METASTATIC HEPATIC EPITHELIOID HEMANGIOENDOTHELIOMA IN 10 YEARS OLD BOY; A RARE CASE REPORT

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ABSTRACT

Epithelioid Hemangioendothelioma is an infrequent vascular neoplasm of intermediate malignant potential oddly affecting children. It is primarily noted in soft tissues, the stomach, breast, spleen, brain, and liver. No definite risk factor is identified in children. However, following WWTR1 -CAMTA1 and YAP1-TFE3 gene fusions are frequently seen in these tumours. We present a case of very rare childhood Epithelioid Hemangioendothelioma of the liver in a ten-year-old boy. A 10-year-old boy presented with abdominal pain, mild weight loss, and abnormal liver function tests. Radiologically, hepatic, pulmonary, and bony lesions are noted. The biopsy report showed Epithelioid Hemangioendothelioma confirmed by an Immunohistochemical panel. Due to the lack of facilities in our centre, palliative treatment was given to the patient. Surgical resection, liver transplant, and radiofrequency ablation were impossible due to widespread hepatic and pulmonary disease. The patient was resistant to any medical treatment. The patient died at the seventh-month follow-up. HEHE is a scarcely seen tumour with no definite management protocol. Surgical resection is the preferred treatment for resectable tumours. In non-resectable extensive bifocal tumours, like in our case, the preferred treatment is radio-frequency ablation and hepatic transplant. The overall survival is trivial due to the non-compliant nature of the disease.

KEYWORDS: *Diagnostic Accuracy, Interstitial Lung Diseases, HRCT, Chest Radiograph, CXR*

INTRODUCTION

Epithelioid Hemangioendothelioma (HEHE) is an unusual soft tissue tumour of vascular origin that primarily affects females but is also reported in the pediatric population. The approximate prevalence is less than 1/1 000 000. HEHE affects soft tissue and organs like the liver, spleen, brain, stomach, and breast. The selfsame risk factor is unknown, but varied etiological risk factors include chronic liver diseases, oral contraceptives, alcohol, trauma, and viruses.[1] Following translocations of the TFE3 gene, the WWTR1 gene and the CAMTA1 gene fusion are associated with this disease. The clinical features are unrelated and non-specific, such as fatigue, nausea, weakness, jaundice, anorexia, right upper quadrant pain, and weight loss. In addition, epigastric mass, ascites, and hepatomegaly are also found. Baseline investigations are usually non-diagnostic; serology markers can rule out primary and metastatic tumours. Approximately 25% of HEHE patients are asymptomatic. In contrast, symptomatic patients typically present with generalized abdominal pain, moderate weight loss, and a subhypochondrium mass or rarely may present as congestive hepatopathy.[2] Radiologically, HEHE represents a well-defined lesion with hepatic or portal vein peripheral tapering the so-called lollipop sign. The rest of the imaging studies, such as ultrasonography, scintigraphy, and angiography, are also recommended. The diagnosis of HEHE is typically only made through histopathological evaluation with confirmation by an Immunohistochemical panel. The most common differentials in multifocal lesions are Metastatic Carcinoma, Angiosarcoma, Sclerosing variant of Hepatocellular Carcinoma (HCC), and Cholangiocarcinoma.[3] In the case of multifocal disease, a high proclivity for systemic involvement is found. Considering its refractory nature, there is a high degree

of vagueness in selecting a suitable management regimen explicitly sanctioned for HEHE. Since there is no specific guideline regarding management, its treatment is at odds with worldwide, resulting in trivial outcomes.[4]

CASE REPORT

A 10-year-old male presented in a pediatric outdoor clinic with irregular abdominal pain, more on the right-sided location, with non-specific weight loss. On general physical examination, he had an average physique and build. Abdominal inspection showed mild, tender hepatomegaly. Blood investigations showed abnormal liver function tests and a deranged coagulation profile. Serology for hepatitis B, C, hydatid disease, and HIV was negative. In addition, tumour marker alpha-fetoprotein was also within the normal range. The chest, abdomen, and pelvis contrast-enhanced CT scan images and bone scans were done. CT scan of the abdomen showed an enlarged and irregular liver and two hypodense lesions in both the right and left lobes of the liver. The most significant lesion, 65.5 mm, was measured. In comparison, the other lesion was 24.6 mm in size (Fig. 1). Axial slice of the chest CT scan showed multiple hypodense nodules of the variable size seen in the bilateral pulmonary parenchyma (Fig. 2). Axial slices of pelvis CT scan showed a suspicious osteolytic lesion in the right acetabulum of the pelvic bone (Fig. 3). The provisional diagnosis of a metastatic hepatic and pulmonary disease considered. Advised bone scan showed abnormal tracer uptake in osteolytic lesions in the left-sided acetabulum, head of the femur, and iliac bones. Based on these findings, the provisional diagnosis of Langerhans Cell Histiocytosis is rendered. Diagnosis of HEHE was made on histopathological examination. The tumour comprised nests of elongated and stellate cells with irregular ovoid nuclei entrapped in hyalinized and fibro myxoid stroma. A moderate amount of pale eosinophilic cytoplasm is also noted (Fig 4). The neoplastic cells showed positive CD34, ERG, ASMA, and low Ki 67on stains [Fig5,6]. A multidisciplinary consultation was done over the index case, and palliative treatment was preferred in widespread metastatic disease. There were no facilities for liver transplants; radiofrequency ablation was available, and surgical resection was not recommended due to non-resectable widespread illness. Unfortunately, the patient died after seven months of diagnosis at a tertiary care centre due to widespread disease.

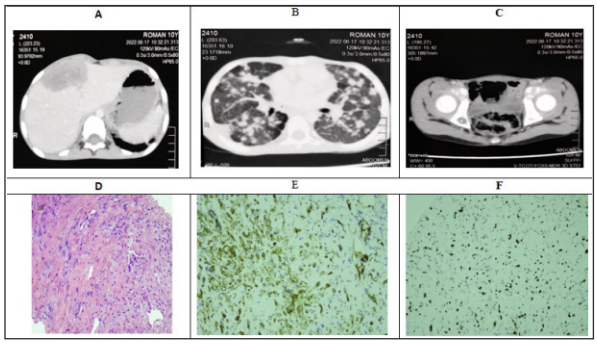

Figure 1: CT-Scan and Histopathological features of Epithelioid Hemangioendothelioma A Two hypodense nodules in the right and left lobes of the liver with peripheral enhancement on arterial phase. B Multiple hypodense nodules in the bilateral pulmonary parenchyma. C Suspicious osteolytic lesion in the right acetabulum of the pelvic bone. D Photomicrograph of H&E stain shows spindle to ovoid neoplastic cells arranged in thin slits. E Strong and diffuse cytoplasmic staining of CD 34. F Strong and diffuse nuclear staining of ERG

DISCUSSION

HEHE is an infrequent vascular tumour with borderline malignant potential. In the pediatric population, HEHE is extremely rare to report globally. It is a multi-organ disease with a prolonged course and non-specific clinical signs and symptoms. Definite diagnosis is made with imaging studies, biopsy, and molecular confirmation of mutations. In addition, there are no specific management guidelines due to the rebellious nature of the disease.[1,5,6,7,8,9] Here, we report a HEHE in a 10-year-old boy, also written by another author **(6)**, although literature reports showed female preponderance.[1,5] No specific clinical signs and symptoms, i.e., right upper quadrant pain, weight loss, hepatomegaly, or any risk factor, were identified in our case, similar to other reports.[5,6,7] In our centre, we only have the facility of contrast-enhanced CT scan, which showed multiple large peripheral hypoechoic nodules with pulmonary and bone involvement reported by other authors.[1,7,8,9] The tumour morphology showed dendritic and epithelioid cells forming slit-like spaces embedded in the fibro-myxoid stroma. Immunohistochemically, tumours are positive for CD34 or CD31, ERG; these observations are consistent with others.[5,6,9] The following prognostic factors of HEHE are size and metastasis. The overall impact of loco-regional versus widespread metastases on prognosis is still controversial. Since there is varied clinical behavior of HEHE from low-grade to high-grade sarcoma, up until now, no reliable molecular studies have been done to evaluate prognosis. Our patient died

after the seventh month of diagnosis due to widespread multi-organ involvement, similarly reported by others. However, according to the literature, most patients survived after 5-10 years of diagnosis. [1,5,6,7,8]

CONCLUSIONS

Our study concludes that CXR has sensitivity, specificity, and accuracy of 76%, 84% and 78.6% compared to HRCT.

CONFLICT OF INTEREST: None

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