

• CASE REPORT •

Very high alpha-fetoprotein in a young man due to concomitant presentation of hepatocellular carcinoma and Sertoli cell testis tumor

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Abstract

Studies reported that there is a close relationship between hepatocellular carcinoma (HCC) and testis carcinoma. Both tumors can be presented as synchronous tumors, or as testicular metastases of HCC or as hepatic metastases of testicular tumor^[7]. HCC is one of the most common malignancies worldwide and the incidence of HCC increases with age^[8]. The relationship between hepatitis B incidence and HCC rates is also well recognized. Alpha fetoprotein (AFP) is produced by 70% of HCC. Though a level of AFP >400 ng/mL is diagnostic for HCC, in the presence of active hepatitis B infection, the cut-off level should be considered to be at least 1 000-4 000 ng/mL. Like HCC, germ cell tumors of the testis also release AFP; but it is shown that some of Sertoli cell tumors of testis can also release AFP^[10]. Herein we have reported about the first case of HCC in the literature which is presented concomitantly with Sertoli-Leydig tumor of testis, leading to extremely high level of AFP in a 21-year-old man.

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Key words: Hepatocellular carcinoma; Sertoli-Leydig cell tumor; AFP; Cirrhosis; Hypercholesterolemia

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INTRODUCTION

Studies have reported that there is a close relationship between hepatocellular carcinoma (HCC) and testis carcinoma. Both tumors can be presented as synchronous

tumors^[1,2], or as testicular metastases of HCC^[3-5] or as hepatic metastases of testicular tumor^[6,7].

HCC is one of the most common malignancies worldwide and the incidence of HCC increases with age^[8]. Alpha fetoprotein (AFP) is produced by 70% of HCC. Like HCC, germ cell tumors of the testis also release AFP^[9]; but it is shown that some of Sertoli cell tumors of testis can also release AFP^[10]. Herein we have reported the first case of HCC in the literature which is presented concomitantly with Sertoli-Leydig tumor of testis, leading to extremely high level of AFP in a 21-year-old man.

CASE REPORT

A 21-year-old man was admitted to our clinic in May 2002, with complaints of fatigue, nausea, vomiting, abdominal distention and weight loss. The patient was well before two months. His mother died of cirrhosis due to hepatitis B. His two sisters were HBsAg seropositive. On physical examination minimal ascites was detected and the abdomen was tender on palpation. The liver was palpated under the rib margin as 10 cm and was also tender. The spleen was palpated as 6 cm. Other systems were normal on examination. On admission, laboratory tests performed reported ALT: 64 IU/L (0-41), AST: 44 IU/L (0-37), fasting plasma glucose: 94 mg/dL, urea: 21 mg/dL, serum creatinine: 0.65 mg/dL, LDH: 500 IU/mL (240-480), GGT: 161 U/L (0-49), ALP: 372 U/L, T prot: 67 g/L, alb: 36 g/L, glob: 31 g/L, D bil: 0.76 mg/dL, I bil: 1.09 mg/dL, total cholesterol: 463 mg/dL, triglyceride: 130 mg/dL, LDL: 413 mg/dL, HDL: 24 mg/dL, VLDL: 38.2 mg/dL, Na: 138 mmol/L, K: 3.9 mmol/L, Ca: 9.4 mmol/L, Fe: 43 µg/dL, total iron binding capacity: 396 µg/dL, hemoglobin: 11.5 g/dL, hematocrit: 34.8%, white blood cell: 2 700, platelet: 215 000, MCV: 83 fL, erythrocyte sedimentation rate: 12 mm/h. Markers of viral hepatitis were HBsAg (+), antiHBs (-), antiHCV (-), HbeAg (-), antiHBe (-).

On ultrasonographic examination, the liver was heterogenous and there were multiple hypodense lesions in the right and left liver lobes. Thromboses were seen in both hepatic and portal veins in Doppler ultrasound. The AFP level was 5 181 000/mL (0-10) and beta-HCG was 0.5 mIU/mL (normal range: 5-10 mIU/mL). Computerized abdominal tomography showed that the craniocaudal sizes of the liver and spleen were 25 and 22 cm respectively. The liver margin was irregular, the right and

left lobes of the liver contained multiple hypodense lesions resembling metastasis or primary HCC. A liver biopsy was done to identify the hypodense lesions of the liver. Diffuse fibrosis and HCC were reported from the histopathological examination. Hepatocytes were positive for keratin and AFP, but negative for vimentin. Because of the young age of the patient, the presence of multiple hepatic hypodense lesions resembling metastasis and the extremely high AFP level, an examination of the testis was also done to exclude a testicular tumor. Physical examination of the testis revealed a painless mass on the left testis. Ultrasound sonography showed a hypoechoic lesion (19 mm×18 mm×17 mm in size) in the left testis. High inguinal orchiectomy was performed. The tumor within the testis was histopathologically diagnosed as Sertoli cell testis tumor. Leydig cells were negative for keratin but positive for vimentin. Finally, the patient who had primary HCC and primary Sertoli cell tumor of the testis (two primary tumors concomitantly presented) was referred to the oncology clinic for further evaluation and therapy.

DISCUSSION

HCC is one of the commonest malignant diseases in the world and the majority of cases of HCC arise in individuals with chronic hepatitis B or C virus infections^[11]. All ages can be affected by HCC. The mean age at diagnosis is 53 years in Asia and 62 years in the United States. Recently, an analysis of 76 HCC cases investigated by Butt *et al.*^[8] showed that the mean age is 52.2±11.3 years and the mean AFP level is 142±155 ng/mL. In contrary, our patient was very young and the AFP level was very high. Transmission of hepatitis B virus from his mother at the very early time of his life might be the cause of HCC development at the very young age.

AFP continues to be the best marker for early diagnosis of HCC. In adults the value of AFP up to 20 ng/mL is considered to be normal. Patients with hepatitis B virus-related cirrhosis having AFP level greater than 100 ng/mL are in the very high risk group for HCC. The AFP level usually correlates with tumor size^[12]. Thus, the very high level of AFP in our patient may be due to the large tumor size, which was multifocal in both lobes of the liver.

Extremely high AFP levels are found in endodermal sinus tumors (yolk sac tumors) also^[13]. Such neoplasms occur in testis, ovary and extragonadal sites. Typically they occur in young subjects. Hence we also examined the testis in our patient and performed orchiectomy after we palpated a testicular mass. The histopathological result was a Sertoli cell tumor of the testis, which was a testicular gonadal stromal tumor. Sertoli cell tumor (SCT) is very rare among testis tumors accounting for lower than 1% of primary testicular neoplasms. It is subclassified into three groups: classic, large cell calcifying (LCCSCT), and sclerosing. Most SCTs are benign, metastases are the only reliable indicator of malignancy, occurring in lower than 10% of cases. The most common sites for metastatic spread are retroperitoneal lymph nodes, lungs, liver, and bone. LCCSCT and sclerosing SCT have minimal

metastatic potential^[14].

The risk for liver cancer is very high in cirrhotic liver. There is also evidence that the risk for extrahepatic cancers increases in patients with cirrhosis. The reason of the increased extrahepatic malignancy risk in cirrhosis is not clear but may be due to many abnormal and metabolic alterations in cirrhosis like hyperestrogenism, alterations in metabolism of lipid and water-soluble drugs and other chemicals, alterations in immune functions and risk of infections in cirrhosis^[15]. In this cohort study, Sorensen *et al.*^[15] also reported that the occurrence of liver cancer, tobacco- and alcohol-related cancers, testicular cancer, stomach and colon cancer is significantly higher in cirrhosis than expected. This study may explain two primary cancers in our young patient which were thought to be cirrhotic due to chronic hepatitis B infection.

Though our case was in a state of decompensated liver failure, he had hypercholesterolemia which was parallel to the change in serum AFP. Hwang *et al.*^[16] also observed that HCC patients with hypercholesterolemia have significantly higher mean serum levels of albumin, triglyceride, and AFP compared with age-sex-tumor volume-matched HCC patients without hypercholesterolemia. It was reported that 11% of HCC patients have hypercholesterolemia, which can be explained by the possible result from the absence of dietary cholesterol suppression feedback regulation in the damaged liver^[17].

In conclusion, this case is an example showing the increased risk of hepatic and extrahepatic tumors in cirrhosis. In the presence of HCC in a cirrhotic patient, there might be multiple primary cancers. The possibility of second primary malignancy in a patient with HCC should be kept in mind especially when a very high level of AFP is encountered and this second primary malignancy may be a kind of a very rare tumor. However, the co-existence of HCC and testis tumor is very rare. As far as we know, this is the first case report showing the co-existence of HCC and SCT in a young boy presented with an extremely high level of AFP.

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