Aberrant epithelial membrane antigen expression in dermal cellular fibrous histiocytoma with central necrosis and epidermal ulceration: a potential mimicker of epithelioid sarcoma

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Abstract

Introduction
We have reported a case of cellular fibrous histiocytoma occurring as a polypoid, dermal nodule in the arm of a 10-year old boy. The tumour was predominantly composed of spindle-shaped cells with a mild degree of nuclear pleomorphism and showed unusual morphological features like central necrosis and epidermal ulceration. Apart from vimentin and CD10, surprisingly, neoplastic cells were diffusely stained with an epithelial membrane antigen. Although expression of the epithelial membrane antigen is absent in conventional fibrous histiocytomas, immunoreactivity for this marker has been reported in about 60% of dermal epithelioid cell fibrous histiocytomas.

Case report
A 10-year old boy presented to our observation with a non-painful, solitary, polypoid, cutaneous lesion; the lesion was focally ulcerated, measuring 1 cm in its greatest diameter, and located in the right arm. This is the first case of cellular fibrous histiocytoma, which exhibited diffused expression of the epithelial membrane antigen. The presence of tumour necrosis and epidermal ulceration, along with an aberrant expression of the epithelial membrane antigen, raised serious diagnostic problems, leading to a speculation regarding the presence of epithelioid sarcoma.

Conclusion
Immunohistochemical analyses, showing diffused nuclear INI1 (hSNF5/SMARCB1) expression and the absence of pancytokeratins, were extremely helpful in ruling out epithelioid sarcoma. Awareness of the possibility that dermal cellular fibrous histiocytoma may concurrently exhibit necrosis, epidermal ulceration and diffused expression of epithelial membrane antigen, is crucial to avoid a misdiagnosis of malignancy.

Introduction
Fibrous histiocytoma is a common fibro-histiocytic tumour which commonly occurs in the dermis and superficial subcutis (dermatofibroma). The diagnosis of dermatofibroma/fibrous histiocytoma is usually straightforward if the typical morphological features are present. However, some diagnostic difficulties may arise when one is dealing with some unusual morphological variants, including cellular, lipidised, haemosiderotic, aneurysmal, keloidal, granular cell, palisading, atrophic, clear cell, myxoid, lichenoid, balloon cell, signet-ring cell, with osteoclast-like giant cells, with smooth muscle proliferation, with prominent myofibroblastic proliferation, with intracytoplasmic eosinophilic globules, plexiform, epithelioid, atypical, epithelioid, and lastly, combined variants. Among these variants, cellular fibrous histiocytoma (CFH) may represent a diagnostic challenge because there is the risk of it being confused with other benign or malignant dermal tumours. CFH, first described by Calonje et al. as a distinct variant of fibrous histiocytoma, accounts to approximately 5% of cutaneous benign fibrous histiocytomas (dermatofibromas). CFH generally presents in young to middle-aged adults as a slowly growing, solitary nodule, ranging in size from 0.5 cm to 2.5 cm, with a slight male predominance. Although CFH has the tendency to develop in the same anatomic sites to those for conventional fibrous histiocytoma, it may occur at unusual sites such as the face, ears, hands and feet. Over the last two decades, there has been increasing evidence that CFH undergoes local recurrence more than the usual fibrous histiocytomas (rates of 25%) especially after incomplete surgical excision. Unlike conventional fibrous histiocytomas, characteristic morphological features of CFH are (i) higher cellularity, (ii) higher mitotic activity (up to 10 mitoses per high-power field), (iii) a more fascicular growth pattern, (iv) a deeper (subcutaneous) tumour extension, (v) a higher tendency to exhibit an epithelioid cell compo-

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nent, (vi) the possibility of undergoing central necrosis (10%–20% of cases), (vii) occasional epidermal ulceration and (vii) myofibroblastic differentiation (variable immunoreactivity for α-smooth muscles actin and desmin)2–4.

We have reported here, a rare case of CFH in a 10-year old boy, exhibiting unusual findings such as central necrosis, epidermal ulceration and an aberrant diffused expression of the epithelial membrane antigen (EMA). This immunohistochemical finding, which has not been reported in CFH, along with the above-mentioned unusual morphological features, may represent a potential diagnostic pitfall in the assessment of malignancy.

Case report
A 10-year old boy presented to our observation with a non-painful, solitary, polypoid, cutaneous lesion; the lesion was focally ulcerated, measuring 1 cm in its greatest diameter, and located in the right arm. The patient had no history of recent trauma. An excisional biopsy was performed. Multiple formalin-fixed and routinely processed sections were stained with haematoxylin–eosin for light microscopy. Histological examination at low magnification revealed an ill-defined, highly cellular, dermal tumour, partly surrounded by a lateral epidermal collarette (Figure 1). The tumour extended from immediately below the epidermis to the deep dermis, without evidence of subcutaneous infiltration. The epidermis above the tumour was focally ulcerated. The tumour was composed predominantly (90%) of a relatively uniform population of spindle-shaped cells (Figure 2), admixed with a minority (10%) of epithelioid cells (Figure 3). Binucleate cells were focally observed. The neoplastic cells had a palely stained eosinophilic cytoplasm, with vesicular nuclei containing prominent nucleoli. A mild degree of nuclear pleomorphism was focally seen. The neoplastic cells, predominantly arranged in short fascicles with a focal storiform growth pattern (Figure 2), were set in a fibrous stroma containing numerous small blood vessels, scattered lymphocytes and plasma cells. Foamy histiocytes, including Tuton cells, were not present. Although mitotic activity was high (10 mitoses per high-power field), no atypical mitosis was found. Notably, a central area of tumour necrosis with haemorrhage, surrounded by neoplastic spindle-shaped cells, was evident (Figure 4). This area was closely reminiscent of the so-called ‘necrotising nodule’ as typically seen in epithelioid sarcoma. Tumour extension into the subcutaneous tissue was not seen.

Immunohistochemical studies were performed with the labelled streptavidin–biotin peroxidase detection system using the Ventana automated immunostainer (Ventana Medical Systems, Tucson, Arizona, USA). A large panel of antibodies was used including the following: vimentin, EMA (Figure 5), pancytokeratins (MNF116; AE1/AE3), INI1 (hSNF5/SMARCB1) (clone BAF47) (Figure 6), CD10, Factor XIIIa, CD45, S-100 protein, HMB45, melan A, α-smooth muscle actin, desmin, myogenin, glial fibrillar acidic protein, P63, CD117,
CD31, CD34, synaptophysin, chromogranin A, neuron-specific enolase, claudin-1, CD99, lysozyme, CD68, CD163, CD45, CD43, CD30, CD56, CD138 and CD117. Immunohistochemical analyses revealed neoplastic cells diffusely stained with vimentin, EMA, CD10 and INI1 (hSNF5/SMARCBC1). Focal staining was obtained with factor XIIIa; however, staining intensity was the greatest in the background stromal cells, making interpretation difficult. No immunoreactivity was obtained with any of the other antibodies. Based on morphological and immunohistochemical features, the diagnosis of 'cellular fibrous histiocytoma (dermatofibroma) with aberrant EMA expression' was rendered. The patient was well and showed no evidence of local recurrence after a 6-month follow-up period.

**Discussion**

Fibrous histiocytoma (dermatofibroma) is the most common diagnosis among benign mesenchymal tumours occurring in the dermis. In its classic form, this tumour is easily recognised but the histological diagnosis can be challenging in daily practice, especially when evaluating unusual variants, including epithelioid, atypical and cellular variants. We have reported a rare case of dermal CFH occurring as a poly-poid nodule in the arm of a 10-year old boy. Notably, it was the unusual occurrence of central necrosis and epidermal ulceration, along with an aberrant EMA expression, that caused some diagnostic problems in the correct interpretation of the tumour as a CFH. In this regard, we admit that epithelioid sarcoma was seriously considered in the differential diagnosis. This is an aggressive malignant tumours that occurs in superficial soft tissues (including the skin) of adolescents and young adults (10–35 years of age). Clinically, like our case, epithelioid sarcoma may present as a relatively small, ulcerated, single, cutaneous nodule. Histological analyses revealed that it is composed of relatively bland-looking, focally atypical, neoplastic cells exhibiting an epithelioid morphology. However, a variable number of neoplastic spindle-shaped cells are usually present in most cases, occasionally representing the predominant/exclusive component (fibroma-like epithelioid sarcoma). A characteristic feature of epithelioid sarcoma is the presence of central necrosis surrounded by neoplastic cells, closely mimicking a granuloma-tous process, such as necrobiotic granuloma. A similar worrisome feature, along with epidermal ulceration and diffused EMA expression in our case, alerted us regarding the possibility of epithelioid sarcoma. In fact, it is widely known that this sarcoma typically co-expresses vimentin and diffused epithelial markers such as cytokeratins (low- and high-molecular-weight isoforms) and EMA. In this regard, our case was completely negative for cytokeratins, raising questionable diagnosis of epithelioid sarcoma. The absence of CD34, a marker which can be found in about 50% of

**Figure 4:** A granuloma-like necrosis with haemorrhage is seen in the central tumour region. Magnification × 100.

**Figure 5:** Neoplastic cells are strongly and diffusely stained with EMA. Staining of the overlying epidermis served as an internal control. Magnification × 100.

**Figure 6:** Retention of INI1 (hSNF5/SMARCBC1) nuclear expression in neoplastic cells argued against the diagnosis of epithelioid sarcoma. Nuclear staining, detected in the keratinocytes, stromal and endothelial cells of the native dermis, served as internal controls. Magnification × 150.

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epithelioid sarcomas, also argued against the diagnosis of this malignant tumour. However, we admit that the retained INI1 (hSNF5/SMARCB1) nuclear expression, more than other immunohistochemical markers, was crucial in ruling out epithelioid sarcoma. In fact, the loss of INI1 (hSNF5/SMARCB1) expression is highly characteristic in the apro-priate morphological context of both conventional and proximal-type epithelioid sarcoma, being detected in >90% of cases.

The most striking feature of the present case was the diffused expression of EMA. Although conventional fibrous histiocytoma is typically negative for this epithelial marker, focal to diffused EMA staining was found in 64% of epithelioid fibrous histio-cytomas. The significance of this unusual expression is still unclear. We are the first to report a diffused expression of this marker even in a case of dermal CFH. Whether CFH is another variant of fibrous histiocytoma, which exhibits a significant EMA expression, should be demonstrated in future studies including a large series of cases.

Conclusion
Awareness of the possibility that CFH may occur in the dermis of adolescents, exhibiting necrosis, epidermal ulceration and diffused EMA expression, is crucial to avoid a misdiagnosis of malignancy. Although the immunohistochemical profile of dermal fibrous histiocytoma, including its more unusual variants, is not specific, similarly a wide panel of antibodies, including INI1 (hSNF5/SMARCB1), is mandatory for a correct diagnostic approach.

Abbreviations list
CFH, cellular fibrous histiocytoma; EMA, epithelial membrane antigen.

Consent
Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

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References

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