Hepatoblastoma in Infant: A Rare Case Report and Literature Review

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ABSTRACT

Introduction: Hepatoblastoma is the most common liver malignancy in children. Hepatoblastoma in infants is rare and usually presents as an abdominal mass without specific symptoms. Diagnosis is difficult, supported by adequate imaging modalities, liver biopsy, and hepatoblastoma marker testing.

Case Presentation: A 3-month-old boy presented with a chief complaint of abdominal mass 3 days after birth without any other complaints. Nutritional status was normal. Vital signs were stable. Physical examination revealed anemic conjunctiva, hepatomegaly, and a palpable lump in the right upper quadrant of the abdomen. The laboratory results were Hb 8.2 g/dL, AST 45 U/L, ALT 13 U/L, gamma-GT 218.2 U/L, alkaline phosphatase 200 U/L, total bilirubin 3.00 mg/dL, direct bilirubin 1.40 mg/dL, Rubella IgG Reactive (20.60 IU/mL), CMV IgG Reactive (145.1 AU/mL), LDH 404 U/L, and Alpha-fetoprotein 5720.45 ng/mL. Abdominal ultrasound was consistent with a malignant liver mass, possibly hepatoblastoma, with a heteroechoic mass +/- 6.57 x 7.21 x 6.76 cm in the right and left liver lobes. A computed tomography scan of the abdomen confirmed the hepatoblastoma in segments V, VI, VII, and VIII of the right lobes with hepatomegaly.

Conclusion: The possibility of hepatoblastoma should be considered when an infant presents with a complaint of an abdominal mass without specific symptoms. In children younger than 2 years, radiologic confirmation of hepatoblastoma is sufficiently accurate, especially when supported by elevated AFP in facilities with limited liver biopsies.

INTRODUCTION

Hepatoblastoma is the most common pediatric liver malignancy. Hepatoblastoma is the third most common solid abdominal tumor in young children after neuroblastoma and nephroblastoma.1 Hepatoblastoma is difficult to diagnose early because it usually presents as an asymptomatic abdominal mass with no systemic symptoms.2 The case of a 3-month-old boy diagnosed with hepatoblastoma is reported. This article briefly reviews hepatoblastoma.

CASE PRESENTATION

A 3-month-old boy presented to the Hepatology Clinic of Dr. Soetomo General Academic Hospital, Surabaya with the chief complaint of an abdominal lump. The parents found a lump on the right side of the abdomen. The lump had been present for 3 days after birth. The patient had no jaundice, pale stools, fever, or vomiting. The patient is the second child born by cesarean section, full term, weighing 2700 grams, birth length 42 cm, crying at birth, yellow at 2 days of age, and disappeared after that. The patient's immunization history is routine and complete. The patient is currently breastfeeding until 2 months of age and formula feeding. The patient's development is age-appropriate, and the patient can lift his or her head and smile. There is no family history of malignant disease. The patient's general condition was comos mentis. Body weight was 6600 g, body length 62 cm. Based on the anthropometric status, a normal nutritional status was obtained. The vital signs were stable. Physical examination revealed anemic conjunctiva and non-icteric sclera. Abdominal examination revealed distended, palpable hepatomegaly and a lump in the right upper quadrant. Laboratory examination showed Hemoglobin 8.2 g/dL, HCT 24.4%, White blood cells 19.00 x10³/µL, platelets 549 x10⁵/µL, MCV 98.0 fl, MCH 33.6 pg, MCHC 29.7 g/dL, AST 45 U/L, ALT 13 U/L, Gamma GT 218.2 U/L, Alkaline Phosphatase 200 U/L, Total Bilirubin 3.00 mg/dL, Direct Bilirubin 1.40 mg/dL, Albumin 2.49 g/dL, BUN 3.0 mg/dL,
Creatinine serum 0.4 mg/dL, FT4 1.05 ng/dL, and TSH 6.0300 uIU/mL. Immunology examination showed Toxoplasma IgG Non-Reactive (0.0), Toxoplasma IgM Non-Reactive (0.09 IU/mL), Rubella IgG Reactive (20.60 IU/mL), Rubella IgM Non-Reactive (0.04), CMV IgG Reactive (145.1 AU/mL), CMV IgM Non-Reactive (0.09 index), Lactate Dehydrogenase (LDH) 404 U/L, and Alpha Feto Protein (AFP) 5720.45 ng/mL.

Abdominal ultrasonography revealed a heteroechoic mass with multiple hypoechoic lesions inside, well-defined borders, lobulated edges, size +/- 6.57 x 7.21 x 6.76 cm (AP x ML x CC) on the right and left lobe of the hepatic which on CDUS showed intra and perilesional vascularization; the mass pushed the right kidney to the inferior side. The lien measured longitudinal length +/- 4.92 cm, echo intensity of parenchyma appeared normal, and no mass/cyst was seen. The gallbladder, pancreas, and kidney were within normal limits. Abdominal ultrasound showed a heteroechoic mass +/- 6.57 x 7.21 x 6.76 cm in the right and left liver lobes supporting a malignant liver mass, probably hepatoblastoma.

Decreased gallbladder contraction index suggestive of biliary atresia. Liver, pancreas, and right and left Kidneys were normal.

The Abdominal CT Scan revealed a solid mass (50 HU) in the liver with a necrotic area in the center (23HU), irregular edges, partially indistinct borders, with a calcified component inside (123HU), size +/- 3.4 x 3.1 x 4.8 cm impression in segments V, VI, VII, VIII of the right lobe of the liver, which on contrast administration showed contrast enhancement (98 HU) in the solid component; the mass impression was feeding from the right a. hepatica; no v. porta/hepatica thrombus image was seen. In the lien, there was a picture of kissing lien (+), normal parenchymal density, no mass/cyst was seen. There was extraluminal free fluid density (14 HU) in the abdominal cavum. There was no locoregional KGB enlargement. No osteolytic/osteoblastic process was seen. The abdominal CT scan showed the above findings supporting the hepatoblastoma segments V, VI, VII, and VIII right lobes. There was hepatomegaly and ascites (minimal).

**Figure 1. Abdominal ultrasound**

**Figure 2. Abdominal CT scan**

**DISCUSSION**

Malignant tumors of the liver are very rare in children. Pediatric malignant liver tumors, consisting of hepatoblastoma and hepatocellular carcinoma, account for approximately 1.3% of all pediatric malignancies. Together, they account for nearly 80% of primary liver malignancies in...
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children and adolescents. In children younger than 5 years, the incidence of hepatoblastoma, acute lymphoblastic leukemia, acute myeloid leukemia, ependymal tumors, and neuroblastoma is increasing. However, hepatoblastoma showed rising in all regions except South Asia. The incidence of hepatoblastoma has increased over the past 30 years. The annual incidence rate of hepatoblastoma in the United States is 1.76 per million people, and the incidence is increasing over time. The incidence of hepatoblastoma is highest in infants and children under 5 years old, but cases above 5 years old have also been reported. Studies mention the increased incidence of hepatoblastoma in patients 2 to 4 years of age and males. Hepatoblastoma is most commonly present in infants and young children. Hepatoblastoma occurred in a 3-month-old infant in this case. Studies suggest that very low birth weight (<1,500g) preterm infants have an increased risk of hepatoblastoma. However, an explanation for this unintended or causal association cannot be determined. This was different in patients born full-term with a birth weight of 2700 grams.

Hepatoblastoma usually presents as an asymptomatic abdominal mass without systemic symptoms. As in this case, there was a complaint of an enlarged abdomen with a palpable mass without specific symptoms. Hepatoblastoma can remain without symptoms for months. Often, enlargement of the right upper abdomen occurs without pain. When hepatoblastoma begins to cause symptoms, it is almost always a sign that the disease has reached an advanced stage. Diagnosis of pediatric liver tumors is difficult due to their rarity. High-quality cross-sectional imaging is essential for the diagnosis, risk stratification, and treatment of hepatoblastoma. The use of three-phase computed tomography or magnetic resonance imaging is recommended. Magnetic resonance imaging (MRI) is commonly used to characterize focal liver masses in children because of its superior contrast resolution. It helps distinguish common benign entities from other liver pathologies. Imaging is essential for the diagnosis of primary liver malignancies. Ensuring adequate imaging allows for proper management. Liver tumors have a tendency to be aggressive and a complete workup is essential for determination of the extent of disease. The PRETEXT (PRA-Treatment Extent of tumor) system describes risk stratification for hepatoblastoma. The PRETEXT system is made up of two components: the PRETEXT group and the annotated PRETEXT factor. The PRETEXT group describes tumor extent within the liver, while factor annotations help describe related features (either portal vein or hepatic vein inferior vena cava), extrahepatic disease, multifocality, tumor, and metastatic disease. Computed tomography (CT) scans have been the primary imaging modality used to determine tumor characteristics, including tumor size and extent, in most cases to date. Hepatoblastoma is usually unifocal in the right lobe but can be multifocal and develop in all liver segments. In this case, the abdominal CT scan showed the hepatoblastoma segments V, VI, VII, and VIII right lobes.

Histopathology is usually required for definitive diagnosis. However, the risk of post-biopsy bleeding requiring transfusion may occur in up to 26% of cases. Another study found that percutaneous liver biopsy is safe and effective for diagnosing hepatoblastoma, and the complication rate is very low. A liver biopsy was not performed in this case because the family refused. With the abdominal CT scan results supporting hepatoblastoma along with elevated AFP levels, the diagnosis of hepatoblastoma can be made. Laboratory workup for hepatoblastoma includes blood tests. Mild anemia, leukocytosis, and thrombocytosis may be found in hepatoblastoma. Liver function tests (ALT, LDH, AP may be slightly elevated) include bilirubin. Tumor markers associated with hepatoblastoma include alpha-1-fetoprotein (AFP) and beta-human chorionic gonadotropin (beta-HCG). AFP is elevated in 80% to 90% of patients. In this case, the laboratory showed anemia Hb 8.2 g/dL with thrombocytosis 549x10^9/µL. However, liver enzymes were normal (AST 45 U/L and ALT 13 U/L). Gamma GT 218.2 U/L which is slightly elevated. There were slightly elevated bilirubin levels (total 3.00 mg/dL, direct bilirubin 1.40 mg/dL), hypoalbuminemia (albumin 2.49 g/dL), with lactate dehydrogenase (LDH) 404 U/L and alpha-feto-protein (AFP) 5720.45 ng/mL. In children under 2 years of age, radiologic diagnostic accuracy for liver malignancies was 81.8% (95% CI, 72.2 to 89.2%), which increased to 92.1% (95% CI, 84.3 to 96.7%) after correlation with AFP. Hepatoblastoma is associated with variable elevated alpha-fetoprotein (AFP) levels at diagnosis. AFP levels of less than 100 ng/mL at the time of diagnosis of hepatoblastoma are associated with a poor prognosis, with lower survival rates. Hepatoblastomas are considered aggressive and have a poor prognosis when AFP levels are low (<100ng/ml). For most cases of primary liver tumors, preoperative neoadjuvant chemotherapy, surgical resection, and postoperative chemotherapy were used. Minimal postoperative chemotherapy such as using cisplatin, fluorouracil, and vincristine is also given to control hepatoblastoma that is resected at the time of diagnosis. Today, the survival rate for patients with hepatocellular carcinoma is more than 90% for patients with standard tumors and 45-80% for patients with metastatic disease. Disease-free survival varies depending on the stage of the disease, from chemotherapy and surgical resection to liver transplantation. The overall survival rate at ages 5 and 10 years was 81.5% and 81.0%, respectively. However, younger age (2-4 years) was associated with shorter overall survival. In another study, it is stated that the 3-year event-free survival rate of children with hepatoblastoma is 88%, and among them, there is a recurrence. The 5-year event-free survival rate was 88% and overall survival was 95% for hepatoblastoma receiving chemotherapy without complete resection at diagnosis. A complete surgical resection is
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usually necessary for survival improvement. Significantly, the size of the tumor was found to be a strong predictor of overall survival in pada hepatoblastoma. According to the Children’s Hepatic Tumors International Collaboration-Hepatoblastoma Stratification (CHIC-HS) system introduced in 2017, the 5-year event-free survival rates were 90.0%, 82.8%, 73.5%, and 51.3% in the very low, low, intermediate, and high-risk groups.

REFERENCES


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