

Primary Yolk Sac Tumor of the Liver in an Adult Man

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ABSTRACT

Primary yolk sac tumor of the liver is extremely rare in adults. We report a case of a young man with an unresectable primary yolk sac tumor of the liver, who had a platinum-refractory disease that progressed despite 2 lines of chemotherapy. We review the literature pertaining to primary yolk sac tumor of the liver and its management.

INTRODUCTION

Extragenital germ cell tumor (GCT) is a neoplasm located outside the gonads with histology associated with gonadal origin. The common sites of extragenital GCT are midline structures including the mediastinum, retroperitoneum, and sacral region. Primary yolk sac tumor of the liver is extremely rare, and less than 15 adult cases have been reported to date.¹⁻⁵ Therefore, the collective description of clinicopathological features and outcomes of this tumor is sparse. We present a case of an unresectable primary yolk sac tumor of the liver in a young man, along with the review of literature, and peculiar features of this tumor.

CASE REPORT

A 27-year-old man presented with a 1-month history of progressive jaundice. Examination revealed icterus and a large intra-abdominal mass in the right hypochondrium, measuring approximately 7 × 7 cm. External genitalia were normal on palpation. Investigations revealed deranged liver function tests with hyperbilirubinemia at 16.2 mg/dL, conjugated bilirubin 11.7 mg/dL, aspartate aminotransferase 118 U/L, alanine aminotransferase 40 U/L, serum alpha-fetoprotein (AFP) 120,000 U/L, lactate dehydrogenase 180 U/L, and human chorionic gonadotropin <1.20 mIU/mL. Ultrasound of abdomen showed multiple ill-defined heteroechoic lesions in both lobes of the liver with central necrosis and intrahepatic biliary radicle dilatation. Magnetic resonance imaging of abdomen revealed a large lobulated mass 13.6 × 10.6 × 10.6 cm in the right lobe of the liver, extending to both left and caudate lobes causing intrahepatic biliary radicle dilatation. The mass was hypointense on T2 within a large hyperintense area, which is suggestive of necrosis.

Percutaneous transhepatic biliary drainage for biliary decompression was performed. The biopsy of the liver mass revealed it to be a nonseminomatous GCT, which is suggestive of a yolk sac tumor. The tumor cells were immunopositive for pancytokeratin and SALL4, negative for CK7, CK20, CD30, Hep Par1, and Arginase 1 (Figure 1). Ultrasound of the scrotum was normal. CECT chest, abdomen and pelvis were done to rule out extragenital germ cell tumor of mediastinum and retroperitoneum. A final diagnosis of the unresectable primary yolk sac tumor of the liver was performed. The patient was started on a bleomycin, etoposide, and cisplatin regimen. After 4 cycles, his AFP level was 14,462 ng/mL and his CECT abdomen showed persistence of lesions in the liver, which is suggestive of suboptimal response (Figure 2). Second-line chemotherapy was initiated with a paclitaxel, ifosfamide (with mesna), and cisplatin (TIP) regimen. After the fourth cycle of TIP, there was clinical deterioration; the tumor was stable on imaging although AFP increased to 20,006 ng/mL. The next step for clinical management is a gemcitabine and oxaliplatin (Gem Ox) regimen.

DISCUSSION

Yolk sac tumor is a highly malignant histological subtype of GCTs. The primary yolk sac tumor of the liver usually presents with abdominal pain, an abdominal lump, and less frequently, jaundice. The serum AFP is usually highly increased in these tumors.

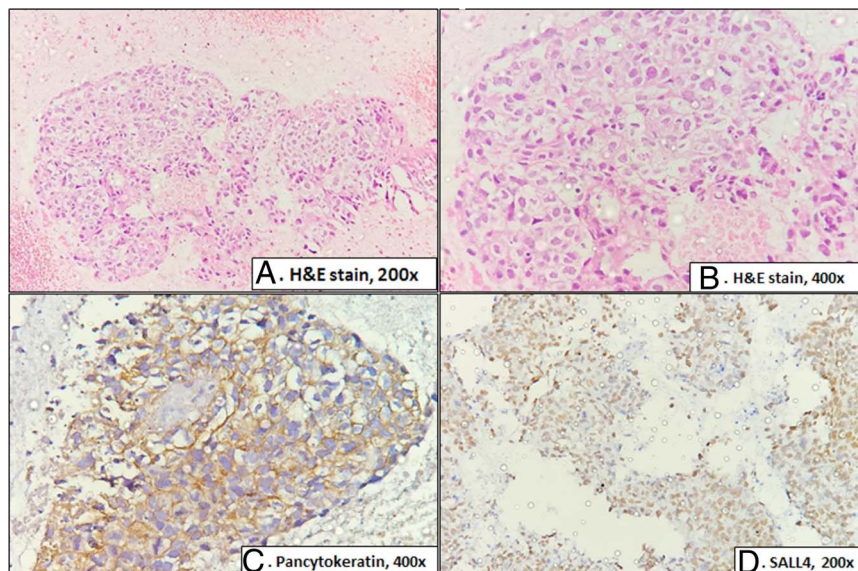


Figure 1. Hematoxylin and eosin stain at (A) 200 \times and (B) 400 \times of the liver mass showing a tumor arranged in nest and a sheet of polygonal cells having pale eosinophilic to clear cytoplasm with well distinct cytoplasmic boundaries. The nuclei are round to oval with marked pleomorphism, vesicular chromatin, and prominent nucleoli. There is brisk mitotic activity in the tumor. The tumor cells are immunopositive for (C) pancytokeratin (400 \times) and (D) SALL4 (200 \times).

Female gender, cystic liver lesion, young age, and high AFP were consistent with yolk sac tumor of the liver according to Wong et al after they reviewed the first 7 cases.¹ A routine testicular biopsy is not recommended if ultrasound of the scrotum is normal. The common features of extragonadal and gonadal GCT are that they occur in young men and metastasize to the lung, liver, and bones, with the presence of 12p karyotype abnormality and sensitivity to cisplatin-based chemotherapy.⁶

The existing hypotheses for pure extragonadal GCT include aberrant migration of primordial germ cells or reverse migration of transformed germ cells from the testes, which later arise in extragonadal sites, and persistence of pluripotent cells in extra

gonadal sites.⁷ The typical radiological features of yolk sac tumor of the liver are not well defined owing to its rarity. On computed tomography, it is usually described as a huge liver mass with heterogeneous enhancement, central necrosis, and in some cases with intratumoral calcification if associated with a teratoma. The tumor cells are immunopositive for AFP, glypican-3, SALL4, and AE1/3 and are immunonegative for CD30, CK7, CK20, Hep Par1, and Arginase 1, which rule out the close histomorphological differentials such as metastatic carcinoma, embryonal carcinoma, and hepatocellular carcinoma (HCC). HCC is characterized by the presence of bile, strong Hep Par1, arginase, albumin, polyclonal carcinoembryonic antigen in canalicular pattern expression, and low SALL4 staining. Shiller-Duval body

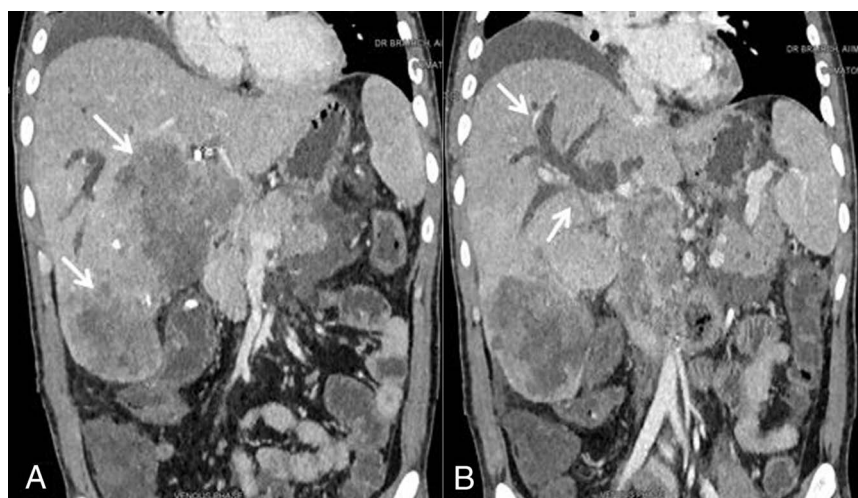


Figure 2. Coronal reformatted contrast-enhanced computed tomography image showing (A) large hypodense masses in both lobes of the liver (arrows) and causing (B) dilatation of the biliary tract (arrows).

is pathognomonic of a yolk sac tumor if identified and can be used to differentiate from HCC.

Most reported cases were managed with surgery along with chemotherapy.^{1,2,4} Our patient had an unresectable disease at presentation and was planned for chemotherapy, followed by a local therapy. The prognosis of this tumor is unclear. One patient was reported to have responded to neoadjuvant chemotherapy.⁸ However, many other reported patients died of the disease despite the use of an aggressive therapeutic strategy.^{9,10} Similarly, our patient responded poorly to the first 2 lines of chemotherapy. The options for platinum refractory GCT are high-dose chemotherapy with stem-cell rescue and a newer gemcitabine-based regime. Our patient was planned for gemcitabine and oxaliplatin, considering his ECOG performance status 3. Nonseminomatous histology, extragonadal site, and presentation with jaundice which delayed chemotherapy, unresectable disease, and platinum refractoriness can be considered as poor prognostic features in the present case.

Although rare, primary yolk sac tumor of the liver should be considered as a differential diagnosis in young patients with large cystic tumors with necrosis and significantly elevated AFP in noncirrhotic patients.

DISCLOSURES

Author contribution: All authors collected data and wrote the manuscript. I. Vanidassane is the article guarantor.

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Informed consent was obtained for this case report.

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