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Case Report

Pathology Section

Hepatic Epithelioid Hemangioendothelioma in an Eight Year old - A Case Report

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ABSTRACT

Hepatic epithelioid haemangio-endothelioma (HEHE) is a rare vascular tumour of endothelial origin. The etiology of this tumour is unknown and has a variable clinical outcome. It usually affects adults and is extremely rare in children. Histologically, HEHE is characterized by epithelioid to dendritic tumour cells with intracytoplasmic lumina containing RBCs and a myxoid to sclerotic stroma. Being a rare entity, awareness and a high degree of suspicion is required to correctly identify this tumour. We report a case of hepatic hemangioendothelioma in an 8-year-old child.

Keywords: Endothelial, Epithelioid haemangio-endothelioma, Liver

CASE REPORT

An 8-year-old boy presented with dragging abdominal pain over left subcostal area which worsened on exertion. He had a history of weight loss and reduced appetite since four months. On examination, he had abdominal distension and hepatosplenomegaly. The liver was enlarged (liver span – 13 cm) with hard and nodular surface and sharp borders. Blood investigations showed abnormal liver function tests with mild elevation in aspartate transaminase and alanine transaminase, reversal of albumin:globulin ratio and deranged coagulation profile. However, the platelet counts and D dimer levels were normal with absent fibrin degradation products ruling out consumptive coagulopathy. The patient was started on vitamin K supplements in view of deranged coagulation profile. Ultrasonography of the abdomen showed hepatomegaly with diffusely scattered multiple target lesions in both the lobes, largest lesion measuring 4 x 3 cm. Splenomegaly, multiple mesenteric lymph nodes and ascites were also noted. Serology for hydatid disease, hepatitis B and HIV was negative. Based on radiology, provisional diagnosis of Non Hodgkin lymphoma and metastatic liver disease were considered. Ascitic fluid sent for cytological examination contained only mature lymphocytes. Laparotomy and open biopsies were obtained from the largest nodule (4 x 4 cm) in segment IV and segment V and sent for histopathologic examination. On microscopy, liver biopsy showed a tumour composed of cords, nests and small islands of spindle and numerous epithelioid cells with small ovoid, irregular nuclei showing anisonucleosis, binucleation and few with nucleoli. The cells had moderate amount of pale eosinophilic cytoplasm with variably sized cytoplasmic vacuoles few of which contained RBCs [Table/Fig-1]. The hyalinised fibromyxoid stroma contained entrapped bile ductules and the tumour cells were seen to infiltrate in between and replace hepatic parenchymal cells. On immunohistochemistry, the tumour cells were positive for CD34 [Table/Fig-2]. A final diagnosis of hepatic hemangioendothelioma was rendered.

The patient was advised monoclonal antibody therapy or liver transplantation and referred to a higher centre for further treatment.

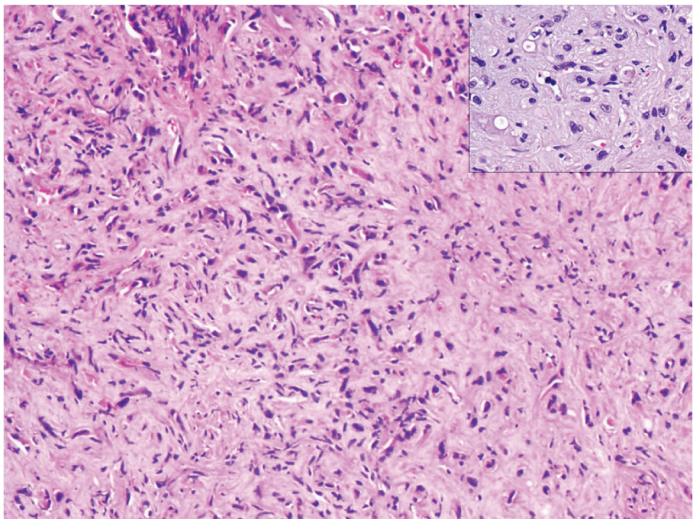
DISCUSSION

Epithelioid hemangioendothelioma (HEHE) is an uncommon vascular soft tissue tumour affecting many organs including spleen, brain, soft tissue, stomach, breast and liver. HEHE is extremely rare with an incidence of <0.1 per 100,000 population [1]. Various aetiological factors proposed in the pathogenesis of HEHE include oral contraceptives, alcohol, trauma, viruses and chronic liver diseases [1,2]. Recently a specific translocation t(1;3)(p36.3;q25) has been hypothesized to be unique for HEHE but the pathway of how the resulting fusion transcript leads to oncogenesis is not yet elucidated [1].

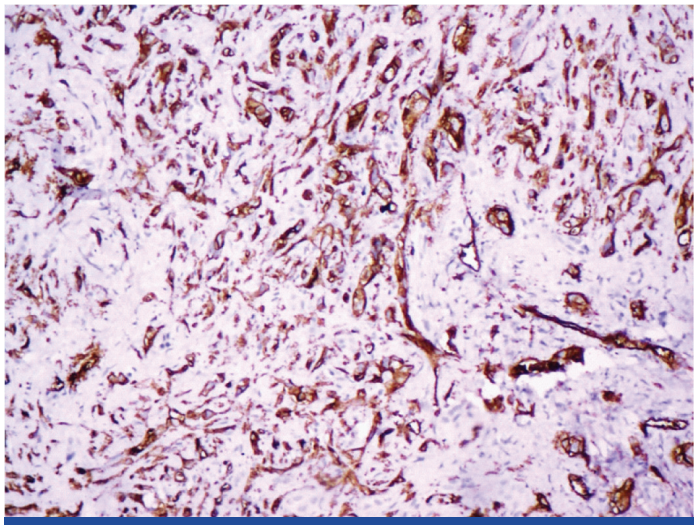
Clinically, manifestations of HEHE are heterogeneous and usually non specific such as right upper quadrant pain, hepatomegaly and weight loss followed by weakness, anorexia, epigastric mass, ascites, nausea/emesis, jaundice and fatigue [2].

Laboratory parameters are usually non diagnostic. Tumour markers have a potential role in ruling out other hepatic neoplasms, both primary and metastatic.

Radiological studies such as ultrasonography, computed tomography, magnetic resonance imaging, scintigraphy and angiography aid in diagnosing HEHE. Based on radioimaging, HEHE is divided into two subtypes. The nodular type indicates early lesion with multiple bilobar hypoechoic nodules while the diffuse type results from coalescence of these nodules resulting in large peripheral masses [1,3,4]. The present case had ultrasonography features of early disease. Multifocality of HEHE have been described more often in the lung and liver; this pattern being attributed to its growth along small blood vessels [5].



[Table/Fig-1]: Photomicrograph showing neoplastic cells in fibromyxoid stroma (H&E, x200) Inset shows tumour cells with intracytoplasmic RBC (H&E, X400)



[Table/Fig-2]: Tumour cells demonstrating CD34 immunoreactivity (X200)

Histopathological examination of the lesion is required for definitive diagnosis of HEHE. These are characterized by epithelioid and dendritic tumour cells with intracytoplasmic lumina (blister cells) which may contain RBCs, vascular invasion with tufting. The stroma is myxoid in actively proliferating lesions and shows hyalinization, sclerosis and fibrosis as the lesion evolves [6]. Calcification may be seen in up to one third of patients. However, no calcification was noted in the current case.

Immunohistochemistry aids in confirming the morphological diagnosis. The tumour cells owing to endothelial cell origin show immunoreactivity for endothelial markers like factor VIII-related antigen (FVIII-Rag), CD34, CD31 [1,6].

Differential diagnosis of HEHE is varied depending on the clinical scenario; cholangiocarcinoma, epithelioid angiosarcoma, hepatocellular carcinoma and metastatic carcinoma being the most common [6]. The hallmark of HEHE which helps to differentiate it from all other entities is the preservation of the hepatic acinar structure despite the presence of an infiltrating tumour [6]. Further, the absence of trabecular pattern with traversing capillaries and the presence of normal bile dutular system in the present case, ruled out hepatocellular and cholangiocarcinoma respectively. The young age of the child and absence of a primary lesion on clinical evaluation, excluded the possibility of metastatic carcinoma. Absence of solid sheet pattern, marked atypia, numerous mitosis and necrosis excludes epithelioid angiosarcoma [5]. Microscopic identification of intracytoplasmic lumina with RBCs, characteristic fibromyxoid stroma and immunoreactivity of tumour cells for endothelial markers help in arriving at the correct diagnosis.

The prognosis of HEHE is highly unpredictable [1]. They have a very slow progression yet a malignant behaviour with local recurrence and distant metastasis [7]. Histological features including pleomorphism, atypia and mitotic activity do not correlate with disease severity or predict outcome. However, cellularity and tumour cell necrosis have been shown to have significant correlation with clinical outcome. Nuclear studies such as DNA content and proliferative indexes are also said to help in predicting the behavior and progression of these tumours [6].

Liver resection is the preferred modality for treating resectable cases. When the tumour is multicentric and metastatic, liver transplantation is offered [8]. Benefit from chemotherapy, radiotherapy and interferon remains unclear and unsatisfactory till date [2]. The tumour is said to pursue a more aggressive clinical course in children with limited role of liver transplantation [7].

CONCLUSION

To conclude, HEHE is a rare vascular tumour. Owing to the paucity of available information regarding its clinical course, pathogenesis, prognostic indicators and treatment outcome, the diagnosis of this tumour is challenging for the pathologist and the management disappointing for the clinician.

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