occur in patients be the end stage of a process beginning with viral hepatitis (Smith and Blumberg, 1969; Sherlock et al., 1970). At present the evidence suggests that H.A.A. may be related to the appearance of primary liver cell carcinoma in Africans (Vogel et al., 1970; Bagshawe et al., 1971), but not related to this in Chinese (Smith and Blumberg, 1969; Simons et al., 1971), or in the cases that occur in Caucasians (Alpert and Isselbacher, 1971).

We report a case of primary hepatoma occurring in a 22-year-old white woman, whose serum was positive for H.A.A. and alpha-fetoprotein. The appearances of liver surrounding the tumour were normal on light microscopy, but electronmicroscopy of the tumour and serum showed particles characteristic of H.A.A. Electronmicroscopy of apparently normal liver around the tumour showed occasional similar particles.

Case Report

A 22-year-old white woman presented in Hobart for routine antenatal care in November 1970, when 36 weeks pregnant. She had been born and lived in Adelaide until 18 and had never lived or travelled outside Australia. No physical abnormality was detected, and she was delivered of a normal infant in December 1970. Three days after delivery she complained of mild right upper quadrant pain, and the liver edge was palpable. Liver function tests showed nothing abnormal except for a raised serum alkaline phosphatase (26 K.A. units). Her symptoms subsided, and she was not seen again until February 1971, when she complained that she had been aware of a lump in the right upper abdomen since the baby was born. At this time the right lobe of the liver was easily palpable, firm, and not tender 6 cm below the right costal margin. A cholecystogram showed normal function of the gallbladder, but it was displaced. A liver scan with the use of 99mTc (Fig. 1) showed a spherical region of diminished uptake in the right lobe about 10 cm in diameter.
A coeliac axis arteriogram showed an abnormal hypervascular pattern corresponding to the scan defect. Routine liver function tests showed nothing abnormal apart from a serum alkaline phosphatase of 18 K.A. units, and bromsulphthalein retention at 45 minutes was 4%. Her haemoglobin, white-cell count, platelet count, and E.S.R. were all normal. Serum was positive for H.A.A. by immunoelectrophoresis and agar gel diffusion, and was also positive for alpha-fetoprotein. A strong presumptive diagnosis of primary liver cell carcinoma was made.

There was no history to suggest a past episode of hepatitis, but four years previously she had received prophylactic gamma-globulin because of contact with probable infectious hepatitis. Her family history was negative for acute or chronic liver disease and malignant disease. Between March 1968 and January 1970 she had donated three units of blood: no cases of jaundice associated with transfusion of her blood were recorded.

The patient returned to Adelaide, and at subsequent laparotomy a vascular tumour of 10 cm diameter was found occupying the anterior segment of the right lobe of the liver. This segment of the liver, including the whole tumour, was excised. Her convalescence was completely uneventful. She remained well 15 months after operation. Her serum was negative for alpha-fetoprotein but remained positive for H.A.A. A liver scan showed an apparently normal liver.

Light microscopy showed that the tumour was a malignant primary liver cell carcinoma, and the histological appearance of the surrounding liver tissue was normal. On electronmicroscopy two types of abnormal particles were seen in the tumour cells. Firstly, the cytoplasm of almost every cell examined contained virus-like particles about 90 nm in diameter and either free
oncogenic appeared to be budding (Fig. 3). They resembled the C-type oncogenic virus described by Bernhard (1960). Secondly, but far less frequently, the nuclei and cytoplasm contained particles about 23 nm in diameter with electronlucent centres (Figs. 4 and 5). These were identical in appearance to the particles which were noted by Huang (1971) and ourselves (Fig. 6) in the liver of patients with H.A.A.-positive hepatitis. Direct staining of frozen sections of the tumour with fluorescein-conjugated human anti-H.A.A. globulin produced fluorescence in a small number of tumour cells.

Both the C-type particles and H.A.A. particles were present in the serum (Fig. 7). Electronmicroscopy of samples of apparently normal liver taken from both right and left lobes showed only very occasional 23-nm particles, and staining with fluorescein-conjugated anti-H.A.A. serum produced no fluorescence.

Comment

Hepatoma is a rare disease in Caucasians. In Australia it is most commonly associated with cirrhosis in chronic alcoholics, although in other Caucasian populations the incidence of hepatoma is higher in cirrhosis of the macronodular or post-necrotic type (MacDonald, 1957; Kew et al., 1971). In East Africans (Maynard et al., 1970; Bagahawe et al., 1971) and West Africans (Morrow et al., 1971) viral hepatitis is common, and is strongly associated with H.A.A. In these populations post-necrotic cirrhosis and of primary hepatoma are also much commoner than in Caucasians. Of 45 patients reported by Vogel et al. (1970), histological specimens of liver remote from the tumour were available for only 25. Of these 25 there was no cirrhosis in six, and in only one of these was H.A.A. found in the serum. Five of the six were positive for alpha-fetoprotein. Of these five, two were young men one of whom had a positive history for acute viral hepatitis, while the serum of the other was positive for H.A.A. The authors suggested that the hepatitis virus may initiate changes leading directly to neoplasia without intermediary chronic parenchymal liver disease.

The question arises whether either of the virus-like particles in the tumour of our patient were related to its development. The larger ones were the more numerous and resembled the free cytoplasmic structures noted by Ma and Blackburn (1966) in a primary hepatoma. They were morphologically similar to the C-type particles of Bernhard (1960). These are a group of oncogenic RNA-containing viruses which include the avian leukaemia virus and the human mammary tumour virus (Sarkar and Moore, 1972).

Spherical particles of about 23 nm in diameter have been found in the liver in H.A.A.-positive patients (Huang 1971), and possibly H.A.A. is in some way related to the appearance of a primary hepatoma in our patient. In Australia the likelihood of a chance association of hepatoma and H.A.A. positivity is remote for the latter is found in only 0.12% of the population (Nelson and Cooke, 1971) and the former is excessively rare (less than 0.001% of hospital admissions in South Australia). If a chance association is dismissed three possibilities remain and apply equally to H.A.A. and to the C-type particle. The first is that an immunologic defect has allowed both persistence of these agents and growth of a hepatoma; secondly, the cells of a primary liver cancer may protect viruses against the normal immunologic defences; thirdly, the presence of either H.A.A. or the C-type particle in the liver cells initiated the neoplastic transformation. Obviously other unknown factors are important in the genesis of primary hepatomas, and indeed H.A.A. may have little part to play in causing hepatomas in Chinese (Simons et al., 1971) or in most cases that occur in Caucasians. In the present patient a causal association of H.A.A. or the C-type particle and hepatoma remains not proved but possible. It is of some interest that the the time of writing both were still present in the patient’s serum.

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MEDICAL MEMORANDA

Miliary Crohn’s Disease

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The macroscopic features of Crohn’s disease are well known. The affected bowel is thickened, soggy, and oedematous, the serosa is a blotchy red, and the mesentery contains numerous hyperplastic nodes (Crohn et al., 1932).

The term “miliary Crohn’s disease” was used by Heaton et al. (1967) in three cases of Crohn’s disease in which at laparotomy the diagnosis appeared to be tuberculous peritonitis or enteritis. The recognition of this unusual appearance is of great practical importance if correct treatment is to be given. A similar case is described below.

Case Report

A 20-year-old chef presented in March 1970 complaining of tiredness and of feeling generally unwell. He thought he had lost weight. Examination showed no abnormality, and the haemoglobin, white count, E.S.R., constituents of the urine, and the chest X-ray picture were normal.

Five months later he developed colicky upper abdominal pain associated with acid regurgitation and borborygmi. Questioning elicited that he had occasional loose stools and a sensation of abdominal fullness. Examination showed the loss of 3 kg in weight since his previous examination but was otherwise unremarkable. Barium-meal examination showed dilatation of the second part of the duodenum; barium-enema appearances were normal.

He continued to lose weight, and more extensive investigations showed: haemoglobin 13-6 g/100 ml; W.B.C. 7,100/mm3; E.S.R. (Westergren) 3 mm in one hour; serum urea 22 mg/100 ml, Na+ 137 mEq/l, K+ 3-7 mEq/l, Cl− 100 mEq/l, HCO3− 29 mEq/l; protein-bound iodine 5-4 μg/100 ml; serum albumin 3-1 g/100 ml; serum iron 25 μg/100 ml; total iron-binding capacity 187 μg/100 ml; xylose excretion 2-1 g/5 hr (5 g dose); faecal fat 6 g/24 hr; serum folate 2 ng/ml; serum vitamin B12 775 pg/ml; pentagastrin test, normal acid output; Synacthen test, normal result; faecal occult blood, intermittently positive.

A further barium-meal examination showed generalized distention of the duodenum and jejunum with multiple “thumb-print” filling defects along the mucosal surface. The appearances were thought to suggest tuberculous enteritis or a resection. Laparotomy showed numerous enlarged yellow fleshy nodes throughout the mesentery. The entire small bowel was thickened and covered with distended lacteals and milary tubercles, the latter lying principally in the line of the lacteals. Along the whole length of the mesenteric border of the bowel thickened areas were palpable. The large bowel was also covered in a pannus of vessels. The appearance of operation was thought to suggest tuberculous peritonitis, and a mesenteric node and a specimen of jejunal tissue were taken for biopsy.

Microscopical examination of the lymph node showed tuberculous granulomata without caseation. The jejunal mucosa showed multiple superficial stellate ulcers with scalloped edges. The serosa was finely granular. Sections of the jejunal specimen showed lymphoid hyperplasia in the base of the ulcers, with scattered non-caseating tubercles throughout the jejunal wall. No acid-alcohol-fast bacilli were seen after prolonged examination, and subsequent culture and animal inoculation proved negative. Postoperative Mantoux testing and bone marrow smears showed no abnormality. The patient was treated with corticosteroids, and his symptoms settled. During the next 12 weeks he gained 4 kg in weight. Barium-meal examination at this time showed normal proximal jejum, but the lower small bowel appearances were distorted by adhesions.

Comment

The distinction between Crohn’s disease and tuberculous enteritis is of obvious practical importance but can be very difficult to achieve. Early descriptions of Crohn’s disease (Crohn et al., 1932; Blackburn et al., 1939) included the presence of minute pale nodules on the serosal surface resembling those seen in tuberculous disease. Later reports (Van Patter et al., 1954; Pollock, 1958) made only brief reference to serosal tubercles, and the presence of these tubercles are not mentioned in standard textbooks of surgery or medicine.

Tuberculous disease of the bowel is becoming uncommon in this country; however, the most granulomatous lesions of the ileocaecal area are now known to be due to Crohn’s disease (Lee and Roy, 1964), but diagnostic mistakes still occur in both directions. Dyer and Dawson (1970) found tuberculosis diagnosed in error in 7% of their cases of Crohn’s disease, and Brenner et al. (1970) described a case of ileocaecal tuberculosis diagnosed initially as Crohn’s disease. Heaton et al. (1967) reviewed the differential features between Crohn’s disease and tuberculous disease at operation. It is worth noting that in miliary Crohn’s disease the tubercles coalesce along the distended lacteals and this was a prominent feature in the present case. Heaton et al. also speculated whether miliary Crohn’s disease represents an early stage of Crohn’s disease. Prompt treatment in the present case resulted in some improvement in the proximal jejunum, but the follow-up period was so short that worthwhile comment is not possible.

References


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