

Case Report

Polycystic liver coexistent with hepatoblastoma: a case report of misdiagnosis

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Abstract: Hepatoblastoma (HB) complicated with polycystic liver disease (PLD) is a rare disease. Herein, we report a 14 years old girl with hepatoblastoma misdiagnosed with polycystic liver with intracystic infection and hemorrhage. Computed tomography (CT) scan showed an enlarged right lobe of the liver and a number of different sizes of circular liquid density shadow. Histopathological examination suggested the liver cell tumor (HB) mixed with the leaf type and fetal type. Right hepatectomy followed by postoperative high dose of cisplatin and doxorubicin chemotherapy were initiated. The patient was followed up for half a year without tumor recurrence. The malignant tumor should be discovered earlier and confirmed to improve the prognosis.

Keywords: Hepatoblastoma, polycystic liver disease, tumor

Introduction

Hepatoblastoma (HB) is a rare malignant tumor in young children which originates from immature embryo cells. Its incidence is around 1.2-1.5 per million children younger than 15 years old in Western countries [1]. The incidence was even lower in developing countries because of the large number of hepatitis B infection which leads to relatively higher incidence of hepatocellular carcinoma. The most common clinical manifestation of HB is abdominal mass or local compression by the large tumor. Some other clinical symptoms include jaundice, abdominal pain, tumor rupture, and hemorrhage.

Hemangioma is the most common hepatic tumor that accounts for up to 60% among all the cases [2]. As the treatment methods for HB is largely different from hemangioma, early diagnosis is the key for successful treatment. However, the clinical features of hemangioma and HB are extremely similar therefore misdiagnoses were common [3, 4]. For the imaging of the HB, computed tomography (CT) scans usually presents as single giant hybrid density mass with liquefaction and necrosis which often locates in the right lobe of the liver. Upon the multidisciplinary treatment including che-

motherapy, surgical resection, and liver transplantation, the survival rate of HB increases from 20% to 80% over the past decades in developed countries [5]. However, in developing countries, the experience of pediatric surgeon is rather insufficient, which is the main reason of misdiagnosis that consequently leads to lower survival rate, especially in non-typical cases [6]. Polycystic liver disease (PLD) typically exists as an extra-renal manifestation of autosomal dominant polycystic kidney disease (ADPKD). Due to the popularization of the imaging diagnostic methods such as B ultrasound and CT, PLD incidence was increased. More than half of the PLD patients combine with polycystic kidney. PLD often affects the whole liver with a small amount of lesions were still limited in one hepatic lobe or semi-liver [7]. Cholangiocarcinoma, a malignant complication of PLD, has been reported in a total of 10 cases [8-10]. While in this report, we present a rare case of polycystic liver coexisted with HB, which has never been reported before (**Table 1**).

Case report

A 14-year-old girl was admitted to our hospital with chief complaint as reiterative fever and anemia for a month. The girl has been diag-

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Table 1. Database search results for polycystic liver disease and hepatoblastoma up to July 17, 2016

Electronic databases	Search strategies	Results
PubMed (NLM)	(Polycystic liver disease) AND (Hepatoblastoma)	No original articles, case reports or review articles
LISTA (EBSCO)	(Polycystic liver disease) AND (Hepatoblastoma)	No original articles, case reports or review articles
Library of congress	(Polycystic liver disease) AND (Hepatoblastoma)	No original articles, case reports or review articles



Figure 1. Computed tomography (CT) scan of the abdomen. The right lobe of the liver was enlarged and a number of different sizes of circular liquid density were found.



Figure 2. The tumor appearance. Right hepatic giant tumor with both solid and cystic components space-occupying. The left liver was normal.

nosed as polycystic liver by ultrasonography and CT since she was 10 years old. Family his-

tory: her mother showed a history of polycystic kidney disease, and no other family history of related disease was reported. Her patients did not have drinking or smoking history during pregnancy. As there was no significant symptom, she received no treatment at that time.

Upon examination, the patient exhibited 146 cm tall and 47 kg on admission. She did not suffer from nausea, vomiting, abdominal pain, cough, or black stool. Menstruation was normal. She presented pale appearance. Physical examination revealed the temperature was 39.5 degrees Celsius, the blood pressure was 125/68 mmHg, and heart rate was 125 bpm. Superficial lymph nodes were not palpable. Abdominal examination demonstrated abdomen bulging without tenderness or rebound tenderness. A soft mass could be touched in the abdominal right upper quadrant. Other physical examination results were normal. Hematologic tests revealed that hemoglobin level was 42 g/L, while the white blood cell (WBC) count was $13.82 \times 10^9/L$, N: 96%. Other laboratory parameters were listed as followed: albumin (ALB) was 25.4 g/L, total bilirubin (TBIL) was 20.4 $\mu\text{mol/L}$, alanine aminotransferase (ALT) was 22 U/L, hepatitis B surface antigen was negative, alpha-fetoprotein (AFP) level was 7.77 ng/ml (reference range: <10 ng/ml), and CA-199 was 680.6 U/ml (reference range: 0-39 U/ml). Urine routine and stool routine were both normal. CT and abdominal ultrasound both revealed a polycystic occupying lesion on the right lobe of liver (**Figure 1**).

She was diagnosed with a polycystic liver with infection, therefore an anti-infection treatment was performed and the symptoms obtained remission and elimination. Before admission, she received 0.5 g imipenem intravenously every 8 hours for 7 days. Seven days later, her temperature showed an upward trend up to 40.5 degrees Celsius, together with progressive decrease in hemoglobin and abdominal mass enlargement. She was then admitted to hospital for further examination.

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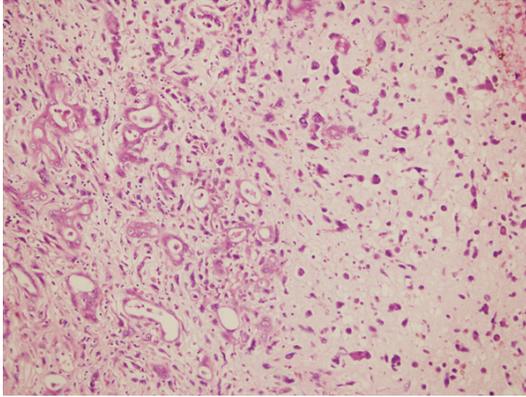


Figure 3. Histopathological examination report. Hepatoblastoma, mesenchymal mixed with a small amount of fetal type (hematoxylin-eosin staining).



Figure 4. Tumor size. The size of the tumor was 18×13×6 cm.

After admission, her fever did not go down. Considering sustained decline of the patient's hemoglobin might be caused by the existence of intraperitoneal hemorrhage or intracystic hemorrhage, we proposed to perform an exploratory laparotomy and resect the possible tumor after correction of her hemoglobin level up to 5.6 g/μL by transfusion. The right hepatic giant space-occupying tumor contained both solid and cystic components (**Figure 2**). The lesion boundary was clear with separated bursa, haemorrhaged central necrotic area, and high inner cyst pressure. Lymph nodes of the hepatic duodenal ligament were enlarged and fused into clusters. The texture of the left liver was

normal, and there were no positive findings in the abdominal cavity.

Pathological diagnosis of frozen section during operation revealed a malignant tumor, with the primary consideration of HB. Therefore, she received a right hemihepatectomy that all of the small branches arising from the right lobe to the inferior vena cava were ligated and dissected. Lymph nodes of hepatic portal, hepatic artery and hepatoduodenal ligament were also dissected.

After the operation, the patient was transferred to ICU for 2 days. The final pathology reported that it was HB composed of mesenchymal mixed with a small amount of fetal-type tumor cells [11] (**Figure 3**). The tumor was weighted 6.3 kg with the maximum diameter of 18.9 cm (**Figure 4**). No tumor cells were found on the cutting edge, and the lymph node of hepatoduodenal ligament showed positive metastasis (1/3). Immunohistochemistry results (**Figure 5**) exhibited positive staining of cellular tumor antigen p53 (P53), Cytokeratin 19 (CK19), Glypican-3 (GPC) and vascular endothelial growth factor (VEGF) [12] and it was negative for alpha-fetoprotein (AFP) and Hepatocyte (hepatocellular carcinoma marker).

The patient showed a good postoperative recovery after the surgery with normal body temperature and blood routine after the surgery. CT scan re-examination demonstrated the increased compensatory of left lobe. According to the intraoperative findings, postoperative pathological examination, and the Childhood Liver Tumors Strategy Group (SIOPEL) in 2014 [13], the patient was diagnosed as a high risk type of HB. She received high dose of cisplatin and doxorubicin chemotherapy after the surgery [14]. No recurrence or metastasis was observed after three months of follow-up.

Discussion

In this case report, we presented a rare case of hepatoblastoma complicated with polycystic liver disease and firstly misdiagnosed as simple PLD. This case report raised the importance of hepatoblastoma recognition and diagnosis in young children.

Hepatoblastoma is the third most common tumor in children, following the neuroblastoma and the neuroblastoma, which accounts

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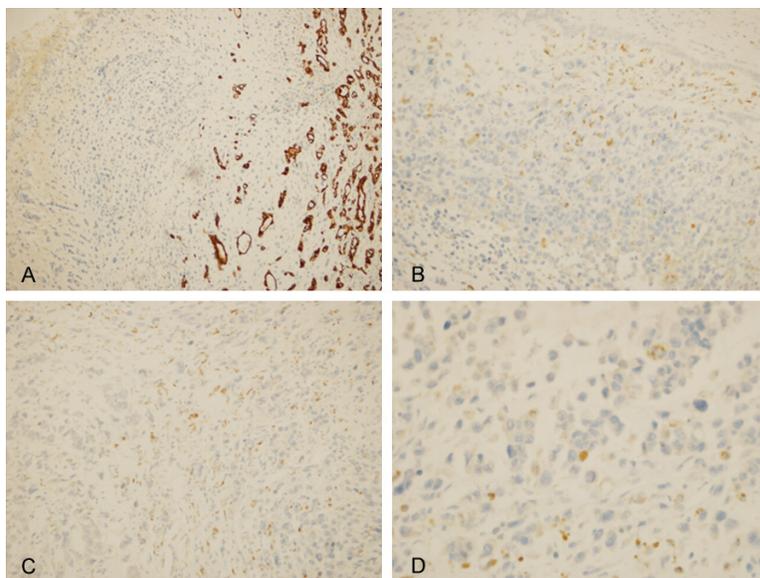


Figure 5. Immunohistochemistry staining of the surgically resected tumor tissue. A. Positive staining for CK19; B. Negative staining for AFP; C. Scattered weak positive staining for GPC-3; D. Negative staining for Hepatocyte (hepatocellular carcinoma marker).

for approximately 1% of pediatric malignant cancer. In recent years, it was found that the occurrence of HB was closely related to pre-term births and low birth weight [15]. In addition, some factors such as drugs (e.g. furosemide and total parenteral nutrition), radiation exposure, familial adenomatous polyposis, and Beckwith-Wiedemann syndrome may also be associated with the onset of HB [16]. It may be also associated with maternal exposure to carcinogens, such as petroleum products, paints, and pigments. Recent findings were mainly focused on lessons learned from the experiences of the Childhood Liver Tumors Strategy Group (SIOPEL). Moreover, it provided current treatment guidelines of HB in different levels of risk [13]. Standard risk HB (SR-HB), defined as tumor confined to the liver and involved within the most three hepatic sectors (PRETEXT I-III), and AFP >100 ng/ml that can be treated by the less-toxic cisplatin monotherapy. High risk HB (HR-HB), defined as tumor involving in all four liver sectors (PRETEXT-IV), vascular invasion (V/P+), extrahepatic disease (E+/M+), or low alpha-fetoprotein (AFP <100 ng/ml) at diagnosis or tumor rupture, which can be treated by intensified chemotherapy called Super PLADO (cisplatin alternating with carboplatin-doxorubicin) [13, 14]. In our case, the pathological finding confirmed the diagnosis of high-risk hepatoblastoma. Therefore, her treatment regimen

was high-dose of cisplatin and doxorubicin chemotherapy.

PLD is an autosomal dominant genetic disorder characterized by congenital polycystic disease with a familial tendency. It usually showed covert morbidity and progressed slowly without clinical symptom at the early stage. Along with the cysts developing, it can cause abdominal pain, fatigue, anorexia, and abdominal mass. In severe cases, some PLD can cause compression of the inferior vena cava, hepatic vein outflow tract obstruction, portal hypertension, and bile duct obstruction. Moreover, they may induce ascites, gastrointestinal bleeding, and jaundice

and complicated with recurrent hemorrhage and infection. PLD was divided into 3 types according to the imaging findings. Type I: Fewer than 10 Cysts larger than 10 cm in diameter. Type II: A small part of liver parenchyma involved. Type III: The major liver parenchyma involved by small and medium-size cysts. At present, the major surgical options are percutaneous puncture cysts fluid drainage, sclerosis treatment, cyst fenestration, Partial liver hepatectomy with fenestration, and liver transplant. In this case, the patient was diagnosed as PLD by CT showing a typical presentation of PLD with diffused distribution of cystic mass in the liver with sharp edges, unequal sizes, and no enhancement after enhancement at ten years old. Four years later, this patient had fever and anemia, which was misdiagnosed as simple PLD complicated with bleeding and infection.

Further differential diagnosis in this patient included hepatitis. This patient showed negative hepatitis B and hepatitis C virus infection, or other liver diseases including autoimmune diseases. Meanwhile, AFP level was normal. AFP would be normal in infants and children with HB under these three conditions. These conditions include: ① Immature HB with high malignancy and AFP regeneration. ② Well-differentiated HB. ③ Fibro-lamellar hepatocellular carcinoma with normal serum AFP. CT plain and

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enhanced scan is an important method for the diagnosis of HB. Combined with clinical manifestations and laboratory tests, the diagnosis and differential diagnosis of typical HB are not difficult. Older children can also occur HB with a variety of nontypical manifestations. After chemotherapy, the patient exhibited a good recovery after surgery and chemotherapy. The future follow-up plan included once hospital visit every 3 month for half a year followed by once visit every half a year.

In conclusion, we reported a patient with hepatoblastoma complicated with polycystic liver. The low incidence of hepatoblastoma in children and non-specific initial symptoms make the diagnosis difficult. It represents a diagnostic challenge since the prognosis could be better upon early detection of hepatoblastoma. It may provide a new idea for the diagnosis of HB by clinicians and radiologists. However, whether the prolonged existence of polycystic liver is the risk factor for hepatoblastoma, or whether hepatoblastoma and polycystic liver share similar etiologic process remains to be investigated.

Disclosure of conflict of interest

None.

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