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CASE REPORT

Primary Yolk Sac Tumor of The Liver: A Case Report

ABSTRACT

Primary yolk sac tumor of the liver is a highly infrequent category of germ cell tumors, especially in adults. Therefore, it is critical to differentiate the disease from more common hepatic cancers that are also characterized by high serum alpha-fetoprotein (AFP) levels, such as hepatocellular carcinoma and hepatoblastoma. We report a male patient in his early 30s who presented with abdominal pain, elevated serum AFP concentration, and a cystic mass on the liver. The patient underwent two lines of chemotherapeutic treatment. We discuss adult patients with primary yolk sac tumors of the liver and the management of their condition in the literature.

Keywords: Liver, tumor, yolk sac

Yolk Sac Tumor (YST), also known as endodermal sinus tumor, is one of the malignant types of germ cell tumors (GCT), whose most common sites are gonads. On the other hand, among extragonadal YSTs, midline structures such as the mediastinum, retroperitoneum, and sacral region are typical locations. Since YST of the liver is a highly infrequent category of GCT, information is scarce in the literature, with few adult male cases (1-5). We present a case of a 31-year-old man with primary YST of the liver who underwent two lines of chemotherapeutic treatment.

CASE

A 31-year-old male patient presented with a 2-month history of abdominal pain that started in the right subcostal region. The physical examination was unremarkable. In family history, no clue for a tendency to any cancer was figured out.

An abdominal ultrasound revealed masses around the liver and peritoneum, along with paracolic lymphadenopathy. Endoscopy showed gastritis, while no abnormality had been identified in the scrotal ultrasound. Among the oncomarkers, only serum alpha-fetoprotein (AFP) was found to be elevated. At first, positive results of the hepatitis B surface antigen (HBsAg) test and extremely high AFP levels led to the preliminary diagnosis of hepatocellular carcinoma (HCC). Therefore, the patient underwent an upper abdominal computed tomography (CT) test to verify if the preliminary diagnosis was correct. In CT, several hypodense lesions, with a maximal size of 46x40x43 mm, were spotted on the left lobe of the liver. On the other hand, magnetic resonance imaging (MRI) showed that the mass on the left side of the liver put pressure on the stomach. Besides, a subcapsular fluid, measured 10 mm in the widest section, was seen around the liver. Since upper abdominal CT and MRI findings were not considered distinctive for HCC, a tru-cut biopsy of the mass on the liver was taken. Malignant epithelial tumor sheets forming a reticular pattern were observed in the biopsy sample (Figure 1). In immunohistochemical studies, the tumor cells were positive for CK8/18 and glypican 3. The neoplastic cells were also noticed to be focal immunopositive for Sal-like protein 4 (SALL-4) and AFP. They were immunonegative for CK7, CK20, HepPar1, arginase1, synaptophysin, INSM1, chromogranin, CD30, and OCT3/4. The sample was a small biopsy (tru-cut) and half of the neoplastic tissue in the biopsy material was necrotic. Most likely for these reasons, Shiller-Duval bodies were not found. However, intestinal differentiation has been demonstrated with CDX2 positivity, which differentiates the Yolk Sac from HCC histopathologically. As no other possible primary location was evident, the final diagnosis became the primary YST of the liver.

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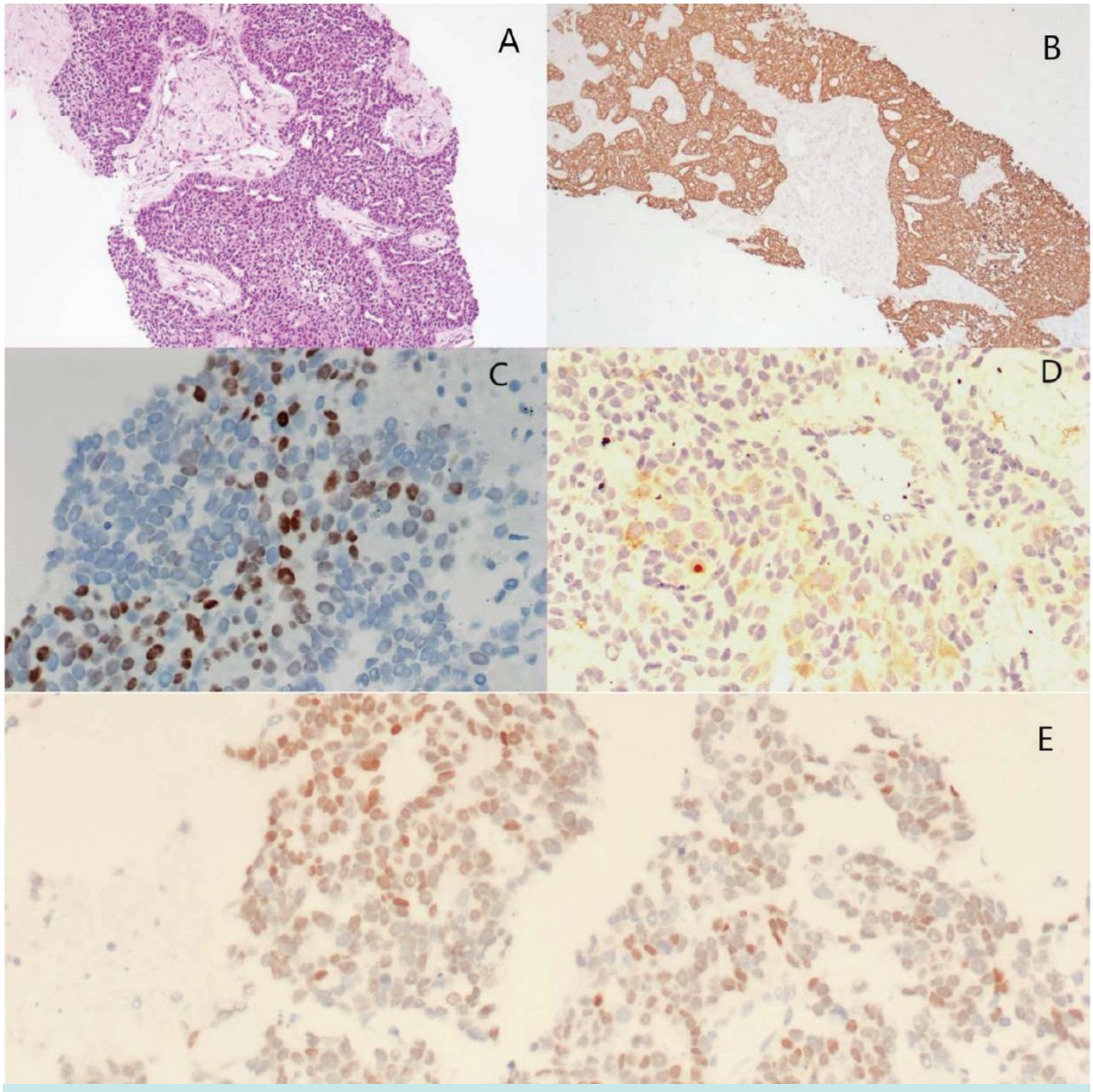

Figure 1. Malignant epithelial tumor showing reticular pattern (A), which forms a network of anastomosing cords of epithelial cells. Tumor cells are immunopositive for CK8/18 (B), SALL4 (C), AFP (D), CDX2 (E) and immunonegative for CK7, CK20, HepPar1, arginase1, synaptophysin, INSM1, chromogranin, CD30, and OCT3/4 (not shown here).

The patient was prescribed four courses of bleomycin, etoposide phosphate, and cisplatin (BEP) regimen. After three courses of treatment, serum AFP levels were unresponsive. Nevertheless, during the BEP treatment, grade 2 chemotherapy-induced toxicity was reported. According to positron emission tomography combined with CT (PET-CT), the metabolic and radiological regression rate of the tumor was between 10% and 20% (Figure 2). Although it is labeled as "stable" in compliance with Positron Emission Tomography Response Criteria in Solid Tumors (PERCIST), we regarded this change as a "mild clinical progression." Yet, there was no prominent amelioration among the patient's complaints. That is why the patient underwent two courses of second-line paclitaxel, ifosfamide, and cisplatin (TIP) regimen at an external medical center. However, this treatment worsened the condition to a certain degree. After the two courses of the regimen, grade 3 neutropenia was evident from blood tests. The patient could not tolerate the treatment and died two months after the last procedure.

DISCUSSION

Although YST of the liver generally presents with symptoms like abdominal pain, jaundice, or an abdominal lump, a pathognomonic examination sign is nonexistent. On the other hand, as it is a rare condition, no typical radiological finding can be directly associated with the disease. In addition, it shares common symptoms, increased serum AFP levels, and higher prevalence for exposure to viral Hepatitis B with more common liver cancers such as hepatoblastoma and HCC (3,4). As a result, the disease is prone to be misdiagnosed, especially as HCC (3,4,6). There is even a case report

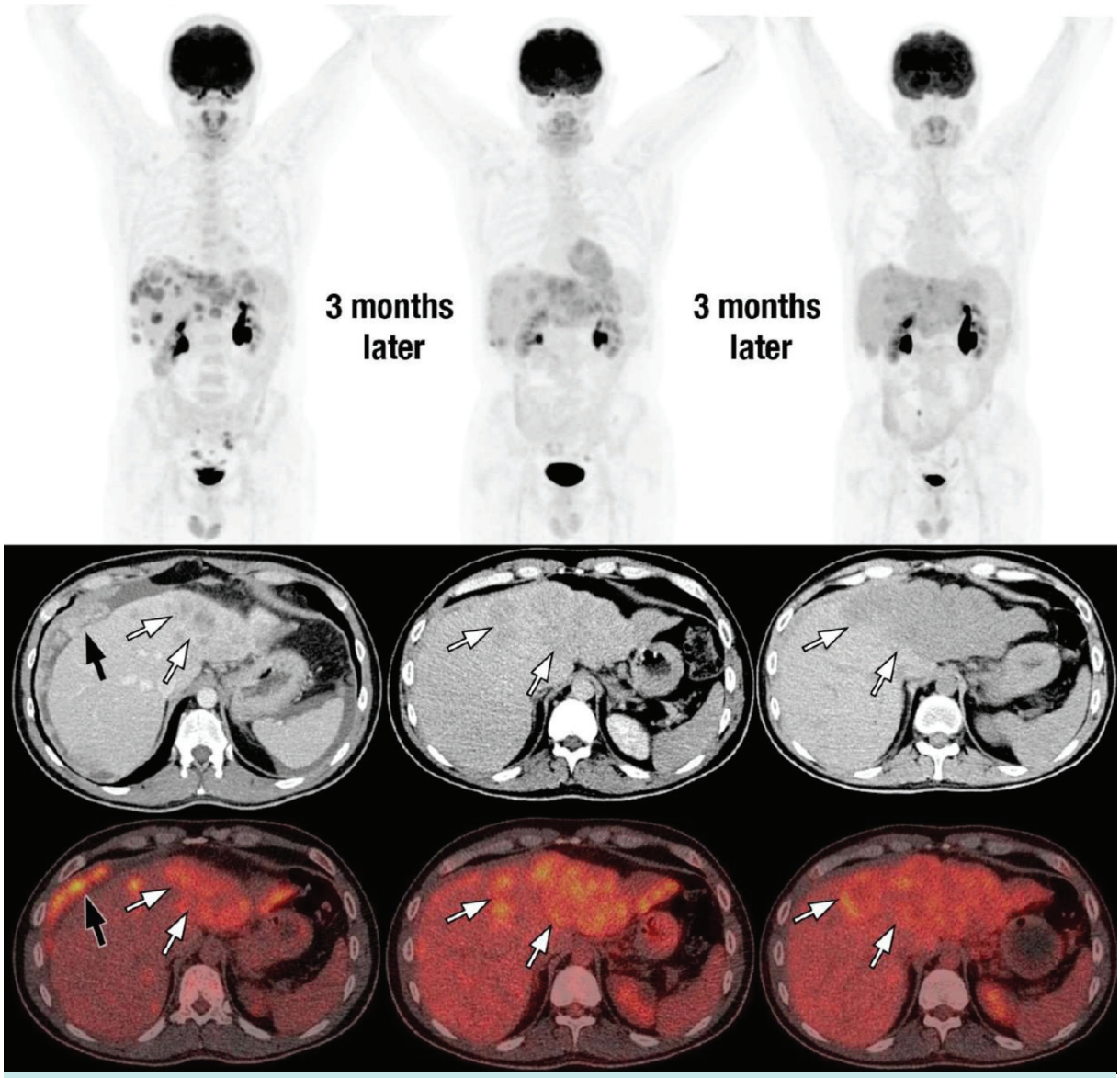

Figure 2. In the sequential imaging (PET-CT) of the same patient taken at three-month intervals, the initial examination reveals perihepatic intraperitoneal malignant lesions denoted by black arrows, which are notably absent in the subsequent images. Conversely, liver lesions, indicated by white arrows, display a progressive increase in size over the observed period.

that pointed out the coexistence of HCC and YST of the liver in the same patient (5).

In fact, CT generally demonstrates large cystic and heterogeneous masses, necrotic areas around the center, and occasionally intratumoral calcifications related to a teratoma (2). MRI is also used in some cases in order to achieve detailed information about the area the lesion spread and possible occlusions it caused (2,6). Still, since primary YST of the liver is a tumor with extremely low prevalence, it is hard to relate radiological findings as typical properties of the disease directly.

Considering that YSTs may have various histological patterns (papillary, reticular, solid, etc.) with pathognomonic pathological features called the Schiller-Duval bodies, YST of the liver sometimes can be detectable without any difficulty via biopsy. However, Schiller-Duval bodies may not always be detected in small biopsies. So, it is crucial to regard YST of the liver as one of the potential diagnoses when confronted with a patient who has high serum AFP levels and common abdominal symptoms with other liver cancers. Otherwise, the disease can often be easily missed. If there is a remarkable suspicion for YST, a biopsy should be taken, as it is the only method that may contribute to a direct diagnosis.

Immunohistochemical features can also be helpful when making a differential diagnosis between HCC and YST (2). While tumor cells of HCC are inclined to be immunopositive for Hep Par 1 and Arginase 1, those of YST are immunonegative for these indicators. The indicators that YST cells tend to be positive for are AFP, glypican-3, SALL-4, and AE1/3. Researchers also reported potential carcinoembryonic antigen positivity in certain YST sites, especially in glandular parts (5,7). In our case, although the pathognomonic Schiller-Duval body was not seen, hepatocellular carcinoma was ruled

out due to CDX2 positivity, no hepatoid differentiation morphologically and immunophenotypically, and no other tumor location.

Alternatively, a study that used fine-needle aspiration biopsy in diagnosis identified common cytomorphological characteristics of extragonadal YSTs, including pleomorphic tumor cells with larger nuclei compared to the cells with the same size of cytoplasm, intranuclear vacuoles, and apparent nucleoli. Moreover, the study emphasized that the tumor cells of YSTs grow in either papillary or microglandular patterns (8). Yet, cytomorphological features can only be used as assistive materials in the diagnosis due to a deficiency of further information.

The most widely accepted treatment is surgery followed by chemotherapy, even though the procedure still has a mortality rate of more than half (9). However, just like in our case, a study used only chemotherapy because of an unresectable tumor (2). At the same time, there are cases that underwent surgery for HCC due to misdiagnosis and a case whose diagnosis of YST was detected after autopsy (3,10).

Among chemotherapeutic approaches, several reports demonstrated the BEP regimen's positive initial response as the first-line treatment by gradually decreasing serum AFP levels (2,6). Though this procedure contributed to a 10% to 20% regression of the tumor in our patient as well, it also caused chemotherapy-induced toxicity. Nevertheless, while different second-line treatments are attempted in the literature, there is hardly any proof of their long-term benefits.

CONCLUSION

To sum up, despite its extremely low rate of prevalence, YST of the liver should be taken into consideration when confronted with large cystic tumors and significantly high serum AFP levels in young patients. In this way, early diagnosis may improve the treatment's possibility of cure.

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