Alpha fetoprotein in metastatic gastric carcinoma

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SUMMARY Two patients with primary gastric carcinoma and multiple liver secondaries who developed alpha fetoprotein in the serum are reported. Both had clinical features which were initially suggestive of primary liver cell carcinoma. Fetoprotein levels fell after ligation of the hepatic artery in one patient. Alpha fetoprotein may occur in the serum of adult patients with tumours of the foregut, other than primary liver cell carcinoma, when such tumours have metastasized to the liver.

Fetal antigens were first described in adult serum in patients with a primary hepatic carcinoma (Tatarinov, 1966). The presence of these antigens in adult serum was initially considered diagnostic of primary hepatic carcinoma or embryonal testicular tumour (Abelev, Assenitova, Kraevsky, Perova, and Perovodchikova, 1967; Foli, Sherlock, and Adinolfi, 1969). More recently, however, there have been reports of alpha fetoprotein occurring in the serum of some patients with metastatic liver disease who had primary gastric carcinomas (Bourreille, Metayer, Sauger, Matray, and Fondimare, 1970; Jeffroy, Metayer, Denis, Philippe, Matray, Sauger, Launonier, and Duval, 1970; O'Connor, Tatarinov, Abelev, and Uriel, 1970; Alpert, Pinn, and Isselbacher, 1971; Kozower, Fawaz, Miller, and Kaplan, 1971; Mehlman, Bukley, and Wiernik, 1971; Castleden and Davies, 1972). We report two further patients with primary gastric carcinoma and liver secondaries who had persistent alpha fetoprotein in the serum.

Case Reports

In May 1972 this 55-year-old white man presented with weight loss, lassitude, and anorexia. There was a history of excessive intake of alcohol. The erythrocyte sedimentation rate was 53 mm per hour and serum alkaline phosphatase was 68 KA units. He was first seen in St Finbarr's Hospital in August 1972. There was obvious weight loss. The liver was large, irregular, and extended 6 cm below the costal margin. There was no bruise over its surface. The spleen was not felt and there was no ascites.

Investigations showed: serum bilirubin 0-8 mg %, SGPT 30 iu, alkaline phosphatase 160 KA units. Stools were positive for occult blood. Percutaneous liver biopsy showed prominent fatty change but no evidence of new growth. A liver scan (99 Tc) confirmed an enlarged liver with at least one filling defect in the right lobe. Alpha fetoprotein was strongly positive when measured by counter current immunoelectrophoresis. A barium meal showed a deformed prepyloric area from which gastroscopic biopsies were inconclusive. Laparotomy was carried out on 10 October in the hope that the patient's hepatic lesion would be a resectable primary liver cell carcinoma. The liver was replaced with secondary tumour and the primary carcinoma was in the antrum of the stomach. The hepatic artery was tied off and a biopsy taken from a tumour nodule in the right lobe of the liver. The patient became jaundiced within 24 hours, the bilirubin rising to 9-8 mg %. Alpha fetoprotein levels were again measured in the postoperative period (see table). The patient died on 6 November 1972 in hepatic and renal failure. Necropsy confirmed the laparotomy findings. The

Methods

Counter current electrophoresis using Cellogel was employed to identify alpha fetoprotein. Ten μl serum from fasting blood samples was applied to the cathode end and the antiserum (5 μl) at a point 5·5 cm from the same end. Electrophoresis was carried out at 150 volts for 45 minutes. Positive results were seen as a sharp precipitin line between the application sites. Behring M-Partigen immunodiffusion plates and standards were used to quantitate the positive results.

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<table>
<thead>
<tr>
<th>Time of Measurement</th>
<th>Alpha Fetoprotein (mg/100 ml)</th>
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<tr>
<td>Preoperative</td>
<td>4-4</td>
</tr>
<tr>
<td>Postoperative 2 days</td>
<td>3-8</td>
</tr>
<tr>
<td>14 days</td>
<td>3.0</td>
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Table Alpha fetoprotein levels in patient 1

The liver was virtually replaced by metastatic tumour (weight 3400 g, fig 1). The primary site was confirmed as the antrum of the stomach. The tumour was an adenocarcinoma of undifferentiated type (fig 2). Serial sections of the liver showed no evidence of primary liver cell carcinoma in that organ.

Case 2

This 65-year-old white housewife presented in August 1972 with a six-week history of abdominal swelling and repeated episodes of coma. When seen in St Finbarr's Hospital, she was found to be in hypoglycaemic coma. The liver extended 10 cm below the costal margin and was hard and irregular. There was a soft bruit over its surface. Bilirubin was 0.7 mg%, alkaline phosphatase 72 iu, SGPT 12 iu. Percutaneous liver biopsy showed an undifferentiated metastatic adenocarcinoma. She had repeated episodes of hypoglycaemic coma which appeared to result from disordered hepatic neoglucogenesis (Kelleher, O'Sullivan, Doyle, and Whelton, 1974). Serum alpha fetoprotein was repeatedly weakly positive; quantitative measurement gave a level of 0.3 mg%. She died on 31 October. At necropsy, the liver was totally replaced by anaplastic carcinoma.

Fig 1 Macroscopic appearance of liver in case 1 showing multiple metastatic deposits. The primary carcinoma was in the stomach. The liver weighed 3400 gm (scale in mm).

Fig 2 Metastatic adenocarcinoma in the liver of case 1 (A). On the left is normal hepatic parenchyma with diffuse fatty infiltration. Histologically, the tumour did not appear unusually anaplastic (haematoxylin and eosin × 40).
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The stomach was adherent to the liver where a malignant ulcer had penetrated its wall.

Discussion

Alpha fetoprotein, a normal fetal alpha 1 globulin, is detectable in trace amounts (less than 30 ng per ml of serum) by radioimmunoassay in adult serum (Seppälä and Ruoslahti, 1972; Waldmann and McIntire, 1972). It is not detectable in normal adult serum by methods such as agar gel precipitation and counter current electrophoresis (Waldmann and McIntire, 1972). High concentrations in adult serum were initially considered to be specific for primary liver cell carcinoma (Tatarinov, 1966; Alpert, Uriel, and de Nechad, 1968; Foli et al, 1969). It is now clear that alpha fetoprotein may occur in high titre in some patients with primary gastric carcinoma and liver secondaries (Bourreille et al, 1970; Geffroy et al, 1970; O’Conor et al, 1970; Alpert et al, 1971; Kozower et al, 1971; Mehlman et al, 1971; Castleden and Davies, 1972). There is a single report of its occurrence in association with carcinoid tumour of the stomach (Žižkovský, Kordač, Orovská, and Masopust, 1972). This patient also had extensive liver secondaries. Thus, with the exception of teratoblastoma of ovaries or testes in children (Abelev et al, 1967), tumours associated with high levels of alpha fetoprotein have uniformly been present in organs derived from the foregut at a stage where these tumours had metastasized to the liver.

The production of fetoprotein in patients with gastric carcinoma is almost certainly from the tumour or its liver secondaries. All reported cases have had massive secondary deposits in the liver. In one of our patients (case 1) serum levels fell after ligation of the hepatic arteries suggesting that the hepatic secondaries were responsible in part, at least, for the production of fetoprotein in this man. Histologically, the tumours in our patients, and in those previously described, have not appeared unusually anaplastic although they may have been so functionally. It is not clear why gastric carcinoma should be associated with the production of alpha fetoprotein. Antigenic reversion and resynthesis may be the mechanism (Gold, 1971).

Clinically, the finding of alpha fetoprotein in patients with secondary tumours of the liver is unlikely to lead to diagnostic problems. The liver will be markedly enlarged and there will be no stigmata of chronic liver disease. In our first patient, however, the history of alcoholic excess, the presence of high titre of fetoprotein and of a single, clear-cut filling defect on scintiscanning made primary liver cell carcinoma a likely possibility. In the second patient, although secondary tumour seemed likely at all times, the presence of fetoprotein in the serum and of bruit over the liver surface (Clain, Wartnaby, and Sherlock, 1966) might have led to diagnostic problems.

References


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