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Case Report

Pathology Section

Embryonal Hepatoblastoma with Co-existent Glycogen Storage Disease in a Seven-month-old Child

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ABSTRACT

Hepatoblastoma is an uncommon malignant liver tumour diagnosed usually during the first three years of life. It presents as abdominal mass with elevated alpha fetoprotein levels. The definite diagnosis requires histopathological confirmation. Although conditions like Familial Adenomatous Polyposis (FAP) or Beckwith-Wiedman Syndrome may be associated with hepatoblastomas, storage disorders are uncommonly documented. We describe a rare case of hepatoblastoma with co-existent glycogen storage disease in an infant male who presented with a progressively increasing mass in abdomen along with failure to thrive.

Keywords: Hepatomegaly, Primary liver cancer, Storage disorder

CASE REPORT

A seven-month old male infant presented to the emergency department with progressive distension of abdomen noticed by his parents since the age of 4 months. A disproportionate increase in size was noticed in the past 3 days. There were multiple episodes of non-projectile vomiting in the previous 2 days. There was no haematemesis or rash over the body. His weight was 7 kg and length was 66cm.

On examination, he was afebrile and had massive hepatomegaly; the spleen was not palpable and there was no lymphadenopathy. Routine haemogram showed moderate anemia (7.2 g/dl) and high ESR (46 mm/1st hour). Serum aspartate transaminase was 78 IU/ml, total bilirubin 1.6 mg/dl and indirect bilirubin 1.03 while Alpha Fetoprotein (AFP) was high (302ng/ml). Abdominal CT scan showed a large mass measuring 72 x 68 mm involving almost the entire liver [Table/Fig-1].

Considering the age, clinical symptoms and radiological findings, a provisional clinical diagnosis of hepatoblastoma was made. Consent for open liver biopsy could not be obtained however needle biopsy was performed using Menghini needle and under the cover of diluted intravenous ketamine. Biopsy was immediately fixed in 10% formalin and sent for histopathological examination.

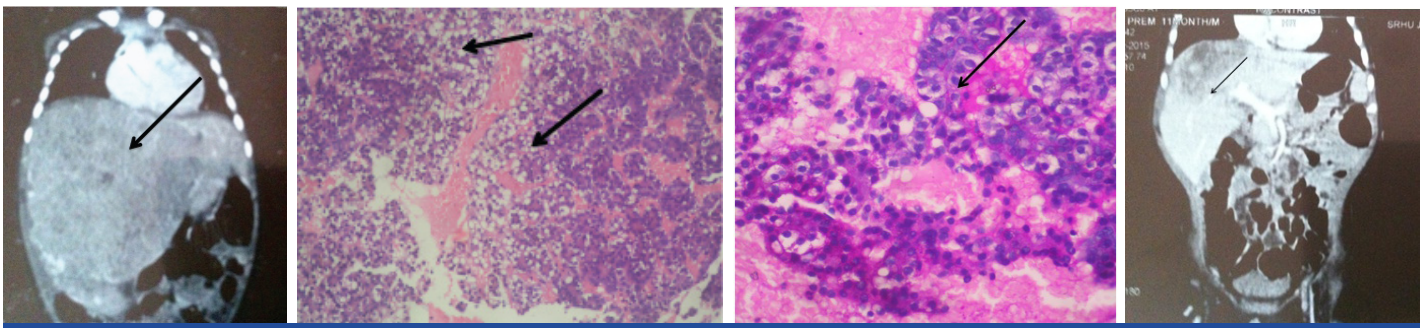
Gross Examination: Liver biopsy was received in two bits together measuring 10x4x4mm.

Microscopic Examination: Both the bits showed a cellular tumour. The tumour cells were arranged in rosettes, trabeculae and sheets [Table/Fig-2]. Many cells showed abundant intra-cytoplasmic vacuoles with peripherally pushed nuclei. Periodic Acid Schiff staining with diastase digestion showed intra-cytoplasmic positivity for glycogen [Table/Fig-3]. A diagnosis of embryonal type of Hepatoblastoma with Glycogen Storage disorder was made.

The patient was given 3 cycles of chemotherapy with intravenous injection Doxorubicin 5 mg in 50 ml Normal Saline (NS) over 6 hours for 3 days and injection Cisplatin 4mg in 50ml NS over 4 hours for 5 days. One unit of Fresh Frozen Plasma (FFP) was administered at the time of admission. Post chemotherapy CT scan showed a reduction in the size of liver mass [Table/Fig-4]. The child has tolerated chemotherapy well and is attending follow up clinics.

DISCUSSION

Primary paediatric liver tumours are rare and comprise 0.5 to 2% of all paediatric malignancies and are the tenth most frequent tumours in children [1]. Approximately 15% of all the abdominal tumours in childhood are primary liver tumours; 66% of these are malignant, the commonest being hepatoblastomas (HB). Hepatoblastomas present earlier than 2 years in the majority of the patients though some may be diagnosed in older children and even adolescents [2]. These tumours may be associated with other conditions like Familial Adenomatous Polyposis (FAP) and Beckwith-Wiedman Syndrome [3] however glycogen storage disease is uncommonly associated. Glycogen storage disorders are rare and incompletely understood. They are characterized by defective breakdown of liver glycogen to glucose due to deficiency of glucose-6-phosphorylase enzyme. The association between glycogen storage disease and hepatoblastoma was earlier described in siblings by Ito et al., in 1987 [4]. Previous studies have postulated that metabolic disorder of Glycogen Storage Diseases may play an important role in the development of hepatoblastoma and hepatocellular carcinoma by the proposed mechanisms in isolation or combination [5], these are:



[Table/Fig-1]: Pre treatment CT film showing massive hepatomegaly. **[Table/Fig-2]:** H&E: 10x10X: Sheets and rosettes of embryonal hepatoblastoma with many clear cells. **[Table/Fig-3]:** PAS stain: 40x10X: Cells showing cytoplasmic positivity for glycogen. **[Table/Fig-4]:** Post chemotherapy CT film showing regression of liver size.

1) glucagon/insulin imbalance; 2) cellular glycogen overload; and 3) proto-oncogene activation [6]. Genetic and molecular studies have documented recurrent chromosomal abnormalities and aberrant activation of developmental and oncogenic signaling pathways in hepatoblastomas [7]. Alternatively, the "toxic-metabolite" model of pathogenesis proposes that metabolic disorders initially present with characteristic histologic and ultra-structural patterns on liver biopsy but chronic injury over months or years may lead to cirrhosis or hepatic neoplasia [8]. There are very few studies which have described the association between hepatoblastoma and glycogen storage disorders and apparently none reported from the Indian subcontinent [4,5,8]. A large study carried out by Ramakrishna et al., in 1993 in Vellore, South India studied 128 paediatric liver biopsies out of which only one case was that of hepatoblastoma not associated with any other condition [9].

Hepatoblastomas may either be epithelial with purely foetal or embryonal histology, or mixed with mesenchymal elements like osteoid. Other rare histological patterns are macro-trabecular, small cell or anaplastic. Pure fetal type carries an excellent prognosis while the rare anaplastic variant that is usually accompanied by low serum AFP carries a poor prognosis. Treatment with 6 cycles of chemotherapy administered every 2-4 weeks is the treatment of choice. AFP levels are used to determine response to therapy. Children with unresectable hepatoblastoma may undergo liver transplantation with post-transplant survival of 80% [10]. The present 5-year survival rate in children is 75% which was 30% about 30 years ago [11,12].

CONCLUSION

This case report supports the theory that Glycogen Storage Diseases may increase the risk of development of hepatoblastoma and hepatocellular carcinomas. Further studies are needed to delineate the pathogenesis of the rare association of hepatoblastomas in Glycogen Storage Diseases and to further define their risk of malignant transformation in relation to age and other possible co-factors.

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