CASE REPORT

Pseudomyogenic (epithelioid sarcoma-like) hemangioendothelioma - a rare vascular neoplasm with deceptive morphology and distinctive immunophenotype

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Abstract

Pseudomyogenic (epithelioid sarcoma-like) hemangioendothelioma is a rare, low grade vascular (endothelial) neoplasm typically presenting as multicentric, superficial to deep nodules in extremities with a slight tendency of affecting young adult males. We report a case of pseudomyogenic hemangioendothelioma in a 15-year-old boy presenting initially with a 1 cm right thigh painless cutaneous lump. The lump was excised with the clinical impression of a sebaceous cyst. On microscopy, a poorly circumscribed, mild to moderately atypical spindle cell lesion in fascicular and storiform patterns with strikingly myoid-like eosinophilic cytoplasm was identified. The spindle cells were highlighted by pancytokeratin AE1/AE3, CD31, and ERG with retained INI-1, while being negative for MNF116, S100, CD34, EMA, desmin, SMA, caldesmon, myogenin, MyoD1, HHV-8 and CD163.

Following the first diagnostic report, a positron emission tomography–computed tomography (PET-CT) scan revealed another 4 cm ill-defined nodule accompanied by a smaller adjacent 0.7 cm ipsilateral satellite nodule within the right psoas muscle that displayed similar morphology and immunophenotype as the cutaneous lump, supporting the multicentric feature of this unique entity. It is an uncommon yet increasingly recognised neoplasm of endothelial origin possessing a misleading myoid morphology and distinctive immunophenotype worth notifying.

Keywords: pseudomyogenic hemangioendothelioma, epithelioid sarcoma-like, myoid-appearing vascular neoplasm, FOSB

INTRODUCTION

Pseudomyogenic (epithelioid sarcoma-like) hemangioendothelioma is a rare, low grade vascular (endothelial) neoplasm typically presented in young adult males as multiple superficial to deep nodules in extremities which display a deceiving myoid-like histomorphology and classic immunophenotype. We report a case of pseudomyogenic hemangioendothelioma diagnosed in Singapore General Hospital.

CASE REPORT

A 15-year-old boy of Chinese descent with no previous history of malignancy presented to our institution with a 1 cm painless right thigh subcutaneous lump. It was subsequently excised based on the clinical impression of a sebaceous cyst. The lesion grossly appeared as ill-defined yellowish fibrofatty tissue. On microscopy, there was an infiltrative lesion (Fig. 1) comprised of atypical spindle cells arranged in fascicles and storiform pattern (Fig. 2) in the background of haemorrhage with admixed conspicuous stromal neutrophils as well as scattered lymphocytes (Fig. 3). The tumour cells exhibited pleomorphic spindle to ovoid, vesicular, hyperchromatic nuclei and prominent eosinophilic cytoplasm resembling smooth muscle fibres, with occasional rhabdoid and epithelioid cells noted (Fig. 4). Few mitoses were identified. Neither discernable vascular lumina formation nor intracytoplasmic vacuoles were seen. Chondroid or osteoblastic differentiation was not evident.

Immunohistochemical study revealed multifocal positivity on pancytokeratin AE1/AE3, diffuse and strong positivity on CD31 and ERG while being negative for MNF116, S100,
FIG. 1: Lesional tissue with infiltrative borders (H&E x20)

FIG. 2: Spindle cells in fascicles with entrapped nerve bundles (H&E x100)

FIG. 3: Spindle cells with strikingly eosinophilic cytoplasm and background admixed inflammatory cells (predominantly neutrophils) (H&E x200)
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FIG. 4: Atypical, pleomorphic spindle cells with occasional rhabdoid cells (red arrow) (H&E x600)

CD34, desmin, caldesmon, SMA, myogenin, MyoD1, HHV-8, and CD163. INI-1 expression was retained (Fig. 5).

The diagnosis of pseudomyogenic hemangioendothelioma was made based on the classical clinical presentation, histomorphology and immunophenotype of this entity. Following the release of the report, a PET-CT scan was done and showed a separate 4 cm ipsilateral intramuscular nodule accompanied by an adjacent 0.7 cm satellite nodule deep within the right psoas muscle, both of which were entirely excised (Fig. 6). The intramuscular tumour showed extensive necrosis and hemorrhage (Fig. 7), apart from displaying a similar histological picture and immunophenotype, and hence was reported as the same entity as the previously excised cutaneous lesion.

DISCUSSION

The entity initially proposed with the name of ‘fibroma-like’ variant of epithelioid sarcoma\(^1\) in 1992 when 5 similar cases were first reported is currently designated as pseudomyogenic (epithelioid sarcoma-like) hemangioendothelioma since 2011 with 50 cases being reviewed\(^2\). It is an uncommon low to intermediate grade, rarely metastasizing vascular neoplasm predominantly affecting young adult (mean age 30 years) males (male to female ratio of 4.6:1), and often involving lower extremities (60%); with upper limbs, trunk, face and scalp being less affected.\(^2\) The lesion can be found in all planes of tissue including dermis (31%), subcutis (20%), muscle (34%) as in this case, and even bone (14%).\(^2\) Patients can present with painful or painless nodules (often multifocal or single mass with satellite nodule) for months before getting noticed. The tumour usually ranges from 1 to 2.5 cm in size, with only 10% being larger than 3 cm.\(^2\) Grossly, it typically has ill-defined borders with firm, grey or whitish appearance. On microscopy, it shows an infiltrative lesion composed of mild to moderately atypical spindle cells in fascicles or sheets, occasionally containing myxoid stroma. 50% of the reported cases including this case show prominent stromal neutrophils. On higher power of magnification, it reveals vesicular nuclei, small nucleoli and easily appreciable, strikingly eosinophilic cytoplasm resembling smooth muscle fibres which gives rise to its current interim name. Rhabdoid or epithelioid cells are occasionally identified. Mitotic activity is usually low (median 1 per 10 hpf).

On immunohistochemical study, the tumour usually expresses pancytokeratin AE1/AE3, thus can potentially be mistaken as sarcomatoid carcinoma or epithelioid sarcoma. The retained INI-1 expression distinguishes this entity from epithelioid sarcoma, and hence resolves the confusion arisen two decades ago. In contrast to pseudomyogenic haemangioendothelioma, sarcomatoid carcinoma occurs more often in older patients (median age 59 years), originates from the viscera and demonstrates a more aggressive cytology (marked nuclear pleomorphism and abundant mitoses). Despite the myoid appearance, smooth muscle or skeletal muscle markers including desmin, caldesmon, MyoD1 and myogenin are negative in pseudomyogenic haemangioendothelioma. However, smooth muscle actin (SMA) positivity is observed in one third of reported cases\(^2\), which again, in those
FIG. 5: Immunohistochemistry (IHC) of the tumour cells. Positive: AE1/3, CD31, ERG, INI-1 (red blocks). Negative: MNF116, S100, CD34, MyoD1, desmin. Other Negatives (not shown): SMA, myogenin, HHV8, CD163

FIG. 6: PET-CT shows two heterogenous nodules (red arrows) within the right psoas muscle. Inset: Scar tissue of previous buttock cutaneous lesion (blue arrow)
situations, might reasonably create a pitfall for making a false diagnosis of leiomyosarcoma or leiomyoma in view of its relatively bland cytology. Spindle cell rhabdomyosarcoma is one of the differentials based on its morphology, however, more mitoses should be identified apart from the positive desmin and myogenin stains. Endothelial markers such as FLI-1 and ERG are usually positive in pseudomyogenic haemangioendothelioma; and 50% of cases have diffuse CD31 positivity, suggesting its vascular origin though vascular lumina formation is not evident. CD34, MNF116, S100 and EMA are consistently negative. High grade angiosarcoma is a possible differential diagnosis, but it occurs in an older age group and shows much higher grade nuclear atypia. Dermatofibroma should be considered in cutaneous lesions, yet it does not exhibit abundant myoid-like, eosinophilic cytoplasm and shows Factor XIIIa positivity. In addition, FOSB stain has recently been found to be a novel immunohistochemical marker that displays diffuse and strong nuclear positivity in pseudomyogenic haemangioendotheliomas, and distinctively separates them from the histologically mimicking epithelioid hemangioendothelioma, or angiosarcoma.

As for cytogenetics, only a single case showing a balanced t(7;19)(q22;q13) as the sole anomaly was identified, with another case of unbalanced der(7)(7;19) in one out of 9 additional cases detected.

Conclusion
Pseudomyogenic hemangioendothelioma is a rare, low to intermediate grade neoplasm of endothelial origin that is especially liable to be misdiagnosed morphologically as a malignant tumour of smooth muscle or skeletal muscle derivative. In addition, its expression of keratin and endothelial markers could mislead some into a diagnosis of sarcomatoid carcinoma or high grade angiosarcoma. Correct appreciation of clinical features, morphology and immunohistochemistry is crucial to make an accurate diagnosis which is very important for management of the patients.

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REFERENCES