Epithelioid Hemangioendothelioma in a Child

Epithelioid hemangioendothelioma (EHE) is a rare tumour arising from the vascular endothelium of soft-tissue, bone and viscera. Skin involvement is rare. The disease has an indolent course, with the potential for recurrence and often associated with multi-systemic localisations. We present a rare case of cutaneous EHE without systemic involvement in 9-year-old boy. The tumour was completely excised and histopathologic diagnosis was consistent with EHE. Complete systemic assessment showed no internal localisation. Wide excision is the mainstay of therapy and regular follow-up is suggested due to the potential for recurrence. The majority of documented cases of EHE is in adults and has developed in association with an underlying systemic involvement. To the best of our knowledge, this is the second reported case of isolated cutaneous EHE in paediatric age group.

KEYWORDS: Childhood, epithelioid hemangioendothelioma, vascular tumours

INTRODUCTION

Epithelioid hemangioendothelioma (EHE) is an uncommon vascular tumour of soft tissue arising from the endothelium and it was first reported by Weiss and Enzinger in 1982. The histological and clinical features of tumour are intermediate between benign vascular tumours such as haemangiomas and frank malignant tumours like angiosarcomas.[1] It is most commonly found in soft-tissues, but can arise in any organ.[2] We present 'an exceptionally' rare case of primary cutaneous EHE on 'the left iliac' region without systemic involvement in a child.

CASE REPORT

A 9-year-old boy presented with an asymptomatic gradually enlarging nodular lesion since 5 months. Patient's past medical and family history were insignificant. On palpation, the lesion was non-tender, freely mobile and firm in consistency. It measured 3 cm × 2 cm and was situated in left iliac region [Figure 1]. The overlying skin was slightly thickened, reddish blue and attached to the lesion. There were no palpable lymph nodes. Based on the clinical examination, dermatofibroma, hemangioendothelioma and arteriovenous malformation were considered as differentials. The routine investigations were within the normal limits. The lesion was completely excised and sent for histopathological examination.

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Microscopic examination revealed well-circumscribed tumour localised in the dermis, composed of mass of plump epithelioid shaped endothelial cells arranged in "nest-like" pattern with minimal vascular differentiation. The epithelioid cells showed intracytoplasmic vacuole (Primitive Lumina) and erythrocytes were seen in some of the lumina. Few vascular channels containing erythrocytes were seen on peripheral portions of the tumour. There was no cellular atypia and necrosis [Figures 2 and 3]. On Immunohistochemistry, CD 31 was positive, other endothelial markers were not done due to lack of facilities and our patient was not affordable. Other investigations such as chest X-ray, ultrasound abdomen and a whole-body bone scan were performed to exclude multicentric location and distant metastasis, but were found to be normal. Patient is on regular follow-up for the last 10 months with no signs of local recurrence or metastasis.

DISCUSSION

EHE is an uncommon, well-differentiated endothelial vascular neoplasm of low grade malignancy. The

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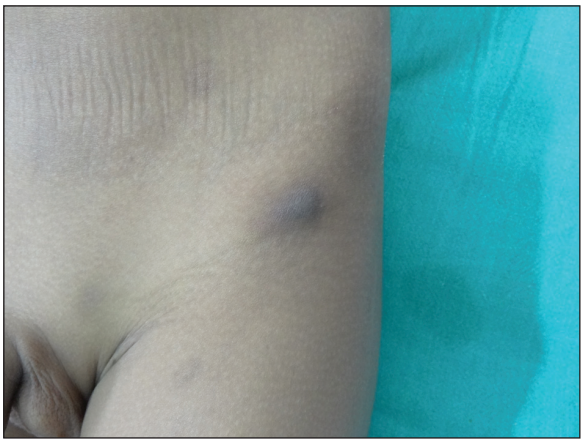

Figure 1: Swelling of 3 cm × 2 cm with violaceous hue, located on left iliac region

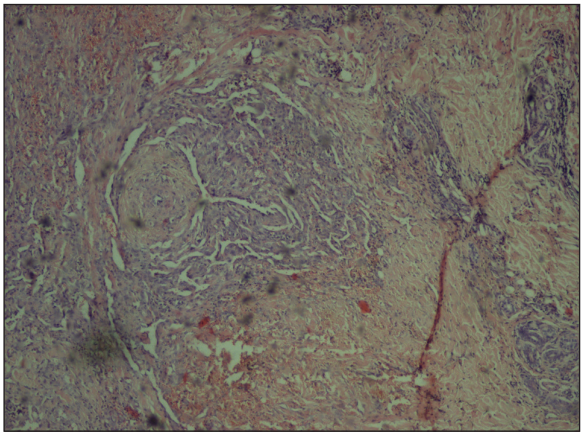

Figure 2: Mass of plump endothelial cells distributed in myxohyaline stroma with minimal vascular differentiation (H and E, ×10)

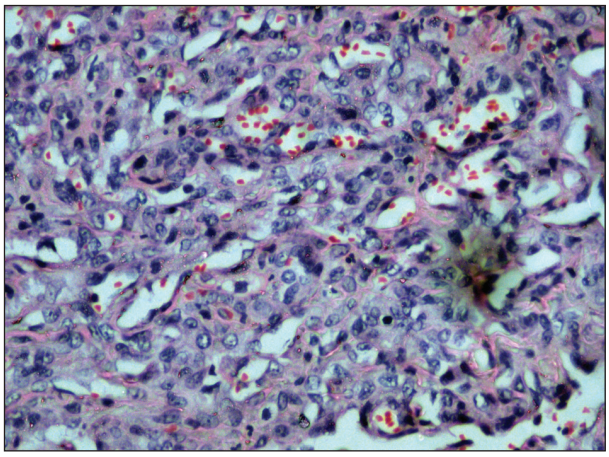

Figure 3: Plump endothelial cells with intracytoplasmic vacuole (primitive lumen) arranged in nests, few lumen show red blood cells (H and E, ×40)

Epithelioid haemangiomas represent the benign end of the spectrum, whereas epithelioid angiosarcomas represent the malignant end. The EHE is an intermediate variant of the family of vascular tumours.[1,2] It presents frequently during the second and third decades of life, but rarely occurs during childhood.[3,4] Both sexes are equally affected, though liver and lung lesions are more common in females.[1] The neoplasm usually presents as a solitary, rarely multiple, erythematous papule, nodule, plaque or nonhealing ulcers. The lower extremities are most commonly involved.[1] It not only involves soft-tissue, but also involves other sites such as liver, lung, bone, skin, lymph nodes, brain and heart.[1] EHE of the skin is extremely rare, it can be isolated or associated with systemic involvement. Majority of cases show multifocal localisations. The tumour arises from a medium-sized vessel mainly in superficial or deep soft-tissue, about 10%, arise within dermis.[3] The chromosomal translocation involving chromosomes 1 and 3 (t[1;3] [p36.3;q25]) is known to occur in EHE.[5]

There are no predisposing factors, but possible associations with trauma, therapeutic radiation and hormonal factors have been postulated. EHE shows multifocal involvement in 10% of cases, but isolated skin involvement is rarely described.[6] Clinically it has to be differentiated from a haemangioma, pyogenic granuloma, arteriovenous malformation and hamartomas.[1,4]

Definitive diagnosis relies on its histopathologic and immunohistochemical features. The tumour is composed histologically of epithelioid, round, to slightly spindle shaped endothelial cells with abundant eosinophilic cytoplasm and round vesicular nucleus. Nuclear pleomorphism is minimal. Intracytoplasmic vacuolisation and occasional intraluminal erythrocytes are regular features. Cytoplasmic vacuolisation probably represents primitive lumen formation by a single cell. Tumour cells are arranged in cords, short strands, small nests with minimal vascular differentiation and are embedded in fibromyxoid stroma.[6] In one-fourth of cases, there can be significant atypia, mitotic activity, focal splindling of cells and necrosis, which correlates with aggressiveness of tumour. Ultrastructural study has revealed the endothelial nature of the tumour cells surrounded by basal lamina, dotted with surface pinocytotic vesicles, intracytoplasmic lumina and occasionally containing Weibel-Palade bodies.[7] Immunohistochemical staining of tumour cell is positive for vascular endothelial markers (CD 31, CD 34 and factor VIII, vimentin and UEA-1 and mostly negative for cytokeratin).[2,3,6] Cases are always positive for at least one vascular endothelial marker, but not usually all. The cytokeratin is positive in only one fourth of patients with EHE.[7,8] Sensitivity of CD31 for diagnosing EHE is 100%, specificity is 62%.[9] CD31 is positive in kaposiform hemangioendothelioma, composite hemangioendothelioma, epithelioid sarcoma-like hemangioendothelioma, retiform

hemangioendotheliomas, epithelioid haemangioma, tufted angioma, reactive angioendotheliomatosis and angiosarcoma.[7-9]

About 19 cases of EHE with skin involvement have been reported in the literature [Table 1][1-4,6,10-13] and the majority of them show systemic localisation and most of them are adult patients. Isolated EHE of skin is reported in only four cases. Roh *et al*. (2000),[4] reported isolated cutaneous EHE in an 8-year-old female child, who presented with erythematous plaque on the left frontal area of the scalp. The lesion was excised with 3 mm margin. There was no evidence of recurrence or metastasis after a follow-up of 20 months. To the best of our knowledge, our case is the second case of EHE involving skin without systemic involvement in paediatric age group.

The detection of skin lesions should lead to a complete assessment of the extension of the disease to detect any internal localisation. Lymph node is the usual site of metastases. Thus wide excision is recommended with evaluation of regional lymph nodes and if they occur here, further surgery may be curative. Adjuvant treatment with interferon therapy and radiotherapy or chemotherapy may be used to restrain growth of incompletely removed tumours or in patients with multi system involvement.[14,15]

The prognosis of EHE is variable and uncertain. EHE displaying features of cellular atypia, mitotic activity (>1 mitotic figure per 10 high-power fields), necrosis and extensive spindling favours an aggressive course and correlates with poor prognosis.[7] Mentzel *et al*.[2] showed local recurrence in 3 cases and systemic metastases in 21% of patients, of which 17% died of their tumours; hence the authors suggested that EHE of the soft tissue should be better regarded as a fully malignant, rather than borderline, vascular neoplasm. Patients with cutaneous EHE have a favourable outcome than their more centrally located counterparts and isolated EHE of the skin probably behaves in a more benign fashion. However, In virtue of its malignant potential and infiltrative growth pattern, a close follow-up is recommended.[4] In our case, there was no evidence of distant metastasis or multifocal involvement, so after wide surgical excision and favourable histopathology report, we proceeded with close follow-up of patient clinically, once in 6 weeks for 6 months and every 3 months later on. As it was isolated EHE, literature says it probably behaves as benign lesion and so we are assessing him clinically for local recurrence, lymph node examination and any systemic complains.

Table 1: Reported cases of EHE

Author's name	Case reported
Tyring *et al*.,[10]	Reported a case in an adult, with violaceous nodules on the skin of the thigh and involving femur
Malane *et al*.,[11]	Reported cutaneous EHE with underlying calcaneus involvement
Resnik *et al*.,[3]	Reported solitary EHE on palm without systemic involvement
Mentzel *et al*.,[2]	Reported skin involvement in 4 cases of EHE
Quante *et al*.,[6]	Reported eight patients with an age range of 29-84 years, who presented with primary cutaneous tumours at a variety of sites including the palm, shin, neck, knee, nose, back and penis. Follow-up ranged from 4 months to 3 years and none of the lesions recurred and there have been no metastases
Roh *et al*.,[4]	Reported isolated cutaneous EHE in an 8-year-old female child, who presented with erythematous plaque on the left frontal area of the scalp. Systemic involvement was absent
Fenniche *et al*.,[12]	Reported EHE in a 34-year-old female involving right forearm and liver
Lakshmi *et al*.,[1]	Reported EHE involving skin and involving the underlying bone with diffuse osteolysis, in 16-year-old female who presented with painful progressive swelling and erythematous skin lesions involving the whole of her right lower limb since birth
Kato *et al*.,[13]	A case of multiple cutaneous EH was reported in a 52-year-old male, who presented with purplish-red nodules on both lower extremities. No other extracutaneous tumours were found

EHE: Epithelioid hemangioendothelioma

CONCLUSION

EHE is a unique vascular neoplasm of intermediate aggressiveness and unpredictable prognosis, which usually appears in adults. It generally affects soft-tissue and less frequently, the viscera such as lungs and liver. Cutaneous involvement is rare. To the best of our knowledge, this is the second reported case of childhood onset EHE arising from skin without systemic involvement. Clear resection of margins and regular follow-up is recommended as a treatment. We would like to point out that clinicians should be aware of this rare presentation in paediatric age group.

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