PATHOLOGICA 2014;106:327-329

ORIGINAL ARTICLE

A peculiar fibroma-like lesion of superficial soft tissue: morphologic and immunophenotypic evaluation

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Key words

Mesenchymal tumours • Immunohistochemistry

Summary

Apeculiar lesion of superficial soft tissue characterised by fibroma-like morphology and an immunohistochemical profile consisting of CK+, VIM+, CD34+, CD31+/-, FLI1+ and INI-1 retained is described. The lesion entered into differential diagnosis with the so-called fibroma-like variant of epithelioid sarcoma, with the entities defined as ES-like/pseudomyogenic haemangioendothelioma and the recently identified entity defined as superficial CD34+ fibroblastic tumour. All of these entities share a common morphological structure, but differ in their immunophenotypic profile.

A 26-year-old man presented for a subcutaneous slow-growing, painless swelling on the left wrist lasting about two years. The patient was subjected to the surgical excision of the mass located in subcutaneous tissues, close to the tendons of the extensor muscles.

Materials and methods

At macroscopic examination, the surgical specimen was oval shaped, measured 1-8 x 1 cm, and the sectional area showed a pearly, homogeneous appearance. The outer surface was smooth. The formalin-fixed, paraffin-embedded sample was stained with haematoxylin-eosin and investigated with the following immunohistochemical antibodies: VIM (monoclonal 1:50 Dako), CK AE1-AE3 (monoclonal 1:50 Dako), EMA (monoclonal 1:50 Dako), SMACT (monoclonal 1:50 Dako), CALP (monoclonal 1:50 Dako), DESM (monoclonal 1:50 Dako), MYOGL (polyclonal 1:500 Sigma Aldrich), S100 (polyclonal 1:400 Dako), Ki-67 (monoclonal 1:75 Dako), CD34 (monoclonal 1:20 Dako), CD31(monoclonal 1:20 Dako), INI-1 (polyclonal 1:500 Ventana Riche), FLI-1 (polyclonal 1:50 Santacruz Biotech).

Results

Histologic findings: a solid proliferation with a spindled cellular fibroblast-like component (Fig. 1a) was seen that was sometimes myoid-like (Fig. 1b). Among these elements pleomorphic, atypical cells with voluminous, hyperchromatic, irregular nucleus, sometimes multiple (Fig. 1c, d) were found with faintly acidophilic cytoplasm. Mitotic activity was virtually absent. The stroma was very loose and faintly fibrillar. The elements were assembled into variously oriented fascicles.
The results of immunohistochemistry are summarized in Table I and show the following immunophenotypic profile: CK+ (Fig. 2a),VIM+ (Fig. 2b), CD34+ (Fig. 2c), CD31 (Fig. 2d), INI-1-retained (Fig. 2e), and Fli-1+ (Fig. 2f).

Discussion

In the interpretation of this case numerous diagnostic hypotheses were considered that were progressively discarded.
The age of the patient, localisation of the lesion, its slow and indolent growth and the immunophenotypic profile,

Acknowledgements
The authors thank Dr. AP Dei Tos for collaboration in the interpretation of the lesion, Dr. Al Folpe for prompt reprints of his work, and Prof. J. Rosai for valuable advice.

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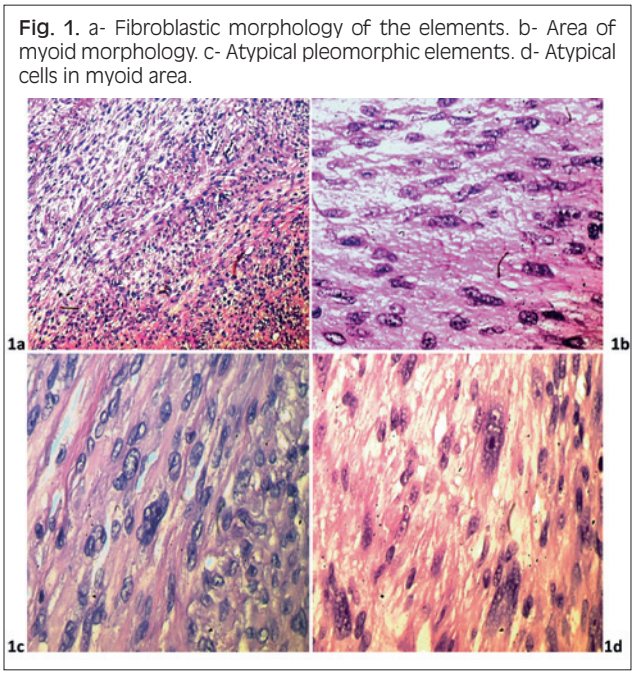


Fig. 1. a- Fibroblastic morphology of the elements. b- Area of myoid morphology. c- Atypical pleomorphic elements. d- Atypical cells in myoid area.

characterized by the simultaneous expression of cytokeratin, vimentin and CD34, would support a diagnosis of epithelioid sarcoma (ES). The morphological structure, predominantly spindle-celled, is different from the classic description of this tumour, lacking the pseudogranulomatous aspects, scalloped necrosis and the epithelioid cellular component.

Since 1992 there have been five cases with the same morphologic characteristics and simultaneously expressing VIM and CK reported in the literature. These lesions were labeled as "fibroma-like variants of ES [1].

In 1999, in a review of 112 cases of ES, seven were attributed to the aforementioned variant [2], 50% of which had documented expression of CD34.

In 2003, seven cases with similar morphologic characteristics and expressing an immunophenotypic profile consisting of VIM+, CK+, CD34-, CD31+ and FLI-1+, were categorised as "ES-like haemangiendothelioma" [3].

In the fifth edition of Enzinger & Weiss's *Soft Tissue Tumors* (2008), two separate entities were reported; one was described as a fibroma-like variant of ES, and the other as ES-like haemangioendothelioma. The former is CD34+ and CD31-, and the latter CD34- and CD31+ [4].

In the same year, a brief report of 29 cases with the same morphology and immunophenotypic pattern (CK+, VIM+, CD34-, INI-1 intact) were considered to be "pseudomyogenic (fibroma-like) variants of ES" [5].

In 2011, based on a study of 50 cases, the same authors, using a wider panel of antibodies, giving an immunophenotypic profile consisting of CK+ (100%), CD34+(0%), CD31+ (50%), FLI-1+ (100%), INI-1 intact (100%), redefined the lesion as "pseudomyogenic haemangioendothelioma" [6]. In a comment on this report in the same journal, in a Letter to the Editor [7], the authors of an earlier report [3] suggested that the morphologic and immunophenotypic identity of the lesion termed by them as ES-Like haenmangioendothelioma was the same as the one called by the authors as pseudomyogenic haemangioendothelioma [6].

Very recently a study entitled "Superficial CD34-Positive Fibroblastic Tumor" [7] was published in which, on the basis of 18 cases, a peculiar neoplasm of the superficial soft tissues was described, hitherto not reported. The neoplasm was found in adult subjects, mainly located in the extremities, and was morphologically characterised by a fascicular growth pattern of spindled cells, with striking, often bizarre cellular pleomorphism. All cases showed strong, diffuse CD34 positivity, focal cytokeratin expression (69%), SMARGCB1 (INI-1) retained, and Ki-67 < 1%. S100, SM-act, desmin and FLI-1 were all negative. Thirteen patients were available for follow-up; 12 were alive without evidence of disease. Only one patient developed locoregional lymph node metastases seven years after marginal excision of the tumour. The authors concluded that this was a distinctive low-grade mesenchymal neoplasm of intermediate (borderline) malignancy.

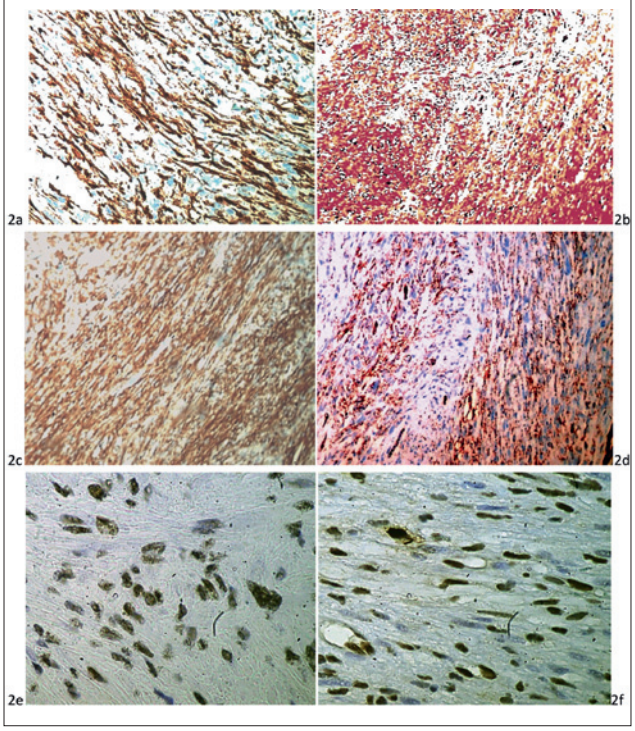
A literature review shows that over time, around the core basis of a lesion morphologically defined as fibroma-like and immunophenotypically characterised by the simultaneous expression of CK and VIM, a variety of antibody associations have been created. Different denominations have also been assigned to such associations. The differences occur mainly in the expression of CD34, CD31, FLI-1 and INI-1. Currently, according the Stanford's criteria [9], classic ES shows positivity for CD34 in 50% of cases, associated with loss of INI-1, and negativity for CD31 and FLI-1. In fact, in one of the aforementioned reports [2], 50% of the cases showed positivity for CD34 and negativity for CD31, consistent with classic ES. In other reports [3 5 6], constant negativity for CD34 is seen, associated with CD31+, FLI-1+ and INI-1 retained. From these data it is evident that it is justifiable in the first case the definition of fibroma-likeES and, conversely, in the second that of ES-Like/Pseudomyogenic Hemangioenothelioma. While on one hand the loss or retention of INI-1 is currently considered a discriminating element to establish or exclude an ES [10], the expression of CD31 and FLI-1 supports an endothelial histogenesis [11 12]. The recently described entity [8] with its distinctive immunophenotypic profile (CK+, VIM+, CD34+, Ki-67 < 1%, FLI-1- and INI-1retained) adds a

Tab. I. Immunophenotipic profile.

VIM	CK	EMA	SMA	CALP	DESM	MYOGL	S100	Ki67	C34	CD31	INI1	FLI-1
+diff	+diff	rare	neg	neg	neg	neg	neg	<1%	+diff	+f	ret.	+diff

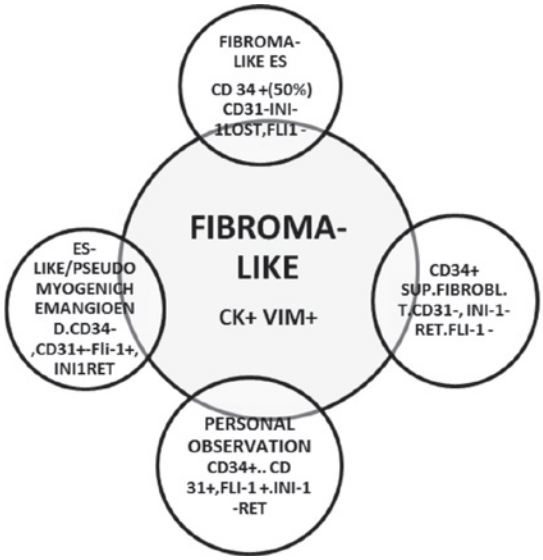
f: focal; diff: diffuse; neg: negative; ret: retained.

Fig. 2. a - CK AE1-AE3. b - VIM. c –CD34. d- CD31. e- INI-1. f- FLI-1



new subgroup to this complex group of lesions. With regards to the prognosis of these lesions, the literature does not mention differences between the classical form of ES and its fibroma-like variant, while the ES-like/pseudomyogenic haemangioendothelioma and the superficial CD34+ fibroblastic tumour are considered low-risk lesions (borderline).

Fibroma – like tumour group



Conclusions

The lesion that we observed with its immunophenotypic profile (CD34+, CD31+, FLI-1+, INI-1-retained) cannot be compared to any of the above-described fibroma-like entities with which it shares a common morphological structure for the following reasons: - It cannot be considered as a fibroma-like variant of ES because it has intact INI-1; It cannot be considered as an ES-like/pseudomyogenic haemangioendotelioma because it has intense expression of CD34. - It cannot be considered as a CD34+ fibroblastic superficial tumour because it has intense expression of both CD31 and FLI-1. It is unclear if these various immunophenotypic expressions are indicative of different pathological entities or variants of a single entity, and further study will be needed to better to define this entity.

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