Angiomatoid fibrous histiocytoma (AFH) is a very rare tumour entity, which predominantly affects adolescents and young adults with a slight female predilection (1–3). As the tumour often appears as a non-characteristic, skin-coloured, slowly growing nodule, mostly on the extremities, the recognition of AFH can be challenging and may require sophisticated diagnostic techniques including immunohistochemistry and molecular genetic analysis. Here, we present a child with a long-standing solitary nodule on the right thigh, which was initially misdiagnosed as interstitial granuloma annulare (GA). The correct diagnosis of solid variant of AFH could only be established after complete excision of the nodule.

**CASE REPORT**

A 13-year-old girl presented with a 16-months history of a solitary, asymptomatic, slowly growing skin-coloured nodule, measuring 1 × 1.5 cm in size located on the ventral aspect of her left lower thigh (Fig. 1A). Nine months ago, a punch biopsy suggested interstitial GA. Various topical treatments including glucocorticoids, pimevansam, and subcutaneous injection of histiocytes in the upper and mid dermis, compatible with interstitial GA (Fig. 1B). However, histological investigation of the lower dermis and subcutis revealed a well-circumscribed tumour consisting of multiple nodules comprised of atypic spindle and epithelioid cells with a marked nuclear pleomorphism (Fig. 1C, D). The tumour cells were surrounded by an inflammatory infiltrate composed of plasma cells and small lymphocytes arranged as secondary lymph follicles with prominent germinal centres. The nodule was encased by a dense fibrous pseudo-capsule (Fig. 1C). Immunostaining showed a strong cytoplasmic positivity for Vimentin, a multifocal positivity for Desmin as well as focal expression of SMA, while EMA was negative, consistent with a solid variant of angiomatoid fibrous histiocytoma (Vimentin+, Desmin−, sm-Actin−, CD20−, CD23−, CD43+, CD3+, CD4−, CD56−, CD30−, CD123+, TCL1+, MNI16+, KL1+, EMA−, S-100−, HMB45−, MelanA−, MIC2+, Calretinin+, AE1/AE3−, Caldesmon−, MyoD1−, Myf-4−, CD34−, CD68−, CD45RA−, Ki-67 2%).

Recently, recurrent chromosomal breakpoints in the **EWSR1** locus (22q12) and the **FUS** locus (16p11) leading to a **EWSR1/CREB1** (t(12;22)(q13;q12)), a **EWSR1/ATF1** (t(12;22)(q13;q12)) or a **FUS/ATF1** (t(12;16)(q13;p11)) gene fusion have been identified in AFH (3). To determine the presence of these chromosomal translocations, we performed interphase fluorescence in situ hybridization (FISH) on lesional skin targeting the **EWSR1** (22q12) and the **FUS** (16p11) locus (all probes from Abbott/Vysis). Evaluation of 200 nuclei showed no evidence for breakpoints affecting these regions (Fig. 1D, Table S1).

Staging procedures, including computed tomography scans and ultrasonography of the peripheral lymph nodes revealed an enlarged lymph node within the right groin as well as a solitary pulmonary nodule (3.4 mm diameter). Since this pulmonary nodule proved stable in a CT-control after 3 months, it was considered benign. An inguinal lymph node biopsy revealed a dermopathic lymphadenopathy.

Fig. 1. (A) Clinical picture of Angiomatoid fibrous histiocytoma (AFH) with cutaneous hyperpigmentation induced by anthralin therapy. Inset: Subcutaneous nodule of AFH. (B) Histology of interstitial granuloma annulare showing infiltrates of histiocytes in the upper and mid dermis (H&E). Inset: Interstitial infiltrates of histiocytes highlighted by CD68 immunostaining. (C) Low power photomicrography showing nodular configuration of tumour cells surrounded by inflammatory infiltrates (H&E). Inset: lymphoid infiltrates forming germinal centres separated by a fibrous pseudo capsule. (D) The tumour consisted of spindle and epithelioid atypical cells with significant nuclear pleomorphism. Inset: Fluorescence in situ hybridization. Interphase nuclei hybridised with LSI **EWSR1** probe (Dual Color, Break Apart Rearrangement Probe; Vysis). The colocalisations of the red and green signals excluded the presence of a translocation affecting the **EWSR1** gene.

1http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1698

© 2014 The Authors. doi: 10.2340/00015555-1698

Journal Compilation © 2014 Acta Dermato-Venereologica. ISSN 0001-5555
adenocarcinoma with no evidence of infiltrating tumour cells. Resection of the area on the left lower thigh with a margin of 1 cm was performed and no tumour relapse has been observed to date.

DISCUSSION

AFH was initially described by Enzinger in 1979 (4). Wide local excision has been proposed as the treatment of choice for AFH (3). As sporadic cases of metastases (<5%) and local recurrences (up to 15%) have been reported, it is important to distinguish this entity from benign processes (2, 5). On the other hand, it is necessary to exclude malignant fibrous histiocytoma and other highly malignant tumours to avoid overtreatment (6). To our knowledge this is the first case of AFH masked by an overlying interstitial GA.

Systemic symptoms such as anaemia, pyrexia and malaise have been reported in association with AFH suggesting cytokine production by the tumoural tissue (1, 4, 5). Since our patient suffered from mild anaemia at the time of diagnosis and induction of interstitial GA by immunomodulatory drugs like interferon-α has been described, one may speculate that in our case the interstitial GA was induced by AFH-derived cytokines (7). It is noteworthy that the existence of the malignant tumour was initially missed due to the too superficial biopsy. Palpation of the subsurface tumour and ultrasound scan must, therefore, lead to a deeper skin biopsy.

Histologically, AFH is characterised by the proliferation of round or spindled cells interrupted by areas of haemorrhage, a surrounding inflammatory infiltrate often forming germinal centres and a fibrous pseudocapsule (1, 2, 4, 5). If blood filled spaces are present, the spectrum of histologic differential diagnoses comprises vascular tumours such as spindle cell haemangioma, cutaneous angioma, spindle cell haemangioma, cutaneous angiosarcoma or no-blood filled spaces are present, the spectrum of histologic differentiation: role in VEGF-induced angiogenesis. Int J Cancer 2010; 128: 2602–2612.

ACKNOWLEDGEMENTS

The authors thank Prof. R. Siebert, Institute of Human Genetics, Kiel, Germany, for support of the study and critical reading of the manuscript. The authors thank Prof. C. D. Fletcher, Department of Pathology, Harvard Medical School, Boston, MA, for confirming the histological diagnosis. The authors declare no conflict of interest.

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