Infantile Hepatic Hemangioendothelioma (IHHE) – An Unusual Presentation.

S Golhar[1], A Madhura[2], Urmila Chauhan[1], P Agrawal[3]

[1]Associate Professor, Department Of Pediatrics, GMCH Nagpur
[2]Assisstant Professor, Department of Pediatrics, GMCH, Nagpur.
[3]Junior Resident, Department of Pediatrics, GMCH, Nagpur.

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ABSTRACT

Hepatic tumours are relatively rare in children, accounting for 1% - 4% of all paediatric solid tumors, commonest amongst them are hepatoblastoma, neuroblastoma, and vascular tumors (hemangioendothelioma/haemangiomas). Infantile Hepatic hemangioendothelioma (IHHE) is classically characterised by hepatomegaly, jaundice, congestive cardiac failure with high cardiac output, skin haemangiomas, haemolytic anemia, thrombocytopenia(kasabach – Merritt syndrome), normal Alfafeto protein (AFP) levels and hypothyroidism.
We report a case of infantile hemangioendothelioma in a 5 day old female neonate with high output cardiac failure, unusually high alpha-fetoproteins, thrombocytosis and polycythaemia, which posed a diagnostic dilemma.
Diffuse IHHE is a rapidly growing benign tumor which can lead to poor clinical outcome if not identified early. Serum AFP can't be relied to exclude IHHE.

Keywords: hemangioendothelioma, haemangioma, hepatic.

INTRODUCTION

Hepatic tumours in children are relatively rare, accounting for 1 to 4% of all paediatric solid tumours.[1] Infantile hepatic hemangioendothelioma (IHHE) is the most common vascular tumour of the liver in children, accounting for 12% of all childhood hepatic tumours with an estimated incidence of about 1/20,000. [2]
Almost 85% of patients with IHHE are diagnosed during the first 6 months of life. Tumour shows a female preponderance, with a female to male ratio of 1.3:1 to 2:1.[3-8] IHHE can present with abdominal mass, hepatomegaly, high-output cardiac failure, skin haemangioma, thrombocytopenia, haemolytic anemia, peritoneal bleeding and low serum alpha-fetoprotein (AFP) levels. Solitary lesions may spontaneously regress but diffuse lesions especially those with heart failure and or jaundice has very high morbidity (up to two-third die).[5-9] It is essential to suspect and identify IHHE early in an infant presenting with hepatomegaly as the outcome could be catastrophic if not treated at the earliest.

Name & Address of Corresponding Author
Dr. A Madhura,
Assistant Professor, Dept of Pediatrics,
GMCH Nagpur, India
E-mail: abhishekmadhura.am@gmail.com

CASE REPORT

We report a case of 5 day old neonate with abdominal distension with CCF with very high serum AFP and thrombocytosis posing a diagnostic dilemma.
A near term (34-36 weeks) female neonate weighing 2100 grams born by emergency caesarean section to a mother suffering from severe pregnancy induced hypertension with uneventful first trimester, cried immediately after birth presented to us on day 5 of life with vomiting, jaundice, abdominal distension, and increased respiratory efforts. She was tachypneic with tachycardia and there was bilateral crepts and rales and a 3/6 grade systolic murmur heard over left lateral sternal border. A firm palpable mass occupying both the upper quadrants of abdomen extending beyond umbilicus causing abdominal compartment syndrome was noted. On day 7 swelling of 3X3 cm over the anterior chest wall, well-circumscribed, soft, skin coloured along the right lateral border of sternum was noted. [Figure 1]
Imaging modalities included 2 D echo which revealed a muscular VSD and patent foramen ovale with left to right shunt. Abdominal ultrasound revealed grossly enlarged liver with almost entire liver parenchyma replaced by multiple well defined rounded heterogenous hyperechoic lesions showing

moderate vascularity suggestive of hemangioendothelioma. Doppler study of chest swelling revealed heterogenous swelling without vascularity. Contrast enhanced CT abdomen disclosed multiple centripetally enhancing lesions of varying sizes involving almost the entire liver consistent with IHHE [Figure 2). Contrast Enhanced CT chest revealed findings compatible with cutaneous hemangioma and diffuse ground glass opacification of lung parenchyma due to pulmonary edema.

Lab investigations are shown in [Table I].

Baby was started on furosemide, digitalis, thyroxin (@10mcg/kg/day) and oral high dose prednisolone (@4 mg/kg/ day) .

On day 6 of admission, she developed sudden pallor with hypotension, seizures, apnoea and her Anterior Fontanelle was tense. CECT brain did not show intracranial bleed or midline shift. Unfortunately, baby died due to cardiovascular instability and intractable congestive heart failure. As the parents did not give consent for autopsy, liver biopsy and CSF sample could not be obtained.

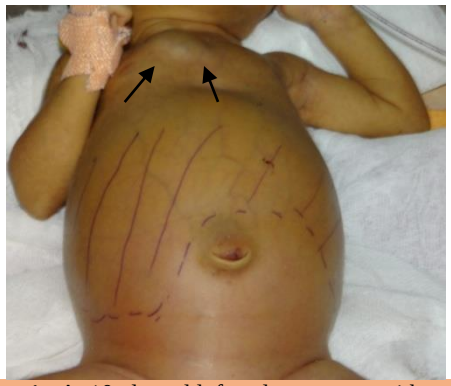

Figure 1: A 10 day old female neonate with massive hepatomegaly (shaded area) and cutaneous haemangioma (arrows) in a case of infantile hepatic hemangioendothelioma (IHHE).

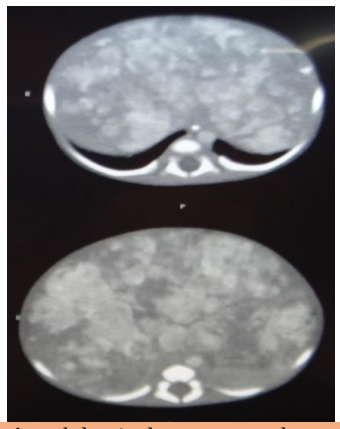

Figure 2: An abdominal contrast enhanced computed tomographic image of Infantile hepatic hemangioendothelioma disclosing grossly enlarged liver with typical multiple ill-defined centripetally enhancing homogenous lesions of varying sizes causing near complete involvement of liver parenchyma.

Table 1: Investigations.

Investigation	Patient value	Reference value
Hemoglobin	9.2 g/dl	13.0 – 19.5 g/dl
White blood cell count	7900 / cumm	5000 – 15000/ cumm
Platelet count	17.0 lac/cumm	1.5 – 4.0 lac/cumm
Serum Albumin	2.2 g/dl	3.5 – 5.0 g/dl
Serum Bilirubin (indirect)	15.3 mg/dl	0.2 – 1.2 mg/ dl
Aspartate aminotransferase	190.6 U/L	0 – 46 U/L
Alanine aminotransferase	98.0 U/L	0 – 38 U/L
Sr. Alpha-fetoprotein	2,22078 ng/ml	See text
Serum TSH	15.22 uIU/ml	1.7- 9.1 uIU/ ml
Serum T3	0.1 ng/ml	
Serum T4	1.9 ug/dl	9.8 – 16.60 ug/dl

DISCUSSION

IHHE should be included in the differential diagnosis of other hepatic masses developing in infancy, such as cavernous haemangioma, hepatoblastoma, and mesenchymal hamartoma. Mesenchymal hamartoma is a developmental anomaly rather than a true neoplasm. Usually, the patient presents with abdominal distension, fever, vomiting and constipation. The alpha-fetoprotein levels are within normal limits. Plain films show a soft tissue mass. Ultrasonography, CT and magnetic resonance (MR) imaging show a predominantly cystic mass with multiple echogenic septae. Cavernous haemangioma rarely presents in infancy. It is the most common primary liver tumour in the older age group and is usually associated with other Haemangioma in the body. It rarely presents with congestive cardiac failure. Hepatoblastoma is the most common symptomatic malignant tumour presenting before the age of 5 years. It may be single or multiple and commonly involves the right lobe of the liver. The child commonly presents with an abdominal mass and is severely ill with weight loss, anorexia, pallor and weakness. The alpha-fetoprotein and human chorionic gonadotropin levels are usually elevated and usually there is thrombocytosis. [10] Hence a very high alpha-fetoprotein levels, thrombocytosis and hemodynamic stability during the initial course of the disease in our patient mislead us to believe this tumor to be a hepatoblastoma but CECT abdomen delineated a hemangioendothelioma.

Although IHHE also termed as liver haemangioma is the third most common type of hepatic tumour and the most common benign vascular tumour of the liver in infants, hepatic tumours are relatively rare in children, accounting for 2%-3% of all paediatric tumors. [1] 10% to 15% of cases present with features of congestive heart failure, including

high cardiac output. [5] Heart failure has high mortality (up to 70%) when lesion is diffuse and non regressive. [11] Enjolras O reported high mortality (100%) in Liver haemangiomas. [12]

The presence of diffuse lesion, anemia and congenital heart defect in the form of a ventricular septal defect had a compounding effect on the high output cardiac failure leading to intractable congestive cardiac failure and ultimately poor outcome in our patient. Hence, it is important to recognise those factors, which can aggravate the congestive cardiac failure early and manage them aggressively.

The serum AFP level, which often increases in primary hepatic malignancies, has been used as an important tumor marker for hepatoblastoma, hepatocellular carcinoma and some germ cell tumors. Alpha-fetoprotein is usually not elevated in hepatic hemangiomas when adjusted for the age.[13] Normal levels of AFP in neonates may be as high as 2500 ng/mL and the adult level of less than 25 ng/mL is not reached until 6 months of age .[11] A Chinese study has reported elevated AFP levels in 80% of infantile Hemangioendothelioma. [14] Serum AFP levels in our case did not help in excluding hepatic haemangioma but can be used to ascertain complete resection of the tumor postoperatively. Various studies[13, 16-18] with Asian subjects including ours' have reported elevated serum AFP levels in IHHE, which is contrary to the current knowledge that IHHE have normal to mildly elevated AFP levels. Further studies are needed to find correlation between elevated serum AFP levels and disease severity.

CONCLUSION

In young infants, a hepatic mass and elevated serum AFP level may not always be associated with hepatoblastoma. IHHE must be differentiated by MRI or CECT or other radiological techniques before performing invasive procedures. Although children with asymptomatic lesions may experience spontaneous regression within a year, due to risk of high mortality with diffuse lesions, aggressive management, which include high dose corticosteroids, interferon-alpha (INF-α), and interventional modalities like embolization and ligation of the hepatic artery, resectional surgery, and/or liver transplantation, is required.

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