

Non-neural Granular Cell Tumour of Uncertain Malignant Potential: A Case Report and Review of Diagnostic Dilemmas

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Abstract

Granular cell tumours are rare, typically benign neuroectodermal neoplasms. While most follow an indolent clinical course, a small subset exhibits aggressive behaviour. We report a case of a granular cell tumour of uncertain malignant potential, non-neural type, in an 87-year-old male, presenting as a rapidly growing, ulcerated forehead nodule. Histopathology revealed high-risk features, including nuclear pleomorphism, increased mitotic activity, and perineural invasion. This case highlights diagnostic challenges in histomorphology, immunohistochemistry and application of conflicting diagnostic criteria—namely the Fanburg-Smith and Nasser frameworks—to determine malignancy in the absence of documented metastasis.

Keywords: Granular cell tumour; cutaneous non-melanoma skin cancer; malignant granular cell tumour; non-neural granular cell tumour

Introduction

Granular cell tumours are rare soft tissue neoplasms, first described by Abrikossoff in 1926. Though initially thought to be of myogenic origin, immunohistochemical and ultrastructural evidence now strongly support a derivation from Schwann cells [1]. Granular cell tumours can occur anywhere but are most frequent in the head and neck, particularly the tongue. While generally sporadic, they are occasionally associated with Noonan's syndrome [2].

The vast majority (98%) are benign. Malignant granular cell tumours are exceedingly rare, accounting for approximately 1–2% of cases [1, 3]. A subset of non-neural granular cell tumors have been identified which may not derive from neural tissue [4–7]. Some, as in this case, show anomalous myofibroblastic staining and include a specific, rare variant known as "primitive polypoid non-neural granular cell tumor" which characteristically presents as S100-negative and SOX10-negative and can display patchy or focal positivity for smooth muscle actin due to myofibroblastic differentiation. Distinguishing between benign, atypical, and malignant GCTs remains a significant challenge for pathologists, as the clinical presentation often mimics non-melanoma skin cancers when ulceration or rapid growth is present [1].

Case Presentation

Clinical History

An 87-year-old gentleman was referred to the dermatology department with a rapidly enlarging, ulcerating nodule on his right forehead. The lesion was clinically suspicious for a high-risk non-melanoma skin cancer. Given the patient's age and the lesion's growth kinetics, an urgent excisional biopsy was performed.

Histopathology

Microscopic analysis showed an atypical epithelioid and focal spindle cell proliferation within the dermis, with areas of overlying epidermal ulceration (Figure 1). The tumour cells exhibited nuclear pleomorphism with prominent nucleoli, multiple mitoses per 10 high-power fields, and perineural invasion (Figure 2 and 3). The deep margin was positive for tumour cells. The immunohistochemistry (IHC) profile showed immunoreactivity for CD68 and smooth muscle actin. Histochemistry with control showed PAS-D positive granular cytoplasmic inclusions (Figure 4). Sox-10 and S-100 were negative confirming non-neural origin. Interestingly, there was also focal positivity for pan-cytokeratin (Figure 5). Tumour cells were negative with Melan A, HMB-45, CK5/6, p63, CD34, and desmin. Ki67 showed proliferation in 80% of cells.

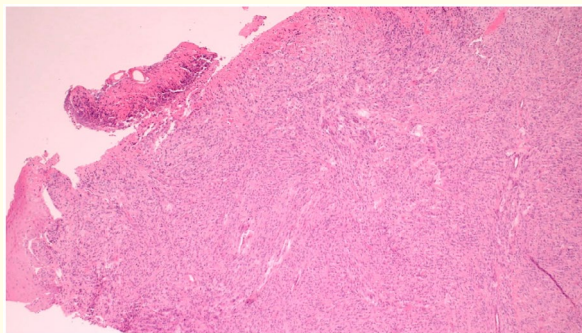


Figure 1: Dermal neoplasm with ulcer, haematoxylin and eosin, low power.

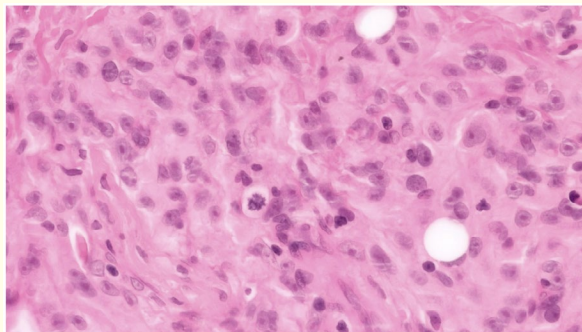


Figure 2: Epithelioid and spindle cells with cytologic atypia and mitoses, haematoxylin and eosin, medium power.

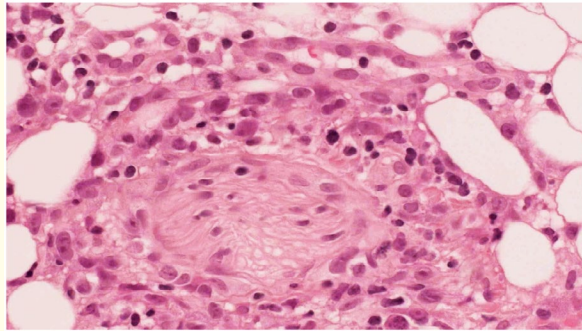


Figure 3: Perineural invasion, haematoxylin and eosin, medium power.

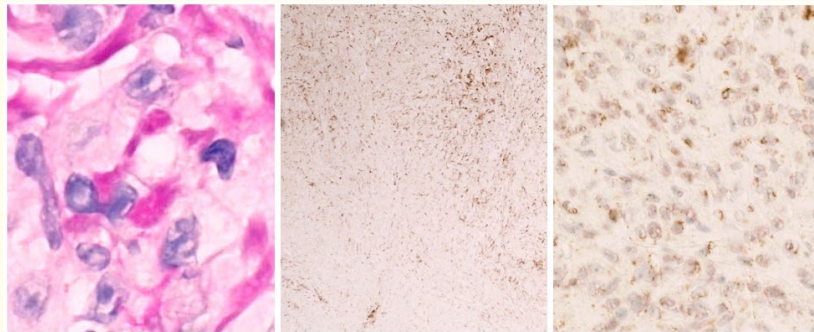


Figure 4: Left: characteristic PAS-D positive granular inclusions, Middle: characteristic CD68 staining, Right: smooth muscle actin staining.

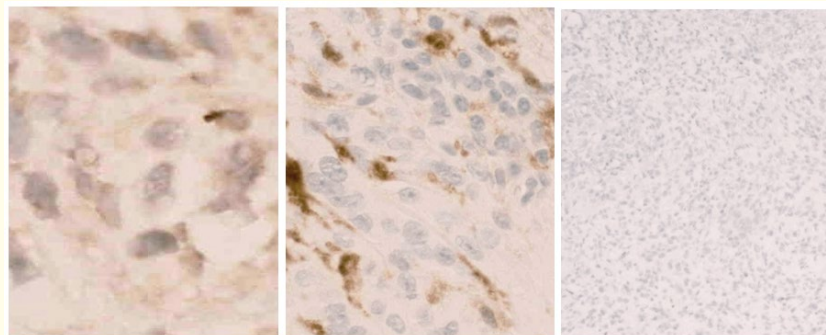


Figure 5: Left: Focal pancytokeratin staining, Middle: S-100 positive dendritic cells, negative tumour cells, Right: negative Sox-10.

Discussion

Determining the biological potential of GCTs relies on specific histological “red flags.” We applied the two most widely recognised criteria sets to this case:

1. **Fanburg-Smith et al. Criteria:** This system evaluates six features: necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 HPF), high nuclear-to-cytoplasmic ratio, and pleomorphism [1].
 - *Classification:* 0 features (Benign), 1–2 (Atypical), ≥3 (Malignant).
 - *Application:* This patient’s lesion displayed spindling, pleomorphism, and high mitotic activity, classifying it as at least atypical, with a high suspicion of malignancy.
2. **Nasser et al. Criteria:** This stricter framework reserves the “malignant” diagnosis for lesions that have already demonstrated metastasis [8].
 - *Application:* Under this set, our case remains of “uncertain malignant potential” as no systemic spread was identified at the time of diagnosis.

The negative S-100 and SOX10 supports that this tumour is one of a subset of non-neural granular cell tumors that have been identified which may not derive from neural tissue [5-8]. Some, as in this case, show anomalous myofibroblastic staining and include a specific, rare variant known as “primitive polypoid non-neural granular cell tumor” which characteristically presents as S100-negative and SOX10-negative and can display patchy or focal positivity for smooth muscle actin due to myofibroblastic differentiation [9].

This, combined with focal cytokeratin expression, necessitates careful exclusion of other spindle cell neoplasms. Squamous cell carcinoma was excluded with negative CK5/6 and p63. Melanoma was further excluded with negative Melan A and HMB-45, the latter also excluding periendothelial cell tumour (PEComa). The unusual cytokeratin expression in this granular cell tumour may relate to the overlying ulceration and degradation of the epidermal layer, allowing tumour cells to take up the stain. The remaining histologic differential diagnoses of dermatofibroma, atypical fibroxanthoma and epithelioid histiocytoma were also excluded. Histology did not show characteristic storiform pattern or peripheral collagen bundles of dermatofibroma. The atypia seen did not show the typically florid atypia or giant cells seen with atypical fibroxanthoma. Epidermal collarette or prominent blood vessels of epithelioid histiocytoma were not seen. However, the classic granular morphology and PAS-D positivity remained diagnostic of GCT. Given the high-risk features (perineural invasion and high mitotic count), one must be cautious; waiting for metastasis to occur (as per Nasser) before intervening may result in a poor prognosis.

Conclusion

This case illustrates the importance of clinicopathological correlation. While the patient opted for clinical surveillance over re-excision, the presence of high-risk histological features suggests an aggressive phenotype. Pathologists should utilise the Fanburg-Smith criteria to alert clinicians to “atypical” lesions that require closer follow-up, rather than relying solely on the presence of metastasis for a malignancy designation. Prudent histomorphologic interpretation, immunohistochemistry and histochemistry should avoid misdiagnosis of this rare entity.

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