Case Report

Pediatric Education and Research
Volume 5 Number 2, May - August 2017
DOI: https://dx.doi.org/10.21088/per.2321.1644.5217.18

Dual Paraneoplastic Syndromes in a Case of Pediatric Hepatoblastoma: A Rare and Challenging Case

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Abstract

Hepatic malignant neoplasms comprise the third most common cause of intra-abdominal malignancies. Apart from the constellation of clinical findings associated with malignancies; liver malignancies have also been associated with perilous paraneoplastic syndromes. This report is about a 10 years old boy presenting with abdominal distension since 1 month with firm massive hepatosplenomegaly. Investigations revealed deranged liver enzymes with HBsAg positive status. CT abdomen was suggestive of heterogenous hepatic lesions. Serum alpha-fetoprotein level came as >90000 ng/ml. Liver biopsy revealed the diagnosis of Hepatoblastoma. Patient subsequently developed paraneoplastic symptoms in the form of hypertensive urgencies and resistant hypoglycaemic episodes manifesting as seizures requiring Nitroprusside drip ultimately and Glucose infusion Rate as high as 12mg/Kg/minute. On PRETEXT staging the tumour was classified as Stage 4 which is the non-resectable variety. The child was started on Cisplatin and Doxorubicin. However, he deteriorated, proceeding to liver failure with deranged liver function tests, raised PT/INR and active bleeding. The parents took a discharge against medical advicedue to financial constraints. As hepatoblastoma is extremely rare in this age group with the disease predominantly presenting as Paraneoplastic syndromes,Doctors should be ready for uncommon and rare possibilities.

Keywords: Abdominal Lump; Hepatoblastoma; Hypertension; Hypoglycemia.

Introduction

Hepatoblastoma is the most common malignant liver neoplasm in the paediatric age group. Typical age of presentation being 6 months to 3 years.It is characterized by organomegaly, deranged liver enzymes, raised alpha-fetoprotein level, along with typical neuroimaging findings and liver biopsy picture.

However, rarely has a case of Hepatoblastoma been reported in the pre-adolescent age group complicated with severe multiple paraneoplastic manifestations posing such arduous management issues.

Case History

A 10 year old male child, tenth by birth order, presented with insidious onset of progressive abdominal distension along with significant weight loss over a period of 1 month.There was no history of abdominal pain, bleeding from any site or any history suggestive of bone pain, altered sensorium, convulsions, respiratory distress, and renal involvement.

On general examination, the child was markedly cachectic with evidence of icterus and grade I clubbing. Dilated veins were seen all over the

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Received on 01.03.2017, **Accepted on** 17.03.2017

abdomen with the abdominal girth being 70 cm. significant bilateral cervical and inguinal lymphadenopathy was noted.Vitals were normal with Blood pressure of 110/60 mm of Hg (between 50th and 97th percentile for age) and JVP being 4 cm (normal). Systemic examination revealed a hard, nodular hepatomegaly with a span of 17cm with a palpable left lobe while spleen was palpable 6cm below the left costal margin with a prominent splenic notch.

Routine haematological investigations on admission were unremarkable but mildly deranged liver enzymes were noted(SGOT- 589 U/L, SGPT-186 U/L). Among the viral markers, HBsAg came positive, however synthetic liver functions were normal.Suspecting a primary hepatic neoplastic cause, AFP levels were done which were >90000 ng/ml (normal – upto 300 ng/ml). CT abdomen showed an ill-defined heterogenous hypoenhancing soft tissue mass lesion measuring 13*12*7 cm with diffuse oval lesions of variable size suggestive of metastasis with partial portal vein thrombosis.Liver biopsy finally revealed the entity as Hepatoblastoma (mitotically active fetal epithelial type).

On day 3 of admission, the child developed severe systemic hypertension which was initially treated with Nifedipine Retard but due to poor control, Labetalol was added. In view of refractory hypertension, Sodium Nitroprusside infusion was started in the intensive care and. Enalapril was added in view of high Plasma Renin Activity. Low Molecular Weight Heparin was started for portal vein thrombosis.

On day 6, the child developed hypoglycaemic seizures (RBS of 32 mg/dl), which were persistent and refractory and required escalation of the Glucose Infusion Rate (GIR) to 12mg/kg/min.Hence, Hydrocortisone and Octreotide were added. During the course of above events, Hepatoblastoma PRETEXT Staging (Pre-treatment extent of disease) was done which classified the tumour as Stage IV which is the non resectable variety.

The refractory hypertension and resistant hypoglycaemia were attributed to the paraneoplastic syndrome caused by Renin and IGF 2 production by tumour cells respectively.

Patient was started on cisplatin based chemotherapy; however he had a stormy course with grave downhill trend evident on the investigation panel; as SGOT/SGPT levels rose to 1285/126 with a Prothrombin time of 24 seconds and INR of 1.6 with active bleeding. Patient had multiple episodes of epistaxis and was started on hepatic drip with fresh frozen plasma transfusions alongwith fat soluble vitamin supplements. Though appropriate therapeutic modalities were instituted, parents took the child Discharge against medical advice in view of personal reasons and financial constraints.

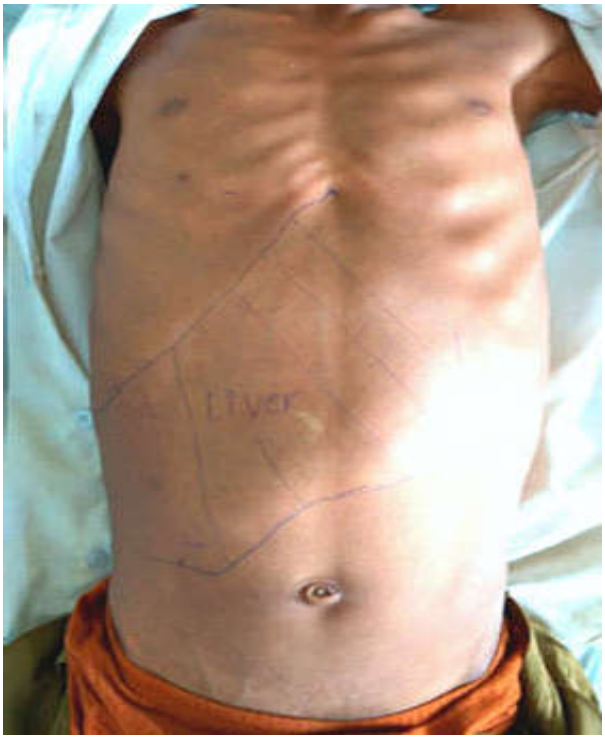

Image 1: Clinical Photograph of Patient Showing Massive Hepatomegaly

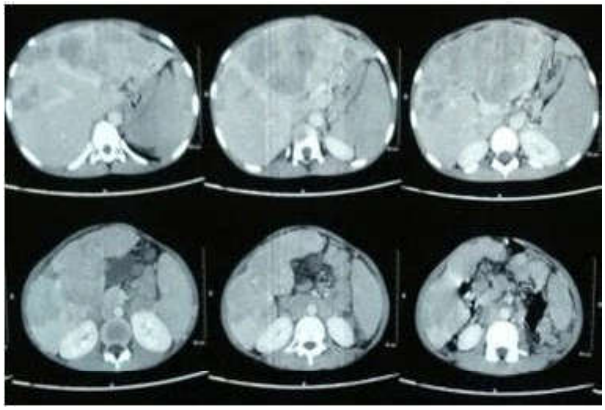

Image 2: Computerised Tomography of abdomen showing an ill defined heterogenous hypo enhancing soft tissue mass lesion measuring 13 × 12×7 cm^3 (TR×CC×AP) s/o Hepatoblastoma or Hepatocellular Carcinoma. Diffuse oval lesions of variable size s/o metastasis with partial Portal vein thrombosis.

Discussion

This communication describes a case of hepatic neoplasm with severe Paraneoplastic syndrome with initial presentation at the age of 10 years.

In our patient, abdominal mass, deranged liver enzymes with raised alpha fetoprotein level suggested a primary hepatic cause. Neuroimaging (CT Abdomen) was significant in portraying a malignant hepatic cause with portal venous extension while liver biopsy was diagnostic of hepatoblastoma.

Hepatic tumors represent approximate 0.5 - 2% of all the tumors in child, and, excluding leukemia and lymphoma, are responsible for 1-4 % of all the solid tumors . Hepatoblastoma, the most frequent malignant hepatic tumor in child, 74% according to certain studies, is however very rare, representing less than 1 case to 100 000 births.The annual incidence of the primary malignant liver tumours is 1 to 1.5 cases per million children in United States[1].Though a rare malignancy it is still a most common paediatric hepatic tumour with maximum cases clustered in the age group of 6 months to 3 years while the Hepato-cellular carcinoma is seen in the age group of 8 years to 14 years [2]. The age of presentation in our patient was 10 years which is unusual and very few such cases been reported in literature.

The etiological factors associated in the genesis of hepatoblastoma include extremely low birth weight and environmental factors (alcohol, drug abuse during pregnancy, mothers' hormonal treatment for sterility, maternal occupational exposure to heavy metal). Important genetic syndromic predispositions include Beckwith–Wiedemannsyndrome, Gardnersyndrome, Familiar adenomatous polyposis and Trisomy 18 [3].

Paraneoplastic manifestations of hepatoblastoma include throcytosis, thrombocytosis, hypocalcaemia, isosexual precocious puberty, hypertension and rarely hypoglycaemia. Though hypoglycaemia is known with hepato-cellular carcinoma, it is an extremely rare presentation in Hepatoblastoma. Madabhavi et al described a 15 years old male presenting with refractory hypoglycaemic seizures ultimately leading to a diagnosis of Hepatoblastoma [4].

Although,Hepatoblastoma is the commonest paediatric malignant liver neoplasm,but the presentation in such an age group has hardly been ever described. Bonehi et al have reported a 18 year old patient with hepatoblastoma with a positive hepatitis B viral status [5].

Apart from routine haematological investigations, Liver function assay with Prothrombin Time remains mandatory.Alpha fetoprotein is a key clinical marker for malignant change,response to treatment and relapse. Beta-HCG Assay is also indicated in cases with suspected precocious puberty/virilisation(as a part of paraneoplastic evaluation). Neuroimaging helps to identify the primary tumor as well as the disease extension which helps in the PRETEXT staging (Pre-treatment Extension of disease) of hepatoblastoma to determine the modality of treatment. Liver biopsy is diagnostic with 'Epithelial type' comprising 67% of the cases. Our case had a rarer histology, suggestive of mixed epithelial and fetal type which accounts for only 20% of the total cases [6].

Treatment options are decided on the basis of liver involvement and metastasis, the favourable option being complete tumourresection. However, other cases of proven hepatoblastoma have been treated with Cisplatin +/- Doxorubicin as in the index case who received 2 cycles of cisplatin based chemotherapy. Non curative treatment options include radiotherapy, trans-arterial embolization and novel Kinase inhibitors like Sorafenib[7].

Conclusion

As exemplified by this case, Hepatoblastoma-patients with Paraneoplastic syndromes have more advanced disease, higher AFP levels and poorer outcome. This case highlights that a patient with Hepatoblastomamay present at an atypical age with atypical symptoms attributable to paraneoplastic syndrome. Therefore, in addition to assessment for tumour extent and prognostic factors, a case of Hepatoblastoma should be evaluated for the presence of paraneoplastic syndromes. Diversions from standard presentations may be misleading. Hence, there is a need to collate all the clinical findings and investigations, which helps in clinching a diagnosis.

Acknowledgment

The authors thank Dr. Ramesh Bharmal, Dean-T.N. Medical College & BYL Nair Hospital for granting permission to publish this manuscript.

Conflict of Interest: None

Funding: None

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