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CASE REPORT

A case of alpha-fetoprotein-producing gastric cancer in a child presenting with rupture of multiple liver metastases

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Abstract We report a 14-year-old boy with alpha-fetoprotein-producing gastric cancer (AFPGC) who was found with ruptured metastatic tumor in the liver. AFPGC is exceedingly rare in pediatric age. It often shows metastases to the liver and should be included in differential diagnoses of liver tumors with increased serum AFP.

Keywords Alpha-fetoprotein-producing gastric cancer · Children · Metastasis · Liver

Introduction

Alpha-fetoprotein (AFP) is a well-known tumor marker for yolk sac tumor, hepatocellular carcinoma, and hepatoblastoma. Other tumors such as gastric cancer (GC) rarely produce AFP. AFP-producing GC (AFPGC) usually occurs in an elderly group, often shows liver metastasis and has poor prognosis [1]. AFPGC in pediatric population is exceedingly rare and only one case has been reported [2]. We report a 14-year-old boy with AFPGC who was diagnosed with ruptured metastatic tumor in the liver. To the best of our knowledge, this is the first reported case of AFPGC with liver metastases under 20 years of age.

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Case report

A 14-year-old boy presented with acute abdominal pain, poor complexion and hypotension. He was urgently admitted to an emergency hospital and computed tomography (CT) was performed. Because CT revealed rupture of multiple liver tumors, transarterial embolization was immediately performed to control the bleeding. Two days later, he was transferred to our hospital for diagnosis and treatment. At first, primary liver tumor was suspected because of increased serum AFP (556.7 ng/mL, normal range 0–20 ng/mL) and no obvious extrahepatic tumors on CT (Fig. 1). At first, he underwent liver tumor biopsy, but only necrotic tissue without any viable tumor cells was observed on frozen section examination. He then underwent resection of the right hepatic lobe for definite diagnosis of the liver tumor. Histologically, the liver tumor was adenocarcinoma showing two cellular and structural patterns: well-to-moderately differentiated tubular adenocarcinoma and solid or tubular growths of cuboidal or columnar cells with PAS-positive clear cytoplasm resembling primitive foregut epithelium (Fig. 2).

Immunohistochemically, the neoplastic cells were diffusely positive for cytokeratin (CK) 8 and CK19, partially positive for nuclear/cytoplasmic beta catenin and AFP, and negative for CK7, CK20 and hepatocyte antigen (Fig. 3). Ki67 labeling was seen in approximately 50 % of the tumor cells. There was no difference in the immunostaining between the two histological patterns. Epstein–Barr virus (EBV)-encoded small RNA (EBER) was negative for tumor cells. No overt point mutation was seen in beta-catenin codon 12 to codon 75. As these findings were consistent with well-to-moderately differentiated tubular adenocarcinoma with AFP production, the liver tumors were suspected to be metastasized from gastrointestinal

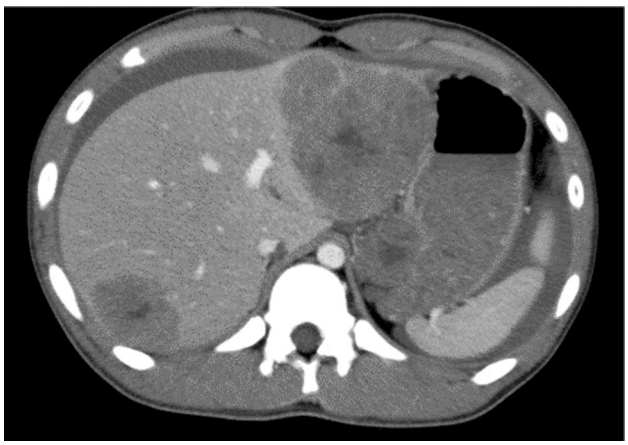

Fig. 1 Abdominal computed tomography. Multiple tumors are observed in the liver

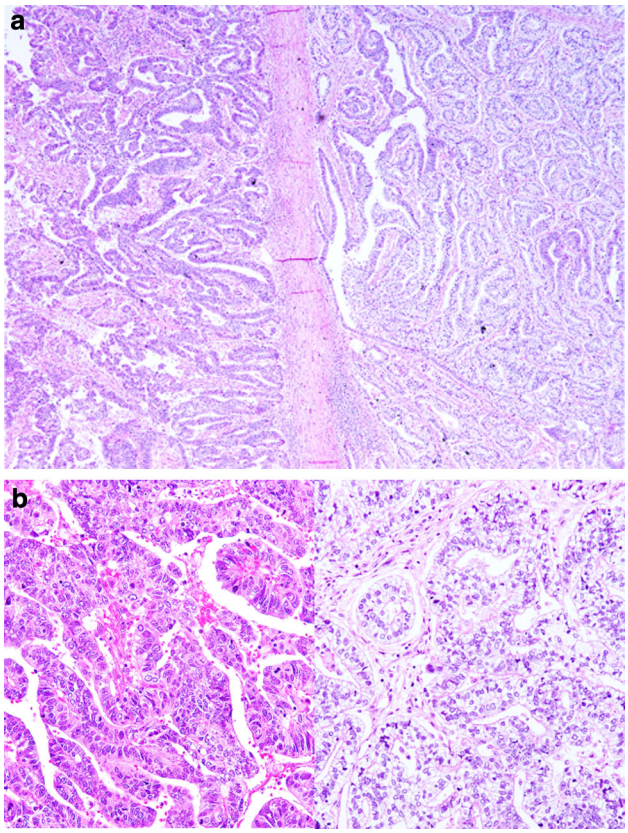

Fig. 2 Histological findings of the liver tumor. **a** Low-power view showing intermixed well-to-moderately differentiated tubular adenocarcinoma and tubular growths of cuboidal cells with clear cytoplasm. **b** High-power view showing adenocarcinoma (*left*) and cuboidal cells with clear cytoplasm (*right*)

(GI) tract (Table 1). Endoscopic examination revealed Bormann type 2 tumor, measuring 30 mm, under the cardia. The biopsy showed well-to-moderately differentiated tubular adenocarcinoma and the neoplastic cells showed almost identical immunohistochemical patterns to the liver tumor. From these findings, the final diagnosis was AFPGC with liver metastases. The patient was transferred to a general hospital to receive chemotherapy, but he died due to progressive disease four months from initial diagnosis.

Discussion

The pediatric gastric cancer (PGC, 15 years old or younger) is extremely rare; the occurrence rate of PGC has been reported to be 0.02 % among GC patients [3]. Most PGC patients are children who are more than 10 years of age [2, 4–6]. They are often discovered at an advanced stage and have poor prognosis. There has been no report that showed a survival rate for 5 years; the average survival after diagnosis period was 5 months [7]. Nakamura et al. reported that the duration of survival for advanced gastric cancer is shorter than that of adults [6]. The reasons why PGC is detected so advanced may be due to the difference in biological properties of the tumor and the low frequency of medical checkup using endoscopy and gastrointestinal (GI) radiography when compared to adults.

Epstein–Barr virus-related GC accounts for approximately 10 % of GC and preferentially occurs in younger men [8], but tumor cells were negative for EBER in our patient. In GC, 27 % of cases have nuclear expression of beta-catenin and 5 % of cases have beta-catenin gene mutation [9]. It is suggested that nuclear expression of beta-catenin is related to poor prognosis [10]. To our knowledge, there has been no report regarding the expression of nuclear beta-catenin in PGC. In the present case, the tumor cells displayed nuclear expression of beta-catenin but no mutation of beta-catenin was found and the prognosis was poor.

In PGC patients, there is an average interval of 2.7 months from the first medical checkup to diagnosis by endoscopic examination. Symptoms include abdominal pain, nausea, vomiting and weight loss. Endoscopy is usually not actively performed in pediatric patients because GI cancer is not strongly suspected and general anesthesia may be needed to perform endoscopy. If these symptoms persist or become worse, it is necessary to suspect GI cancer and to consider endoscopic examination. It should be stressed that CT study is not useful for the diagnosis of GC. In the present case, because CT detected only liver tumors, we did not initially suspect metastasis of GI cancer. GI cancer was suspected after the histological examination of the liver tumor, and then the endoscopy was performed. Similar cases have been reported in the literature (Table 2) [2, 11]. In these two cases, no gastric lesion was detected by CT or GI radiography. They were diagnosed as gastric cancer by endoscopy that was performed after the

Table 1 Comparison of immunohistological and genetic parameters of the present case with hepatocellular carcinoma and hepatoblastoma

	Present case (liver metastasis)	Hepatocellular carcinoma	Hepatoblastoma
AFP staining	Positive, partially	Positive	Positive
CK7 staining	Negative	Negative	Negative
CK8 staining	Positive	Positive	Positive
CK19 staining	Positive	Negative	Negative
Hepatocyte antigen staining	Negative	Positive	Positive
Beta-catenin staining (nuclear/cytoplasmic)	Positive, partially	Occasionally positive	Usually positive
Beta-catenin mutation	Negative	Occasionally positive	Often positive

Table 2 Clinical features of pediatric gastric carcinoma patients whose diagnoses were not made at the first visit

References	Clinical presentation	Age (year)/sex	First diagnostic method	Duration between first visit and definitive diagnosis	The survival period after diagnosis	Serum AFP
Emir et al. [2]	Abdominal pain	12/male	CT	4 weeks	8 months	207 mg/dl
Michálek et al. [11]	Nausea, body weight loss	9/male	GI radiography	4 months	10 days	Unknown

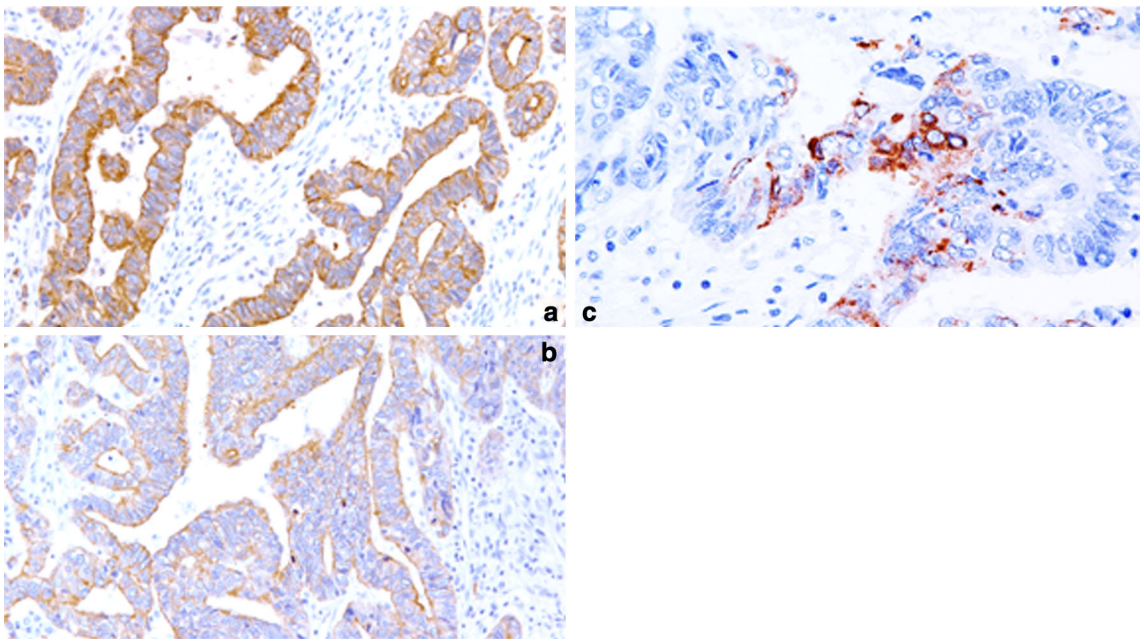

Fig. 3 Immunohistochemical findings the liver tumor showing well-to-moderately differentiated tubular adenocarcinoma. Immunoperoxidase ×40. **a** Diffusely positive staining for CK8, **b** diffusely positive staining for CK19, **c** partially positive staining for AFP

deterioration of the symptoms. These cases suggest that metastatic GC, although rare, should be included in the differential diagnosis of pediatric liver tumors.

This is the first reported case of AFPGC with liver metastasis under 20 years of age. AFPGC occupies approximately 1 % of GC and occurs most frequently in the age group of 50 years or older. There has been only one case of AFPGC in pediatric age group. Most cases of AFPGC show increased serum AFP and have liver metastasis. Liu et al. reported that preoperative serum AFP levels ranged from 10 to 3000 mg/L, and the median value was 41,000 ng/mL [1]. Serum AFP was mildly elevated in our case (556.7 ng/mL). It should be noted that mild elevation of serum AFP may be seen in some AFPGC. For

liver tumors with mildly elevated serum AFP, it is necessary to consider AFPGC as one of differential diagnosis. GI cancer with increased serum AFP can occur not only in stomach but also in colon and esophagus [12, 13]. In pediatric age group, liver tumor with increased serum AFP is mostly hepatoblastoma or hepatocellular carcinoma, but endoscopy with biopsy may be necessary to diagnose liver metastasis from AFP-producing GI cancer.

Conflict of interest The authors declare that they have no conflict of interest.

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