Case report

Dermatofibroma-like granular cell tumour: a potential diagnostic pitfall

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Dermatofibroma-like granular cell tumour (GCT) is a rare entity, with only two cases having been described so far. We report another case in a 62-year-old woman, discuss histopathological features, and review other tumours in which granular changes have been observed. Our tumour was composed predominantly of oval-to-spindle granular cells with prominent nucleoli, arranged in short fascicles and storiform pattern, infiltrating around collagen bundles. Immunohistochemical analysis with antibodies against CD31, CD56, CD68, CD117, S-100 protein, inhibin, calretinin, EMA, p53 and MIB-1 was performed, showing expression of CD56, CD68, S-100 protein, inhibin and calretinin. The diagnosis of atypical dermatofibroma-like GCT was made.

Key words: granular cell tumour, soft tissue tumours, S100.

Introduction

Granular cell tumour (GCT) was first described in 1926 by Abrikssof. It is characterised by epithelioid cells with eosinophilic cytoplasm containing an abundance of eosinophilic granules that ultrastructurally represent lysosomes [1]. Morphologic features of a typical GCT are distinct, and the diagnosis is usually straightforward. However, cases with atypical appearance may be challenging in both the diagnosis and subsequent assessment of biologic behaviour. Moreover, nonspecific granular changes may be present in a variety of other benign and malignant skin and soft tissue tumours [2, 3, 4, 5, 6, 7, 8, 9, 10]. This may lead to serious diagnostic errors if the entities are confused with GCT. Herein we describe an atypical GCT with rare dermatofibroma-like morphology and briefly discuss criteria of malignancy in GCT. Additionally we provide a short review of tumours that may show granular cell changes.

Material and methods

A 62-year-old Caucasian woman with no significant clinical history underwent surgery of a skin tumour on the back under the right scapula. The clinical appearance was that of a dermatofibroma. The tumour formed a vaguely demarcated nodule measuring 18 mm in diameter and was retrieved in skin excision measuring 50 × 30 × 18 mm. No follow-up data are available.

The tissue was formalin fixed and paraffin embedded, and 5-μm-thick sections were made for hematoxylin and eosin (H&E) staining and immunohistochemical studies. Antibodies used included CD68 (Dako Denmark A/S, PG-M1, dilution 1 : 50), CD56 (Cell Marque Rocklin, CA, USA, clone MRQ-42, dilution 1 : 2000), S-100 protein (Dako Denmark A/S, polyclonal, dilution 1 : 5000), inhibin (Cell Marque Rocklin, CA, USA, clone Alpha(R1), dilution 1 : 25), calretinin (Dako Denmark A/S, DAK-calret 1, dilu-

tion 1 : 50), CD117 (Dako Denmark A/S, polyclonal, dilution 1 : 200), EMA (Dako Denmark A/S, E29, dilution 1 : 400), CD31 (Dako Denmark A/S, JC70A, dilution 1 : 50), p53 (Ventana, BP53-11, predilute), and MIB-1 (Ventana, 30-9, predilute). Staining was conducted on a Benchmark Ultra stainer (Ventana/Roche) using the avidin-biotin complex method with horseradish peroxidase as an enzyme and 3,3'-diaminobenzidine for a substrate.

Results

The tumour was located in the dermis, with extension into subcutaneous fat. It consisted of cells with granular eosinophilic cytoplasm, with bland looking nuclei. In some cells, larger eosinophilic inclusions with a surrounding clear halo, which corresponded to pustulo-ovoid bodies of Milian, were observed (Fig. 1). In some areas, prominent vesicular nuclei with nucleoli were seen. Cells in the deeper parts of the tumour had more epithelioid morphology and were arranged in solid aggregates (Fig. 2). However, most of the cells were oval to spindle shaped and predominantly arranged in short fascicles or showing a storiform pattern (Fig. 3), with peculiar growth along the hair follicles. The cells were dispersed in prominently desmoplastic tumourous stroma (Fig. 4), entrapping and encircling hyalinised bundles of collagen, thus simulating classical dermatofibroma morphology. Multiple nerve bundles were located adjacent to the tumour. The lesion showed no mitotic activity. Immunohistochemically, the cells expressed diffusely CD56, CD68, S-100 protein (Fig. 5), calretinin and inhibin (Fig. 6). CD117 and EMA were negative as well as CD31. Staining for p53 was positive in 80% of nuclei, and the MIB-1 assessed proliferation index was 3%. The diagnosis of an atypical granular cell tumour was made, based on Fanburg-Smith criteria [11]. To our knowledge, only two similar cases with prominent dermatofibroma-like morphology have been described in the literature so far [12, 13].

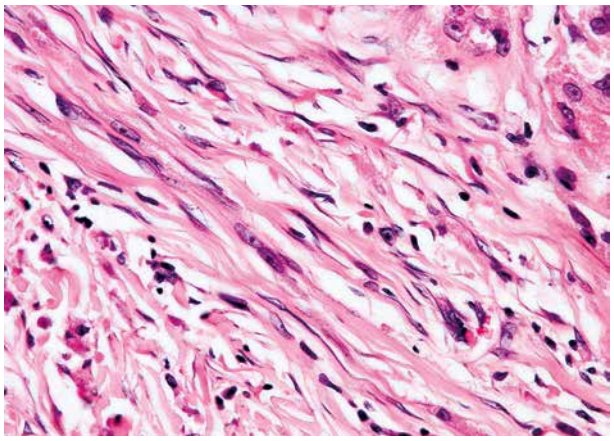

Fig. 1. Spindle-shaped tumour cells with granular cytoplasm, vesicular nuclei with nucleoli and more epithelioid tumour cells with pustulo-ovoid bodies. HE, original magnification 400×

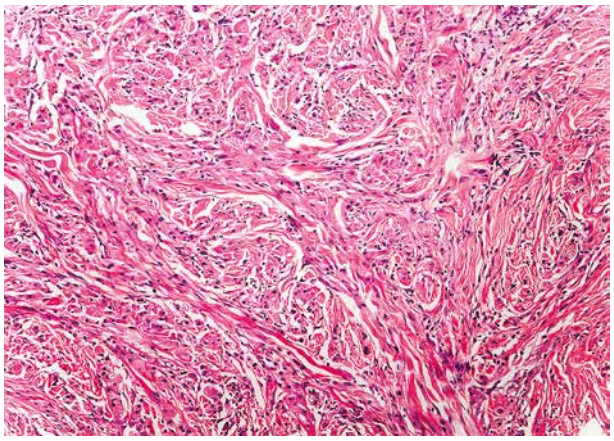

Fig. 2. Less desmoplastic areas with more epithelioid tumour cells. HE, original magnification 100×

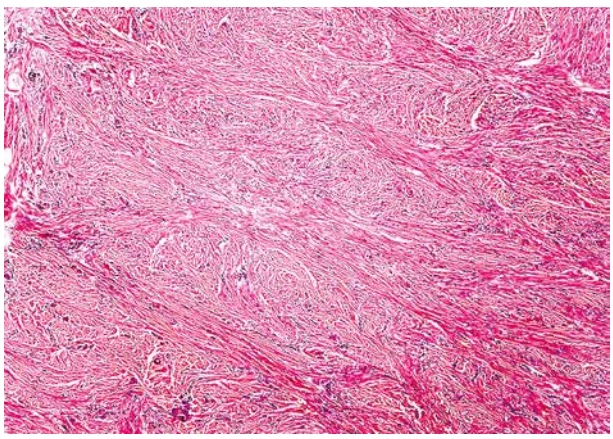

Fig. 3. Spindle-shaped tumour cells arranged in storiform pattern. HE, original magnification 40×

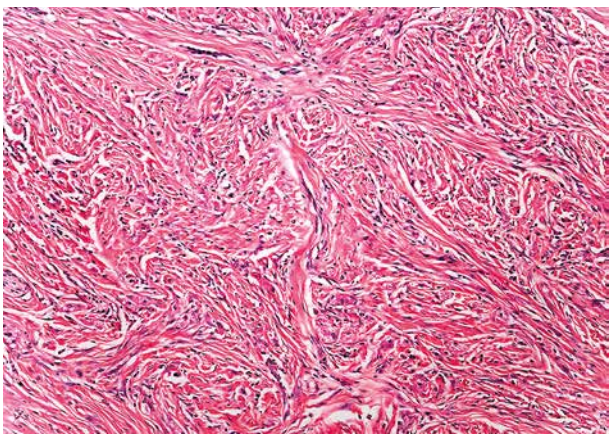

Fig. 4. Tumour cells dispersed in prominently desmoplastic stroma. HE, original magnification 100×

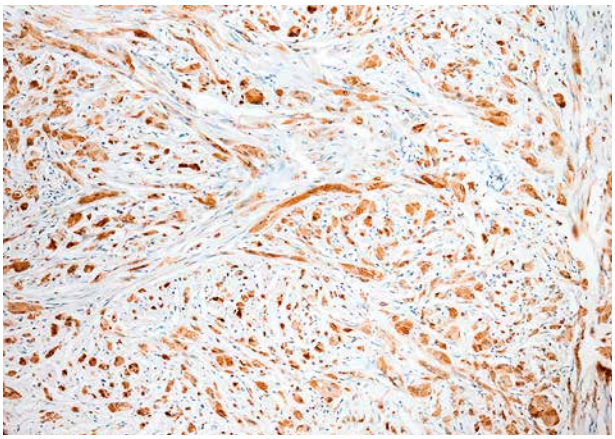

Fig. 5. Strong diffuse expression of S-100 protein. Original magnification 100×

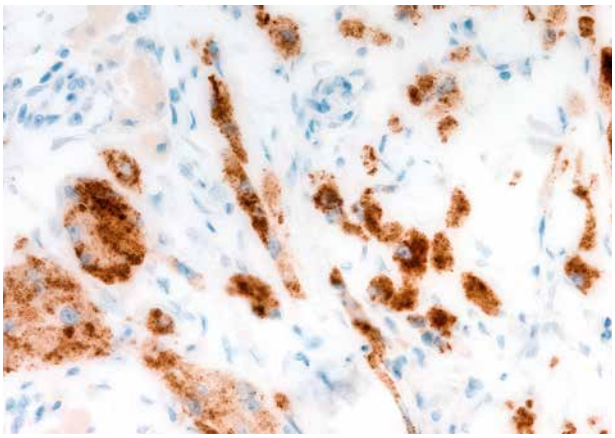

Fig. 6. Strong diffuse expression of inhibin. Original magnification 400×

Discussion

The GCT shows no significant age or sex predilection, and its occurrence has been described in many locations, the organs most frequently affected being skin, soft tissues, oral cavity and oesophagus [1]. Although the morphology is characteristic, granular changes represent a non-specific phenomenon that may be encountered in various soft tissue tumours that must be excluded in differential diagnosis, especially when dealing with cases of GCT with unusual morphology. The reason for granular change is unclear, and reactive or degenerative nature has been suggested as the most probable explanation. The granules correspond ultrastructurally to lysosomes with autogenous phagocytosed material (autophagosomes) [14], and lysosomal origin is further supported by immunohistochemical positivity of CD68, which can be demonstrated in GCTs and also in regions with granular change in other tumours.

Histogenetically, the most accepted theory proposes origin of GCT from Schwann cells, this being supported by its frequent localisation adjacent to peripheral nerves, ultrastructural features [15], myelin sheath components contained in autophagosomes [14] and immunohistochemical expression of S-100 protein, vimentin and CD56. Moreover, GCTs express NSE, PGP9.5, calretinin and inhibin [16].

Table I. Fanburg-Smith criteria of malignancy

Fanburg-Smith criteria
Vesicular nuclei with macronucleoli
Spindle cell morphology
Cellular pleomorphism
High N/C ratio
Necrosis
Mitotic rate > 2/10 fields of 200× magnification

Table II. Immunophenotype of tumours possibly mimicking GCT

	S-100	Melan A/HMB45	SMA/desmin	CD34	AE1/AE3
GCT	positive	negative/negative	negative/negative	negative	negative
Melanoma	positive	positive/positive	negative/negative	negative	negative
MPNST	weakly	negative/negative	rarely/rarely	rarely	rarely
PEComa	rarely	positive/positive	positive/positive	negative	negative
Smooth muscle tumours	rarely	negative/negative	positive/positive	negative	negative
Alveolar soft part sarcoma	negative	negative/negative	variable/variable	negative	negative
Angiosarcoma	negative	negative/negative	negative/negative	positive	rarely
Dermatofibrosarcoma protuberans	negative	negative/negative	negative/negative	positive	negative
Dermatofibroma	negative	negative/negative	negative/negative	rarely	negative
Basalioma, adnexal tumours	negative	negative/negative	negative/negative	negative	positive
Atypical fibroxanthoma	negative	negative/negative	negative/negative	negative	negative
Non-neural GCT	negative	negative/negative	negative/negative	negative	negative

Biological behaviour of GCT is almost exclusively benign. However, several cases with local recurrence and even metastases have been described. Fanburg-Smith *et al*. [11] proposed criteria for evaluation of GCT's biological behaviour based on its morphological features (Table I), thus dividing tumours into benign, atypical (fulfilling at least one criterion) and malignant (fulfilling at least three criteria) categories, with increased risk of recurrence or metastases in the latter two subgroups. Vascular invasion and perineural spreading may be present in a relatively high proportion of GCTs [17], although these correlate neither with morphologic criteria of malignancy nor with malignant behaviour.

Many other tumours may show focal granular change of cells together with morphological features typical for a particular lesion but uncommon in the GCTs. In other situations, however, granular change may be widespread, obscuring clues for the correct diagnosis and leading to the misdiagnosis of benign GCT. So far, granular cell change has been described in neoplasms of soft tissues as well as in tumours of epithelial and neuroectodermal origin, including entities with various biologic behaviour (Table II).

Based on the immunohistochemistry results of our case (strong diffuse S-100 protein positivity, calretinin and inhibin positivity), we excluded possible diagnoses of granular cell dermatofibroma (S100-protein negative), melanoma (inhibin and calretinin negative) and malignant peripheral neural sheath tumour (weak S-100 expression, lack of inhibin and calretinin, mitotic activity).

Only two cases of granular cell tumour with prominent dermatofibroma-like morphology similar to our case have been described in the literature to date [12, 13]. The first case [12] presented on the back of a 60-year-old Afro-American woman, while the second case [13] was localised in the pubic area of a 48-year-old man. All cases showed at least focal cell spindling and nuclei with prominent nucleoli, thus fulfilling criteria for an atypical GCT, although in none of the cases has recurrence been reported.

In conclusion, we presented a rare case of dermatofibroma-like GCT fulfilling criteria of an atypical GCT as defined by Fanburg-Smith. Based on the currently available data, there is no evidence that dermatofibroma-like morphology, even with atypical features, leads to more aggressive behaviour. When dealing with GCTs with unusual appearance, it is however necessary to consider other entities, including those with malignant behaviour.

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The authors declare no conflict of interest.

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