MEDICAL MEMORANDA

Disappearance of Hepatic Cancer after Intra-arterial Fluorouracil

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The presence of cancer in the liver in nearly three-quarters of all patients who die from malignant neoplasms raises in itself considerable diagnostic and therapeutic problems. Systemic and regional chemotherapy have been used for both primary and secondary cancers of the liver (Sullivan and Zurek, 1965; Sullivan *et al.*, 1967). Survival has not been obviously increased but relief of pain has often been noted (Chan, 1967; Anderson, 1968; Provan *et al.*, 1968).

The precise nature of a hepatic growth in a patient under our care, whose clinical course will be described in more detail elsewhere, was not determined but the absence of alternative treatment and the foregoing reports encouraged us in the use of regional chemotherapy.

Case Report

A 49-year-old man who had reported a short-lived episode of jaundice with pale stools and dark urine six months previously was found to have hepatomegaly to four finger-breadths below the costal margin in January 1967. The haemoglobin was 15.6 g/100 ml, the platelet count was 191,000/mm³, and liver function tests showed: albumin 39 g/l, globulin 30 g/l, alkaline phosphatase 27 K.A. units/l, aspartate aminotransferase 50 units/l, alanine aminotransferase 32 units/l, and bilirubin 0.9 mg/100 ml. Cholecystography and barium studies of the upper alimentary tract showed no abnormalities. Two large masses were found in the liver at laparotomy on 21 January. No primary tumour of intra-abdominal organs was detected. Frozen-section histological study showed undifferentiated malignant tumour, probably of epithelial origin. A catheter was placed in the hepatic artery and infusion of fluorouracil 250 mg/day was started immediately after completion of the laparotomy. The infusion was continued for six weeks by means of a portable clockwork pump. The catheter was then withdrawn because of displacement from the artery.

Detailed examination of the paraffin sections of the biopsy specimen of liver showed clear evidence of malignant invasion of the liver by anaplastic tumour (Fig. 1). There were masses of small cells with round hyperchromatic nuclei and vacuolated cytoplasm. Mitotic figures were numerous but no definite opinion on the histogenesis of the tumour was possible; reticulosis and seminoma were considered in addition to anaplastic cancer of the liver.

Repeated thorough clinical examinations and radiography did not reveal a primary growth.

Over the next three years the liver became impalpable, and this could be correlated with an improving uptake of 198 Au on repeated radioisotopic scanning of the liver. In March 1970, however, the patient complained of tiredness and vague upper abdominal discomfort. The spleen had become palpable and the platelet count had fallen from normal levels to 50,000/mm³. A barium swallow showed large gastro-oesophageal varices, and a splenic venogram showed dilation and medial displacement of the portal vein. The minimum intrasplenic pressure recorded was 39 cm of saline. Ascites developed, requiring paracentesis. No malignant cells were seen in the ascitic fluid. The only abnormalities of the serum biochemistry and liver function were low levels of albumin at 34 g/l. and of α_2 -globulin at 5.7 g/l. Frusemide 160 mg/day had no effect but the addition of spironolactone 25 mg four times a day gave a large diuresis and continued control of ascites. A new mass was palpable in the left upper quadrant of the abdomen and a second laparotomy on 12 December showed enlargement of the left lobe of the liver with an apparently normal outward appearance. A biopsy specimen showed normal hepatic architecture. There was no evidence of recurrent cancer.

FIG. 1—Biopsy specimen of liver. Hepatic tissue on left is invaded by anaplastic tumour (Haematoxylin and eosin. $\times 135$.)

The patient thereafter returned to work on maintenance doses of frusemide and spironolactone but anaemia recurred despite blood transfusions and iron. On 11 July 1971 he had a large haematemesis and melaena. Haematemesis recurred and portal decompression of the Valdoni type was performed on 19 July. There was a deep scar in the middle of the right lobe of the liver but no evidence of cancer was seen. Unfortunately recurring haematemesis during the postoperative 48 hours required the use of a Sengstaken tube, but thereafter the patient recovered slowly until 21 days after operation, when another massive haematemesis occurred, the urine output fell, and resuscitative treatment was unavailing. He died on 31 July, 12 hours after the final haematemesis.

At necropsy the vascular anastomosis was satisfactory. A deep scar involved the central part of the right lobe of the liver occluding the right hepatic duct. The tributary ducts were grossly dilated and the scar merged with nodules of liver at the periphery of the right lobe with the appearance of very fine cirrhosis. The left hepatic duct was patent and there was no cirrhosis in the left

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lobe of the liver. The portal vein appeared to have become obliterated by surrounding fibrosis. The hepatic artery was patent. Gastro-oesophageal varices were prominent and an ulcerated varix in the cardia appeared to be the source of recent haemorrhage. Detailed examination showed no evidence of cancer in any organ or tissue throughout the body. There was no enlargement of lymph nodes and the arterial system was remarkably free of atheroma.

FIG. 2—Porta hepatis region of liver at necropsy. There is dense fibrosis but no hepatic parenchyma. Grossly dilated bile ducts with dark biliary debris are prominent. Dilatation of venous and lymphatic channels is also apparent (Haematoxylin and eosin. $\times 55$.)

Microscopical examination of tissue from the region of the porta hepatis showed extensive scarring and complete absence of hepatic parenchyma. Many bile ducts were grossly distended with granular inspissated bile (Fig. 2). Dilated veins and lymphatics were also prominent but the hepatic arterial branches appeared normal. There was no cirrhosis in the left lobe of the liver but some portal fibrosis and dilatation of bile ducts was present.

Sections from numerous blocks of tissue taken from all parts of the liver showed no evidence of new growth. Similar multiple microscopical examination was made of all organs of the body, with particular attention to the thyroid, lungs, and genitourinary tract, and no cancer was seen. The spleen was the seat of congestive splenomegaly only and there was no reticulosis.

Comment

The true histogenesis of this tumour is obscure. The histological findings did not suggest a primary hepatocarcinoma or a cholangiocarcinoma, and it could be presumed that the hepatic tumour was a secondary growth from a primary which had regressed or remained undetected. The disappearance of the cancer is not in keeping with this viewpoint, since only one or two patients in the literature have been reported to survive up to three years among many series of treated hepatic metastases, and no complete therapeutic regressions are on record. Everson and Cole (1966), however, recorded seven cases of spontaneous regression of cancer in the liver.

The clinical and necropsy findings in the case reported here indicate that destruction of the hepatic tumour by chemotherapy had been followed by gross scarring which had obstructed biliary drainage, especially from the right lobe of the liver, and the portal venous drainage, leading to the formation of gastro-oesophageal varices and fatal haemorrhage therefrom.

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