Priya et al., J Clin Case Rep 2019, 9:5
DOI: 10.4172/2165-7920.10001240

Journal of Clinical Case Reports

Case Report Open Access

Hepatoblastoma-An Unusual Presentation: A Case Report

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Abstract

Hepatoblastoma (HB) is the most common primary hepatic malignancy in children and accounts for 43% of the pediatric liver tumors. The usual presentation is the presence of an abdominal mass, vomiting, elevated α-fetoprotein levels and thrombocytosis and it occurs in infants and children under 3 years of age. A 6-year-old male child presented to the outpatient department with complaints of mild to moderate grade fever, vomiting and loose stools for 3 days. The child was otherwise active and there was no palpable abdominal mass. USG abdomen and CT scan revealed the presence of an encapsulated solid hepatic tumor suggestive of HB. Complete blood count showed an elevated WBC count, high ESR and high α-fetoprotein levels (958 ng/ml) but no thrombocytosis. A non-anatomical excisional biopsy of the tumor confirmed it to be hepatoblastoma. The unusual features noticed in this case was presentation at a slightly later age (6 years), absence of abdominal mass and absence of thrombocytosis.

Keywords: Hepatoblastoma; Thrombocytosis; Abdominal mass; Surgery

Introduction

In children, the third most common intra- abdominal site for malignancy is the liver. A report from the United States says that primary malignant liver tumors have an incidence of 1-1.5 per million children and hepatic tumors contribute to 1.3% of all pediatric malignancies [1]. Of these, two thirds of the hepatic neoplasms are hepatoblastoma (HB) and hepatocellular carcinoma (HCC). Hemangioma, hamartoma and focal nodular hyperplasia (FNH) are the other benign liver tumors [2]. HB has shown good survival rates of 70-80% after the introduction of chemotherapy (the earlier survival rates were below 30%) [3]. The annual incidence of HB has gradually increased in the past three decades [4].

In a majority of cases HB presents with elevated α-fetoprotein levels (AFP) which helps in diagnosis and monitoring treatment response and follow-up. It is usually diagnosed in the first 3 years of life. HB is usually sporadic, but it may be associated with genetic abnormalities like Beckwith-Wiedemann syndrome and familial adenomatous polyposis [5]. Premature babies with birth weight below 1 kg have a greater risk of developing HB. While the most common sign is an abdominal mass or an abdominal distention, this case presented unusually with no such clinical sign which made diagnosis challenging. CT, MRI and USG abdomen are the imaging techniques used for evaluation and surgical resection with chemotherapy is the treatment modality of HB. This unusual case presentation may alarm the pediatrician in a way to look for prompt diagnosis even in the absence of usual clinical signs and symptoms and hemogram values.

Case Report

A 6-year-old male child who was well and active till 3 days back reported with his parents to the outpatient department with moderate to high grade fever, vomiting and watery stools for 3 days. The loose stools had 4-6 episodes per day and not associated with abdominal pain and vomiting was non projectile with 5-6 episodes per day. The child had pain in the epigastric region, which was intermittent in nature, griping kind and increases severely after eating. There was no hematemesis and weight loss. General examination revealed a nourished child with height and weight appropriate for age. The weight was 19 kgs (75th percentile) and height was 120 cms (75th percentile). Patient did not have anemia, clubbing, cyanosis or jaundice and had a normal appetite till just before vomiting and loose stools episode. Abdominal examination showed a scaphoid abdomen with no palpable mass in any of the quadrants. There was no distension or free fluid and skin was clear over the abdomen.

Upon eliciting birth history, he was the first child FTND (full term normally delivered). The birth weight is 2.8 kgs and there's no history of neonatal issues or drug ingestion by the mother in antenatal period. The child showed normal physical and mental development and was immunized up to date. There's no history of radiation or drug ingestion. The present complaints were treated with zinc syrup, antibiotics, probiotics and antiemetics.

USG abdomen was done on the 3rd day which showed a homogenous mass in the right hypochondrium measuring 4.5 × 4 × 5 cms. Few enlarged mesenteric nodes were seen and colitis was present. Hematological investigations revealed an increase in total WBC count, elevated ESR and elevated α- fetoprotein levels of 958 ng/dl (normal value <20 ng/dl). CECT abdomen showed a lesion measuring 4.5 × 4.7 × 4.9 cms in segment V of liver suggestive of hepatoblastoma. The tumor looked encapsulated and no enlarged lymph nodes were seen either close to the tumor mass or away from it (Figure 1).

The Hepatitis markers for B and C were negative and HIV screen was also negative. The CT findings and lab parameters were all in favor of a hepatoblastoma. Since the tumor was localized and the location was deep, it was decided to not do a liver biopsy. Surgical examination by a pediatric gastrointestinal surgeon concurred with the diagnosis. A laparotomy with anatomical resection of the tumor mass was planned. A cardiac evaluation and general fitness were obtained pre-operatively.

Then laparotomy with non- anatomical resection of the exophytic lesion in segment V of liver, cholecystectomy and periportal lymphadenectomy was done and tissues were sent for histopathological testing. Histopathology showed liver parenchyma infiltrated by neoplastic cells arranged in nests. Lymph vascular and perineural invasion was not seen and the inked resected margin was free of tumor with a clearance of 1 cm. The gall bladder and the end of cystic duct was free of tumor. So, this tumor was staged as stage 1.

Repeat α-fetoprotein level showed a value of 58 ng/ml post surgically. Repeat USG abdomen showed absence of any residual

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Received April 12, 2019; **Accepted** April 25, 2019; **Published** May 02, 2019

Citation: Priya C, Varshini C, Biswakumar B (2019) Hepatoblastoma-An Unusual Presentation: A Case Report. J Clin Case Rep 9: 1240. doi: 10.4172/2165-7920.10001240

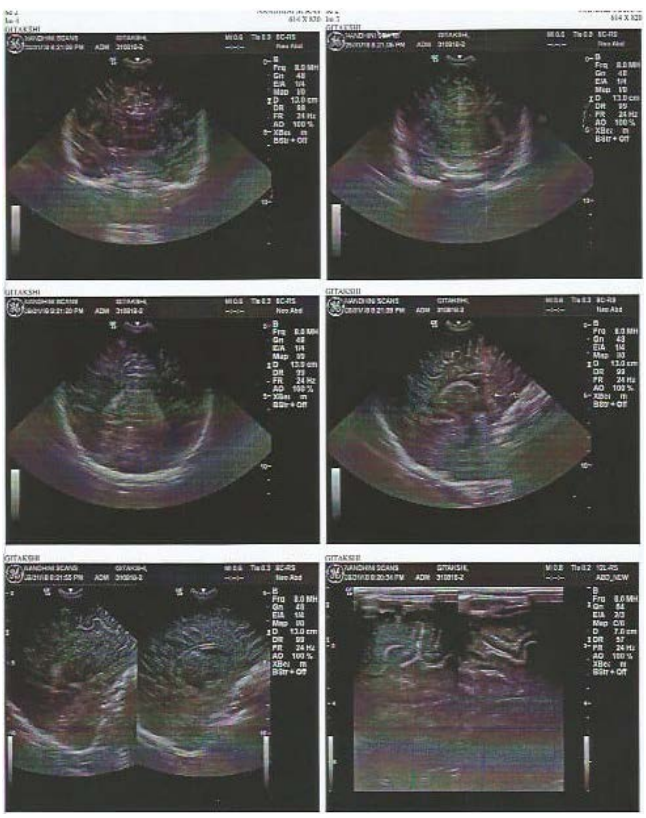

Figure 1: Hepatoblastomas appear as predominantly echogenic soft tissue mass. It also showed a homogenous mass in the right hypochondrium measuring 4.5×4×5 cms.

lesion. As per protocol, 3 doses of chemotherapy with cis-platinum was planned for this child. The unusual features at presentation in this child was presentation at a slightly later age, absence of thrombocytosis and absence of abdominal mass.

Discussion

Hepatoblastoma, the most common liver malignancy in infants and children under 3 years is usually asymptomatic [6]. This leads to the advancement of the disease at diagnosis. HB originates from immature liver precursor cells. They are unifocal and occur in the right lobe of the liver often. They have the capacity to metastasize and the common site for metastasis is liver [7]. The exact cause of the disease is unknown but several genetic conditions like trisomy 18, trisomy 21, Beckwith-Wiedemann syndrome; Familial adenomatous polyposis and Hemihypertrophy are known to be associated with HB. Children affected with Hepatitis- B at an early age and those with biliary atresia are also known to be at increased risk [8]. Parental smoking and low birth weight are other reported risk factors.

The signs and symptoms of HB depend on the size of the tumor and whether it has metastasized to the adjacent tissues. The usual presentations of the disease are an abdominal mass, swollen or distended abdomen, weight loss, decreased appetite, vomiting, jaundice, itchy skin, anemia and back pain [9]. HB is divided histopathologically as epithelial (56%) and mixed epithelial/ mesenchymal [10]. The epithelial type is further classified as fetal, embryonal, macro tubular and small cell undifferentiated subtypes [11]. The subtypes have a direct effect on the prognosis with more favorable outcome in fetal type and the worst in small cell differentiated type [12,13].

Lab findings show an elevation in liver enzymes. α-fetoprotein is an excellent biomarker to help determine the presence of liver malignancy in children. AFP levels are relatively high at birth and falls to normal adult levels by the second year. The normal AFP levels are lower than 50 ng/ml in children and 10 ng/ml in adults. AFP levels higher than 500 ng/ml is a strong indicator of hepatoblastoma [14]. It is also used as a bio-marker to monitor the treatment success and tumor recurrence. AFP levels return to normal when treatment is successful [15]. The variants of HB and HCC such as rhabdoid tumor that has distinct histopathological features may have low or normal AFP levels and show a worse prognosis [16,17]. Some tumors also secrete β-hCG (human chorionic gonadotropin) which manifests with precocious puberty or virilization.

The most useful diagnostic modality is CT scan or MRI. USG abdomen usually reveals a mass in the liver, with satellite lesions and hemorrhagic areas within the tumor. Helical CT with contrast imaging can help diagnose hypervascularity lesions of the liver suggestive of malignant tumor. Histological evaluation of the specimen is also important while some suggest that biopsy may not be necessary for children less than 3 years with high AFP levels [18] due to the risk of tumor seeding or dissemination. Blood tests may show thrombocytosis which is a typical characteristic of HB.

Pre- surgical staging of the tumor is essential to decide the extent of surgical resection. One method is based on the surgical technique of the pediatric gastrointestinal surgeon and staging depends on the findings at or after surgery:

Stage 1: Complete resection with negative margins.

Stage 2: Gross section with microscopically positive margins.

Stage 3: Residual disease after attempted gross resection or biopsy and rupture of the capsule.

Stage 4: Distant metastasis.

The second is the PRETEXT (Pretreatment extension) system designed by SIOPEL (Childhood liver tumor study group of the international society of pediatric oncology) [19,20]. PRETEXT system makes staging more accurate using CT angiography and MRI. This is based on Cournand's system of segmentation of the liver [21] where the liver is divided into four sections:

Segment 1: The caudate lobe was ignored in the original system.

Segments 2 and 3: Left lateral section.

Segments 4a and 4b: Left medial section.

Segments 5 and 8: Right anterior section.

Segments 6 and 7: Right posterior section.

This staging system considers the liver segments involved prior and post surgical resection. In addition to the intrahepatic extent, the PRETEXT system also takes into consideration the extrahepatic structures which are called "additional criteria". This assesses the involvement of inferior vena cava or hepatic veins (V), portal vein (P), extra hepatic abdominal disease (E) and distant metastasis (M). This inclusion of the extra hepatic structures improves the prognostic assessment and acts as a valuable tool for risk stratification. Hence the original SIOPEL risk stratification system has been modified in the current protocols of SIOPEL for HB study [22].

While surgical resection provides the best outcome and is the primary goal of the therapy, CHT has implied a multimodal approach

to treatment from surgery alone. The combination of CHT and surgery has provided promising results in patients with unresectable and metastatic disease and has improved the survival rates. CHT can be used as an adjuvant or neoadjuvant treatment and it helps to differentiate the tumor from the surrounding vascular structure and aids in complete tumor resection. Some of the chemotherapeutic drugs used for the treatment of HB are Cisplastin, vincristine, 5-FU, cyclophosphamide and doxorubicin. Tiao et al. proposed the combination of conventional resection, CHT and transplantation in the management of HB [23]. The treatment strategy is as follows:

PRETEXT Stage 1 tumor: Resectable by most surgeons.

Stage 2: Dependent on surgeon's ability.

Stage 3 or 4 (resectable): CHT recommended prior to resection based on surgeon's opinion.

Stage 3 or 4 (unresectable): Liver transplantation [24].

Heroic attempts to do partial hepatectomy are not encouraged because most HBs can be down staged by chemotherapy. The possibility of chemoresistance of tumor should be kept in mind in such cases. Post transplant chemotherapy has also been tailored in many children, but the benefits are not yet proven. An absolute contraindication for liver transplant is the presence of extra hepatic deposits after CHT that are not amenable to surgery. Patients with lung metastasis and incomplete tumor removal after partial hepatectomy or intrahepatic disease can undergo rescue liver transplantation, but the survival rates are low. In cases of ruptured tumors trans arterial embolization (TAE) is used to control peritoneal hemorrhage. Many controversies do exist in several areas in the treatment of HB.

Conclusion

To conclude excellent results have be achieved in the treatment of HB in the past few decades by a combination of radical tumor resection, CHT and liver transplantation. The overall 5-year survival rates of HB affected children is more than 90% in the absence of metastasis with PRETEXT Stages 1 and 2 while the rates are 90% and 75% respectively with POSTTEXT (post CHT) stages 1, 2 and 3 without liver transplantation.

In this case study the child presented at 6 years of age which is unusual and there was no abdominal mass or thrombocytosis which made diagnosis challenging. The features favorable in the diagnosis of HB were elevated AFP levels and a liver mass as seen in Contrast Enhanced CT. The resected tumor was identified as stage 1 according to children's oncology group staging. So, the pediatric surgeon must be cautious in making a prompt diagnosis even in the absence of usual disease presentation which will help to achieve a good prognosis in children affected with hepatoblastoma.

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