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Case Report

Primary Hepatic Yolk Sac Tumor: A Case Report of a Ruptured Tumor in a 22-month-old Boy

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Submitted: 26 November 2014

Accepted: 18 January 2014

Published: 21 January 2014

Keywords

- Yolk sac tumor
- Germ cell tumor
- Liver

Abstract

Primary hepatic yolk sac tumor is a rare extra-gonadal germ cell tumor in children and adults. Two important differential diagnoses for hepatic tumor in a pediatric patient are hepatocellular carcinoma and hepatoblastoma. A 22-month-old boy presented to our hospital with acute respiratory distress and increased serum alpha-fetoprotein. His symptom was caused by a ruptured massive intraabdominal tumor into the pleural space, which was identified during radiological workup. Surgical resection was performed and histological examination revealed the typical endodermal sinus pattern with additional solid, microcystic, polyvesicular, and hepatoid patterns. Absence of similar lesion in the gonads and other sites established the diagnosis of primary yolk sac tumor of the liver. The patient responded well to the adjuvant chemotherapy, which consisted of cisplatin, etoposide, and bleomycin. Our case illustrates the diagnostic challenge of an extremely rare primary hepatic yolk sac tumor and the improved survival rate with multimodal therapy. Considering this rare entity as a differential diagnosis of liver tumors in children is important for timely diagnosis, appropriate management, and accurate prognostication.

INTRODUCTION

Yolk sac tumor (YST), also known as endodermal sinus tumor, is the most common germ cell tumor in children. Although the majority of the tumors occur in gonads, 10-15% of YSTs arise in extra-gonadal sites. Anterior mediastinum, central nervous system, vagina, retroperitoneal and sacrococcygeal regions are the most common extra-gonadal sites of YST [1]. Primary YST of the liver, first reported by Hart in 1975, are extremely rare [2].

Because of its rarity, YST is often not considered in the differential diagnosis of hepatic tumors. Diagnosticians including pediatricians, pathologists, and radiologists should be aware of this uncommon but important entity. The diagnosis relies heavily on histologic examination due to the nonspecific clinical and radiological findings. The possibility of metastatic YST from gonads or other sites should be ruled out prior to making the diagnosis of primary hepatic YST. The distinction of YST from other types of hepatic tumors is important for appropriate therapy and accurate prognostication. We herein report a case of ruptured YST of the liver into parietal pleura in a 22-month old boy.

CASE PRESENTATION

A 22-month-old male patient who was previously diagnosed with pneumonia presented with worsening respiratory status despite a 7-day course of oral antibiotic (cefprozil). Physical examination revealed decreased breath sounds on the right lung and laboratory results showed leukocytosis (23,000/uL). Right lower lobe consolidation with small pleural effusion was also found on the chest x-ray. He was admitted overnight and discharged to complete one-week treatment of intramuscular ceftriaxone.

During the course of therapy, the patient fell into the right side of his chest and he immediately became pale, tachypneic and tachycardic. Chest x-ray showed left mediastinal shift and total opacification of the right lung. He was admitted to pediatric intensive care unit and chest tube placement yielded 1 liter of serosanguineous fluid. CT scan showed a large tumor (9.3 cm in largest dimension) occupying the right lobe of the liver (Figure 1) and extending through the diaphragm into the right thorax. In addition, his serum alpha-fetoprotein (AFP) level was markedly elevated, 6811 ng/mL (normal < 10 ng/mL). Patient subsequently underwent partial resection of the liver (trisegmentectomy) and lung (right lower lobectomy) in addition to removal of the right parietal pleura and diaphragm.

Pathological examination of the liver tumor revealed a yolk-sac tumor. Histologically, the tumor displayed the typical endodermal sinus pattern (Figure 2) with additional solid, microcystic, polyvesicular, and hepatoid patterns. Prominent mitotic activity

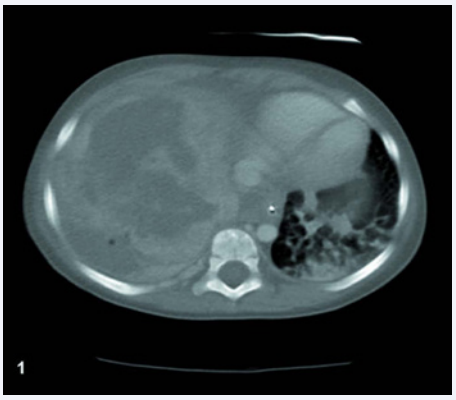

Figure 1 CT scan showed a large intraabdominal tumor occupying the right lobe of the liver.

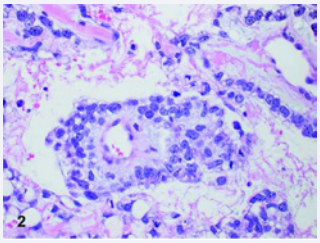

Figure 2 Schiller-Duval body, characteristic of yolk sac tumor (hematoxylin-eosin, 400x).

and focal necrosis were also seen. Immunohistochemistry studies revealed the tumor cells were positive for cytokeratin, alpha-a-antityrpsin, and alpha-fetoprotein immunostains. Gross and microscopic examination revealed the tumor was extending through the diaphragm into the parietal pleura. However, there was no tumor invasion into the lung tissue. The resection margins were positive and lymph nodes were negative for malignancy. Testicular examination and ultrasound revealed no tumor involvement in the gonad. Based on these findings, the patient was deemed to have stage II primary hepatic yolk sac tumor (Children's Oncology Group Staging). Consequently, the patient was treated with adjuvant chemotherapy, consisted of 3 cycles of cisplatin, etoposide, and bleomycin.

His AFP level decreased to 108 ng/ml after the surgery and it became normal (4 ng/ml) after his second cycle of chemotherapy. He was monitored with serial CT scans and serum AFP level during and after the adjuvant chemotherapy. The patient is doing well at the time of writing (3 years after the surgery) with normal serum AFP level and no evidence of tumor recurrence.

DISCUSSION

Primary YST of the liver is an exceedingly rare tumor that occurs in children and adults. Although this entity has been described for decades, its etiology and pathogenesis are still obscure. The tumor is thought to arise from aberrant migration of germ cell tumors during embryonic development [2]. Other explanations include displacement of blastomers in the early stage of embryogenesis and evolution from pluripotent somatic cells [4,5].

The initial presentation of our patient was acute respiratory distress caused by ruptured hepatic tumor. He was known to have hepatic lesion only after he underwent radiological examination during the latest admission. The radiological findings showed a large necrotic or hemorrhagic hepatic tumor and definitive diagnosis of yolk sac tumor was reached on the basis of histological examination.

The diagnosis of this lesion is challenging because of its low frequency and the nonspecific clinical and radiological findings. Enlarging abdominal tumor with space occupying lesion effects are the most common clinical presentations of many hepatic tumors including YST of the liver. A small study reported that 88% of primary hepatic YST showed central necrosis and intratumoral hemorrhage on cross-sectional imaging. However, these findings may also be seen in hepatoblastoma and other hepatic lesions [6].

Hepatoblastoma and hepatocellular carcinoma (HCC), the two most common primary hepatic tumors in children, are the most important differential diagnosis for primary hepatic YST. Increased serum AFP may be seen in all of these tumors, thus it is not a reliable marker to differentiate these hepatic lesions. Histologically, hepatoblastoma and hepatocellular carcinoma may resemble hepatic YST. The embryonal subtype of hepatoblastoma often shows primitive tumor cells and the hepatoid pattern of YST is similar to HCC. Furthermore, it is important to remember that hepatic YST may coexist with other components. Combination of primary YST of the liver with hepatocellular carcinoma, hepatoblastoma, and teratoma have been reported [7,8,9,10].

The characteristic microscopic finding of yolk sac tumor is the AFP-positive epithelial cells, which form Schiller-Duval bodies [11]. The structure has a distinct papillary architecture with central thin-walled blood vessel surrounded by cells with hobnail appearance (Figure 2). Cytoplasmic hyaline globules, which are positive for Periodic-Acid Schiff immunostain, can also be seen in this lesion [3,11].

SAL-like protein 4 (SALL4), a transcription factor in the embryonic stem cells, is a useful marker to diagnose extra-gonadal germ cell tumors including YST [12]. However, SALL4 immunoreactivity has also been seen in hepatoblastoma and HCC. The protein is immunoreactive in the embryonal subtype of hepatoblastoma [13]. Furthermore, Gonzalez-Roibon et al. reported that focal nuclear expression of SALL4 was seen in 46% of HCC cases [14]. Different protein expression pattern was observed in YST and HCC. Diffuse finely granular nuclear expression was seen in YST in comparison to punctuate/clumped nuclear pattern in HCC. SALL4 has also been shown to be a marker for progenitor subclass of HCC with an aggressive phenotype [15].

Definitive diagnosis is essential to determine the management of these patients. Primary hepatic YST and hepatoblastoma are often treated with multimodal therapy including surgery and chemotherapy. Meanwhile, complete surgical resection is often the only curative treatment for HCC because of its chemoresistance [16].

Tumor stage is determined after the surgery. Children Oncology Group classified extra-cranial germ cell tumors into

stage I (localized disease), stage II (microscopic residual disease), stage III (gross residual disease), and stage IV (presence of distant metastasis) diseases.

The recommended adjuvant chemotherapy for extra-gonadal germ cell tumor includes cisplatin, etoposide, and bleomycin [17]. This regimen of chemotherapy has improved the prognosis of patients with extra-gonadal YST. Our patient showed good response to the adjuvant chemotherapy based on his serial serum AFP level, clinical, and radiological evaluation. In comparison, the first case reported was an 18-month old boy who died of widespread metastasis after an extended right hepatectomy, chemotherapy (actinomycin D, methotrexate, and cyclophosphamide), and radiotherapy [2]. Furthermore, Abramson et al. recently reported the first successful orthotopic liver transplantation in a young patient with an unresectable primary hepatic YST [10].

CONCLUSION

Primary hepatic YST is a rare but an important entity to consider in children with liver tumors. Its main differential diagnoses are hepatoblastoma and HCC. Histological examination is the most reliable method to differentiate hepatic YST from other liver lesions. Multimodal therapy including chemotherapy with cisplatin, etoposide, and bleomycin has improved the prognosis of patients with primary hepatic YST.

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Cite this article

Putra J, Ornvold K, Suriawinata AA (2014) Primary Hepatic Yolk Sac Tumor: A Case Report of a Ruptured Tumor in a 22-month-old Boy. JSM Clin Case Rep 2(1): 1015.