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CASE REPORT

Alpha-1-antitrypsin deficiency resulting in a hitherto unseen presentation of hepatocellular carcinoma: Polycythemia but with normal alpha fetoprotein

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Abstract

Polycythemia is a known paraneopastic manifestation of hepatoma, but only in the presence of alpha-fetopro (AFP). We present a case of polycythemia in the absence of AFP, and suggest concurrent alpha-1-antitrypsin deficiency as the cause for breaking this rule. We also suggest a reason for the apparent constant conjunction between polycythemia and AFP in hepatoma.

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Key words: Hepatoma; Polycythemia; Alpha 1 anti trypsin; Ephrin-A; Alpha-fetopro

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INTRODUCTION

Polycythemia is a known paraneopastic manifestation of hepatoma, but only in the presence of alpha-fetopro (AFP). We present a case of polycythemia in the absence of AFP, and suggest concurrent alpha-1-antitrypsin deficiency as the cause for breaking this rule. We also suggest a reason for the apparent constant conjunction between polycythemia and AFP in hepatoma.

CASE REPORT

A 79-year-old man was referred for dizziness with a history of benign prostatic hypertrophy and cholecystectomy. He was taking finasteride and ranitidine. He was an ex-smoker with a forty-pack year history and had never drunk alcohol heavily. Clinical examination was unremarkable but for a smoothly enlarged liver. Full blood count revealed polycythemia (haemoglobin 176 g/L, haematocrit 0.527), with a normal platelet count and white cell count. Chest X ray and ECG were normal. Oxygen saturation was 96% on air.

Abdominal ultrasound revealed a normal spleen and a 47 mm × 57 mm × 49 mm mass in the right lobe of the liver posteriorly, which was compressing the inferior vena cava. A CT scan demonstrated a well-defined rounded mass in the hilum of the liver with a mixed attenuation pattern, consistent with either hepatocellular carcinoma (HCC) or haemangioma. Serum AFP [8 μg/L (normal 0-16)], liver function tests, and hepatitis serology were normal, except IgG antibodies to hepatitis A. MRI of the liver suggested HCC as a more likely diagnosis than haemangioma. With normal AFP and liver function tests, a biopsy of the lesion was carried out. The histology confirmed HCC with adjacent cirrhosis.

He was referred to a specialist centre and further imaging confirmed extra hepatic disease with intra-abdominal and mediastinal lymphadenopathy. There was local vascular invasion but no peritoneal dissemination. A further liver biopsy found underlying fibrosis and DPAS (diastase periodic acid Schiff) positive globular material in the hepatocytes, consistent with alpha-1-antitrypsin (AAT) deficiency. Because of vascular involvement he was deemed unsuitable for surgery and was entered into a trans-arterial embolisation versus chemoembolisation trial.

DISCUSSION

Hepatocellular carcinoma can present with various paraneoplastic manifestations including polycythemia, hypercholesterolemia, hypoglycemia and hypercalcemia[1]. Our case is unique as it demonstrates an unreported phenomenon: HCC with polycythemia, but normal serum AFP. Polycythemia is strongly related to tumour burden and AFP, and is usually associated with markedly raised serum AFP levels[2,3].

Polycythemia is only partly due to increased erythropoietin production, as raised serum erythropoietin can be present in up to 23% of HCC patients[4], yet polycythemia is found only in approximately 1% of patients. This implies that erythropoietin production may be necessary, but is certainly not sufficient for polycythemia, and other factors must be implicated.

One such factor may be the expression of the erythropoietin receptor. This is upregulated by Ephrin-A1, a ligand for the Eph (erythropoietin producing hepatocellular) receptor tyrosine kinase[5]. Ephrin-A1 expression upregulating the erythropoietin receptor and thus resulting in the appearance of polycythemia would explain the constant conjunction hitherto reported in HCC between polycythemia and AFP, as there is a strong correlation between the presence of AFP in HCC with the expression of Ephrin-A1, which is known to induce AFP[5].

We therefore suggest that the association between polycythemia and raised AFP previously noted in HCC is because both arise from the expression of Ephrin-A1.

Our patient's normal AFP (despite his polycythemia) may be related to his AAT deficiency. Previous reports demonstrated high serum AFP levels in neonates with neonatal hepatitis, either idiopathic or due to extrahepatic biliary atresia. However, AFP is not raised in those infants with neonatal hepatitis and AAT deficiency. It was postulated that this is because alpha-1-antitrypsin is a rate limiting factor in the production of AFP[6]. To our knowledge, the possibility of AAT deficiency resulting in normal AFP in HCC in adults has not been raised.

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