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CASE REPORT

A retroperitoneal mass with elevated alpha-1-fetoprotein: not always a testicular carcinoma

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ABSTRACT

High levels of alpha-1-fetoprotein are usually associated with nonseminoma carcinoma of the testis or hepatocellular carcinoma of the liver. We describe a male patient with extrahepatic hepatocellular carcinoma who presented with a large retroperitoneal mass and extremely high alpha-1-fetoprotein levels. The importance of taking an adequate biopsy specimen cannot be emphasised enough since both prognosis and treatment are completely different.

KEYWORDS

Alpha-1-fetoprotein, ectopic tissue, hepatocellular carcinoma

INTRODUCTION

Hepatocellular carcinoma (HCC) is known for its high mortality. It also demonstrates a high variability in incidence around the world. Areas such as sub-Saharan Africa and Eastern Asia have an incidence up to ten times higher than the incidence in, for example, Europe.[1] This is probably due to the local prevalence of risk factors as hepatitis B and C virus. A known yet very rare phenomenon is hepatocellular carcinoma in ectopic liver tissue. The incidence of ectopic liver tissue is estimated at 0.1 to 0.5%.[2] Described locations include the gallbladder, pancreas, diaphragm, thorax and testis. Virtually all cases of ectopic HCC involve the Asian population,[3] although three Caucasian patients have been described.[4] We present a Caucasian male with no relevant medical history and no risk factors for HCC with a retroperitoneal HCC without lesions in his liver.

CASE

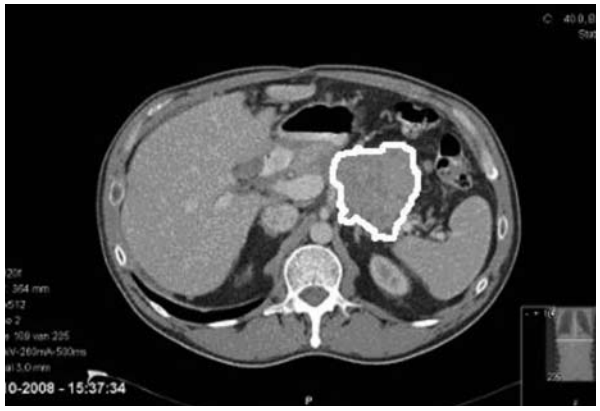
A 46-year-old Dutch male visited our emergency department after referral by his general practitioner with symptoms of stomach ache in his umbilical region that had been progressive over the last three months. Over that period his bodyweight had dropped about 5 kg. He complained of some diarrhoea without blood loss. His medical history comprised a surgical correction of a pyloric stenosis in his first year. He was not on any medication, did not smoke and used alcohol in moderate quantities.

On physical examination, a pale man was seen, in no acute distress with normal vital signs. There were no further abnormalities, aside from some peri-umbilical tenderness on palpation. There was no palpable mass in his testicles.

Biochemical investigation showed a microcytic anaemia (Hb 4.2 mmol/l; MCV 65 fl) and moderately elevated aspartate aminotransferase and alanine aminotransferase (76 U/l and 147 U/l, respectively). Ultrasonography of the abdomen revealed a soft-tissue mass in the upper abdomen. A computed tomography (CT) scan of the abdomen demonstrated a normal liver, but a large retroperitoneal mass in the upper abdomen (*figure 1*) with multiple enlarged lymph nodes in the mesentery. Magnetic resonance imaging did not show any hepatic lesions either. Because a testicular carcinoma was considered a possible diagnosis, an alpha-1-fetoprotein (α-1-FP) level was determined. This was extremely elevated at 24,000 kU/l (reference value <7 kU/l). The ultrasound investigation of his testes, however, was normal.

For further investigation the patient underwent an ultrasound-guided biopsy of the tumour. Microscopic examination revealed a tumour growing in trabeculae and some tubular structures with an aspect of hepatocytes. Some cells showed a positive alpha-1-fetoprotein (α-1-FP) immunostain. No bile production was seen. Further staining showed pankeratin

Figure 1. *Retroperitoneal mass (within white contour) at the location of the pancreatic tail*



and keratin-7 positive cells, suggesting epithelial tissue. Keratin-18, frequently present in normal hepatocytes, and keratin-19, usually absent in hepatocytes, were both negative. Beta-HCG was negative. The sample was concluded to be a poorly differentiated hepatocellular carcinoma. Pathological revision at the Department of Pathology of the University Hospital Nijmegen confirmed the conclusion. After evaluation of the radiological images we concluded the primary tumour to be irresectable. In addition, there were clearly metastases to abdominal lymph nodes; therefore the patient was treated with sorafenib (400 mg twice daily) for a metastasised ectopic HCC. After one week his level of α-1-FP dropped to 13,000 kU/l. During that week he visited the emergency department for the second time. On this occasion he complained of severe abdominal pain and diarrhoea. A CT scan showed an avascular necrosis of the head of the pancreas. The treatment with sorafenib was interrupted. After one week his pain had gone and the treatment with sorafenib was continued at a lower dose (200 mg twice daily). Until now, six months after diagnosis, his condition is stable and repeated CT scans have not revealed any signs of progression. Drug-related side effects are limited to fatigue and mild well-manageable diarrhoea.

DISCUSSION

Although the presence of ectopic liver tissue is rare (estimations below 0.5%) we have to bear in mind that this tissue is probably at a higher risk of developing into a carcinoma. All reviewed cases of ectopic HCC (all Japanese) show no primary hepatic lesions. In addition, more patients with ectopic HCC do not have the usual risk factors (such as HBV infection or cirrhosis) than patients with HCC in normal liver tissue.[2,3] Reasons for this higher carcinogenic tendency are not fully understood. It is suggested that impaired vascularisation or continuous cholestasis contributes to the development of HCC in ectopic liver tissue, although in this case no bile production was observed in the tissue sample. The phenomenon of ectopic liver tissue developing into carcinoma remains a diagnostic challenge. Learning more about the mechanisms leading to this higher carcinogenecity might lead to a better understanding of the principles behind the origin of hepatocellular carcinoma.

Until recently no proven or standard systemic treatment for advanced HCC was available. The SHARP trial, a randomised phase III trial in HCC, performed in the Western population, compared sorafenib 400 mg twice daily with placebo. Sorafenib is an oral multikinase inhibitor with antiproliferative and antiangiogenic effects. Treatment with sorafenib showed a progression-free survival (PFS) benefit of 2.4 months compared with placebo (PFS 5.2 *vs* 2.8 months in sorafenib and placebo respectively). The overall survival (OS) was 10.7 months *vs* 7.9 months in sorafenib and placebo, respectively.[5] Cheng *et al.* also showed a survival and PFS benefit in sorafenib *vs* placebo in 271 patients from 23 centres in China, South Korea and Taiwan (PFS 2.8 *vs* 1.4 and OS 6.5 *vs* 4.2 months in sorafenib and placebo, respectively).[6] The effect of systemic treatment of extrahepatic HCC is unknown. Sorafenib is generally well tolerated although side effects are sometimes severe and dose limiting. The most common drug-related adverse events include hand-food syndrome, diarrhoea, alopecia, fatigue, rash or desquamation and hypertension.

CONCLUSION

A retroperitoneal mass with elevated levels of α-1-FP and no liver lesions does not always mean a testicular carcinoma. Even in otherwise healthy Caucasian patients, ectopic hepatocellular carcinoma is a possibility, although a rare one. The importance of having a good enough biopsy specimen of the tumour for determining its origin cannot be emphasised enough.

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