Synchronous subcutaneous granular cell tumours, a rare presentation

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ABSTRACT

We describe a unique presentation of a rare disease presentation of a granular cell tumour. A 36-year-old woman presents with a large symptomatic left flank mass that had been slowly increasing in size. Multiple synchronous subcutaneous masses were found at presentation on the left breast, right auricle and right cheek. After diagnosis of granular cell tumour by core needle biopsy, the masses were excised with histopathological and immunohistochemical analysis of both specimens confirming the presence of non-malignant granular cell tumours. Granular cell tumours are rare Schwann cell derived tumours that are typically asymptomatic and benign. These tumours are most often located in the head and neck, with multifocal disease present in approximately 5–16% of patients. Final pathology is necessary for diagnosis and frozen section is rarely helpful. Malignancy is present in approximately 2% of cases and can be diagnosed by the presence of a high mitotic rate, large nucleoli, necrosis, spindling and pleomorphism are other suspicious features. Granular cell tumours do not generally require adjuvant treatment. The mainstay of therapy is surgical resection with surveillance.

KEYWORDS

Granular cell tumours – Soft tissue neoplasm – Surgical oncology

Accepted 3 December 2017

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Introduction

Granular cell tumours derive their eponym, Abrikossoff tumour, from Abrikossoff and his description of granular cell tumours of the tongue in 1926, although they were first described in 1854 by Weber.¹ Originally thought to be of muscle origin, it has been shown through immunohistochemical analysis that these tumours are derived from Schwann cells. Granular cell tumours are most commonly benign lesions of the head and neck presenting in the fourth and fifth decades of life. We describe a unique presentation of a rare disease.

Case history

A 36-year-old woman presented with a large symptomatic left flank mass that had been slowly increasing in size. A core needle biopsy was performed showing granular cell tumour with an infiltrative pattern without atypia. An excisional biopsy was performed. Histopathological and immunohistochemical analysis revealed the presence of a granular cell tumour. Multiple subsequent foci were discovered and the patient was sent to a surgical oncologist with expertise in soft tissue tumours. The sites of excision were the left flank and a left lateral breast subcutaneous nodule. Histopathological and immunohistochemical analysis of

both specimens confirmed the presence of non-malignant granular cell tumour extending to the inked superior, medial, deep and inferior margins (Figs 1, 2). Subsequent work-up included positron emission tomography, which showed very low metabolic activity in the region where there was known gross residual tumour (Fig 3). There were also nodular densities in both breasts, larger in the left than the right, which raised a concern about additional tumours. Owing to the rarity of the tumour, next-generation sequencing was ordered, which revealed variants of uncertain significance in three genes: *KIT*, *PRKAR1A* and *TSC2*. *KIT* is associated with autosomal dominant gastrointestinal stromal tumours. *PRKAR1A* is associated with the tumorigenic disease, Carney complex, characterised by altered skin pigmentation and blue nevi. Tuberous sclerosis has been associated with *TSC2*. The specific variants in this tumour have not been reported in any specific disease process.

The case was presented to the multidisciplinary sarcoma tumour board and, based on all prior work-up, the patient was believed to have benign, multifocal disease that would be amenable to surgical resection. She subsequently underwent a radical resection of her left flank mass, including the latissimus dorsi, excision of a left inguinal nodule and re-excision of the nodule in her left breast. She also had an excisional biopsy of a right posterior auricular nodule and right lip nodule. All excised masses were consistent with

Figure 1 Haematoxylin and eosin slide at 2 × magnification, showing a non-encapsulated mass with cells grouped in a typical nest-like pattern, surrounded by thin strands of fibrous tissue

Figure 3 Computed tomography: a contrast-enhanced axial view showing a left posterior soft-tissue mass with homogeneous enhancement

Figure 2 The cells are large and have centrally placed nuclei surrounded by ample, coarsely granular, eosinophilic cytoplasm. Haematoxylin and eosin slide at 40 × magnification

granular cell tumour. Excision margins were free of tumour except for a single peripheral margin of the left groin mass. The right perioral granular cell tumour extended to one peripheral/deep margin. The patient and surgeon elected to monitor it with surveillance imaging. The patient does not currently have signs of recurrent disease.

Discussion

Granular cell tumours are epidemiologically obscure; these tumours have not been well characterised in terms of their natural history.¹ The predominant presentation is a painless mass and these tumours are benign in the large majority of cases.² Granular cell tumours occur most frequently in the head and neck, but have been reported in a large number of visceral and cutaneous sites. Abdominal wall and flank tumours are exceedingly rare and this presentation with multifocal disease even more so. Multifocal disease is present in approximately 5–16% of cases and although this does occur in benign disease, it can be a sign of malignancy or associated with *PTPN11* and *RAF1* gene mutation syndromes, such as LEOPARD or Noonan.^{1–5}

LEOPARD is an acronym for an autosomal dominant genetic syndrome. Lentiginosis, skin discolouration marked by multiple spots ranging in colour from dark brown to black (L). Electrocardiographical conduction defects (E), mostly various heart blocks and abnormalities secondary to hypertrophy of the left ventricle and septum. This may even lead to hypertrophic obstructive cardiomyopathy or pulmonary stenosis if the right ventricle is involved. Ocular hypertelorism, widely spaced eyes, is the (O). Pulmonary stenosis, as mentioned above, would be the (P). Abnormalities of the genitals (A), Restricted growth and short stature (R) and finally deafness (D).⁴

Noonan is also an autosomal dominant genetic syndrome characterised by hypertelorism, down-slanting eyes and a

webbed neck in all but the mildest of presentations. Other characteristic features include congenital heart disease (especially pulmonary valvular dysplasia), deformed chest (pectus carinatum and excavatum), short stature and often developmental delays.⁵

Final pathology is essential for the diagnosis and characterisation of granular cell tumours. Frozen sections are rarely helpful. Malignancy is present in approximately 2% of cases. Malignancy can be diagnosed by the presence of a high mitotic rate, greater than 2 mitoses per 10 fields at 200 times magnification. Large nucleoli, necrosis, spindling and pleomorphism are other suspicious features. Granular cell tumours do not generally require adjuvant treatment. The mainstay of therapy is surgical resection with negative

margins with post resection surveillance.^{1–5} We believe this to be a unique presentation of an already rare disease.

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