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CASE REPORT

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Vulvar granular cell tumour in a recently post-partum woman: a case report

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Abstract

Granular cell tumours (GCTs) are uncommon neuroectodermally derived tumours. Vulvar location is rare with 134 reported cases presenting as a non-specific vulvar mass. They are of low malignant potential and management is local excision. They have a high local recurrence rate if incompletely excised. The GCT diagnosis is often retrospective due to its rarity, its non-specific presenting symptoms and numerous differentials. Here we descibe the case of a 31-year-old woman presenting after an asymptomatic right labium majus mass was noted during a postnatal visit. This was imaged with magentic resonance imaging (MRI) and a biopsy was inconclusive. She was referred for subspecialty consultation at the Chris O'Brien Lifehouse. The lesion was five centimetres, overlying the pubis and inferolateral to the clitoris with no skin changes or epidermal attachment. Wide local excision was performed. Histopathology showed GCT features with no malignant characteristics, but positive margins. Despite positive margins, the decision was made to not complete re-excision and observe for recurrence. This was an unusual case in a young postpartum woman. It highlights the need for clinical suspicion of this tumour type during a postpartum examination and the need for nuanced decision making regarding re-excision based on individual patient needs despite recurrence risk.

Keywords

Vulva; Granular cell tumour; Neuroectodermal tumours; Postpartum period

1. Introduction

Granular cell tumours (GCTs) are uncommon skin and soft tissue lesions [1] which make up less than 0.1 percent of surgical specimens and only 0.5 to 1.3 percent of soft tissue tumours [2, 3]. These tumours are thought to be of nerve sheath origin, likely Schwann cells [4, 5].

They are typically located in the head and neck region, predominantly the oral cavity [6]. Gynaecological locations are uncommon; vulvar lesions represent 5 to 16 percent of such tumours [7, 8] however, cervical, ovarian [3] and clitoral location [9] have been reported. They most commonly affect women in their 40s to 60s [3]. Familial inheritance occurs such as in Noonan syndrome, but this is an extremely rare phenomenon [10, 11].

2. Case presentation

A 31-year-old woman presented with an asymptomatic right labium majus solid mass, inferolateral to the clitoris measuring 6.6 by 1.8 by 2.1 cm on ultrasound.

She described no symptoms. It was incidentally found at her six-week postnatal examination and had not been noted previously during her obstetric care. She had no relevant medical, surgical or gynaecological history. A clinical examination noted no evidence of other lesions.

Her obstetrician performed a fine needle aspiration biopsy and an MRI. The biopsy was non-diagnostic due to an inadequate sample. An MRI showed a 5 by 2.5 cm ovoid mass, isointense to muscle on T1 imaging, demonstrating homogenous enhancement with contrast. It overlaid the pubis and the bone demonstrated reactive changes, possibly associated with her recent pregnancy rather than the lesion itself. There did not appear to be focal bony invasion (Fig. 1).

She was referred to a tertiary referral centre for subspecialty gynaecological oncology consultation. An examination under anaesthesia (EUA) was arranged confirming the prior clinical and imaging findings, mainly on the right anterior vulva but extending across the midline inferior to the clitoris. No inguinal adenopathy was noted.

Subsequently she underwent a wide local excision (WLE) without incident (Fig. 1) and has had an uneventful postoperative course.

Her histopathology noted a tan nodule measuring 52 by 28 by 20 mm. The cut surface was pale and whorled. Soft tissue sections including adipose tissue and medium sized nerves showing diffuse effacement by a GCT characterized by a circumscribed non-encapsulated collection of plump cells with distinctive granular eosinophilic cytoplasm (Fig. 2). Immuno-

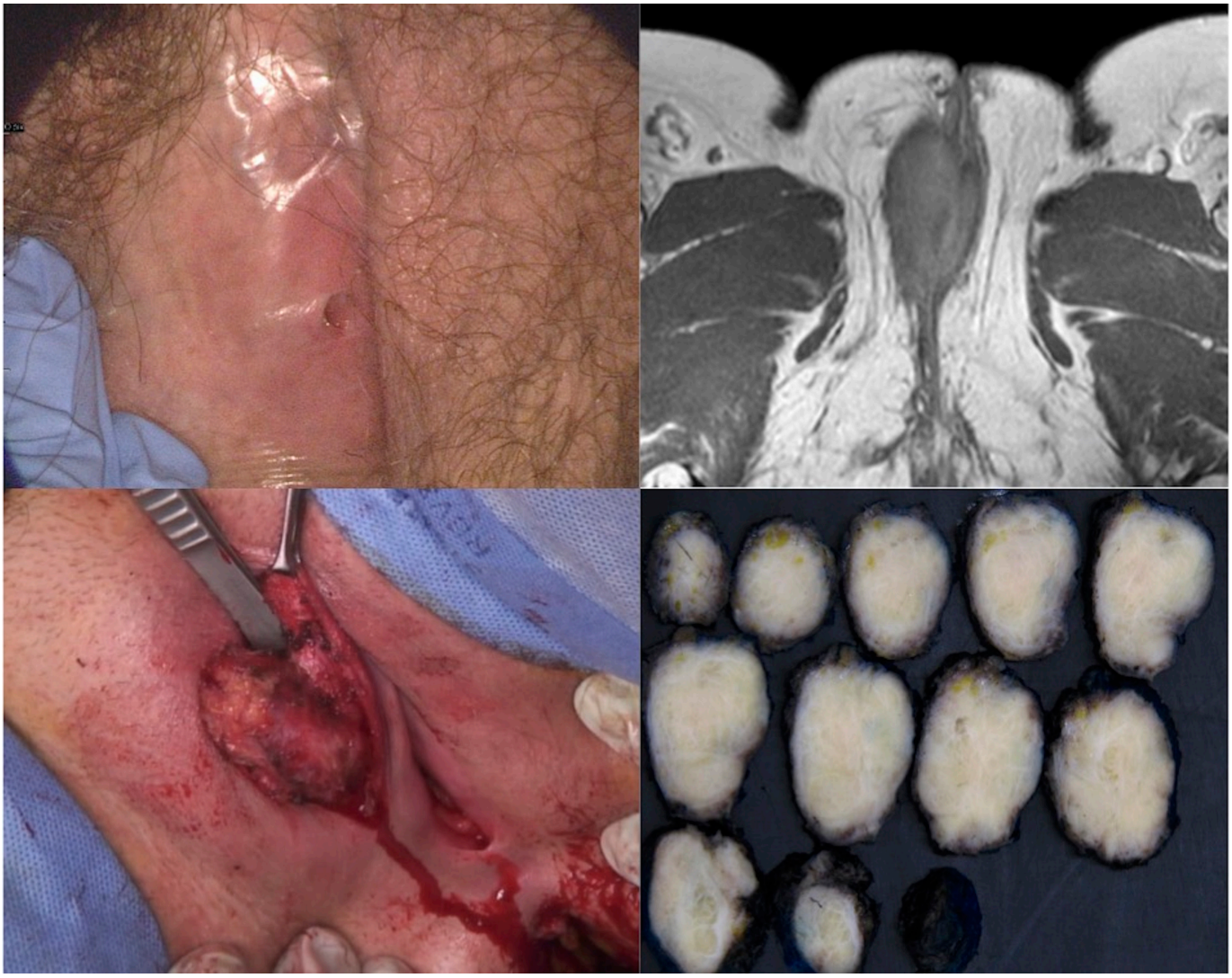

FIGURE 1. The clinical, radiological, operative and pathological findings of the GCT. Right sided labium majus lesion on initial colposcopic examination (arrow) (Top Left). MRI Pelvis noting right labium majus mass (arrow) (Top Right). Operative appearance of the labial mass (arrow) (Bottom Left). Macroscopic appearance of the lesion noting tan tissue measuring 52 × 28 × 20 mm with a pale and whorled cut surface (Bottom Right) (Colour image).

histochemistry showed cells positive for S100 (Fig. 2), cluster of differentiation 68 (CD68), neuron specific enolase (NSE) and microphthalmia associated transcription factor (MITF) showed nuclear staining. The excision margins were not clear with changes extending to the margins.

The specimen did not demonstrate any evidence of malignancy with no sarcomatoid morphology, high mitotic activity or geographical necrosis. After discussion at a multidisciplinary tumour board meeting, it was decided that no further excision was advised given its location, inferior to the clitoris and overlying the pubis, and she was discharged from the service for ongoing follow up with her general obstetrician and gynaecologist for repeat referral if there was recrudescence. She has not currently re-presented with a recurrence at the time of this publication.

3. Discussion

GCTs are usually benign neuroectodermal tumours. In a recent review, there were only 134 vulvar cases to date in 2012 with 7 malignant cases. Mean patient age for benign lesions was 45.81 years and 40.33 for malignant with only 4 pre-pubertal. The majority were vulvar, such as in this case, but there were also five clitoral, two perianal, two perineal, one introital and one episiotomy scar case. Their mean size was 2.6 to 7 cm in benign and on average 6.34 with a range of 1.5 to 12 cm for malignant. In this review, 10 percent had multiple lesions. This potential multifocal presentation should be considered during initial assessment [6]. They also rarely are associated with a familial pre-disposition which should also be considered [12]. The case discussed above is consistent with most of these characteristics including size, benign nature and location (Fig. 1). There was no extra vulvar involvement or a family history of vulvar tumours in our case.

In gynaecology they present as slow growing, solitary, painless and soft nodular lesions of variable size [1], most commonly as an incidental asymptomatic vulvar mass [3] which was the case in our patient. However, they can present with pain or pruritus [6].

Due to these non-specific presenting symptoms, GCTs have

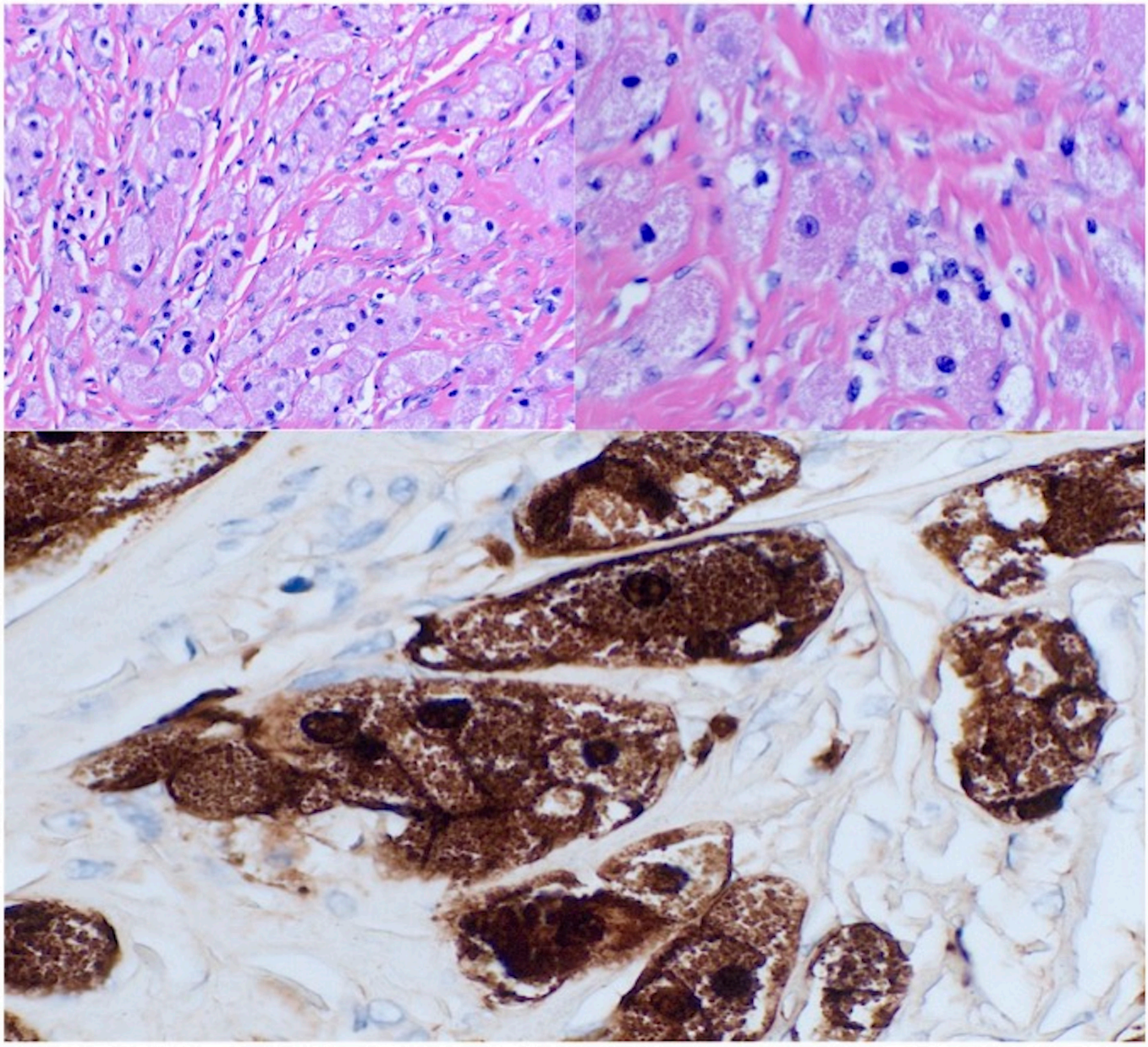

FIGURE 2. The histopathological and immunohistochemical findings in this case. Histopathology of classical polygonal cells with granular eosinophilic cytoplasm, small oval, central nuclei with absent mitotic figures and cell membranes (Haematoxylin and Eosin stained slide, × 200 magnification) (Top). Slender hyalinised bands of connective tissue (Haematoxylin and Eosin stained slide, × 400 magnification). S100 immunohistochemistry showing nuclear and cytoplasmic staining (× 400 magnification) (Bottom) (Colour image).

numerous differential diagnoses. Benign lesions, such as Bartholin gland tumours and sebaceous cysts, and nodular benign tumours, such as lipomas and fibromas, need to be considered. With concomitant ulceration, there may be confusion with carcinomas and sexually transmitted infections [6]. A biopsy may be performed. However, most diagnoses are retrospective [13], this was demonstrated in our case with an inconclusive biopsy and a firm diagnosis only made after surgical management.

GCTs are typically subcutaneous or subdermal [14], less than 5 cm, firm, white and are not encapsulated [2]. However, they sometimes occur in submucosa, smooth and striated muscle; and internal organs [15].

Microscopically GCTs show loosely infiltrating large spindled, round or polygonal cell aggregates with a granular eosinophilic cytoplasm, corresponding to lysosomes [3]. Their nuclei are small, oval and central. Mitotic figures and cell membranes are not visible. There are stromal hyalinised bands which represent vascular networks [2]. The overlying squamous epithelium may undergo pseudoepitheliomatous hyperplasia which sometimes leads to misdiagnosis as a squamous cell carcinoma [3] and also shows similar features to basal cell carcinoma, melanoma, leiomyoma and leiomyosarcoma [14].

Immunohistochemistry results can assist in distinguishing these histological diagnoses [14] and are indicative of Schwannian derivation with immunoreactivity for S-100, NSE, laminin, CD68, vimentin, ki-67 and p53 [3, 4].

Fig. 2 demonstrates the classical histopathological and immunohistochemical appearance found in this case.

Less than 2 percent of GCTs are malignant [15] and this is particularly unlikely in solitary lesions [3] such as our case. Clinical factors that indicate poor prognosis are; older age, large tumour size with rapid growth and ulceration, metastasis and multiple lesions [6]. Malignant GCTs respond poorly to chemotherapy and radiotherapy with radical local surgery and regional lymph node dissection often a mainstay after exclusion of distant metastases [14].

Malignant histopathological features include necrosis, increased mitotic activity, spindling, vesicular nuclei with prominent nucleoli, high nuclear to cytoplasmic ratio and pleomorphism. Immunohistochemical features are high ki-67 and p53 immunoreactivity. Three or more of these features indicate malignancy [3]. The above are referred to as the Fanburg-Smith Criteria formulated in 1998 [15]. None of these histopathological and clinical characteristics were present in our case.

Primary management is complete surgical excision. Wide excision is best practice due to poorly defined borders with cells beyond macroscopic growth limits [3, 4], tendency towards infiltration and no encapsulation [6, 16]. However, this may be impeded by anatomical location and the potential for blood loss and scarring leading to incomplete excision which is not uncommon [17] as in our case. Surgery remains the primary therapy for GCTs [17].

Prognosis is excellent with local recurrences appearing in 2 to 8 percent of patients with clear margins [13]. Positive margins cause higher recurrence rates, up to 20 percent [16]. Additionally, ill-defined tumour edges increase recurrence risk [2].

Immediate re-excision with positive margins is often preferred versus simple clinical observation due to this [16]. However, the evidence related to this management is limited, indeed, Rose *et al.* [18] (2009) stated that resection margins or tumour depth were not related to malignant transformation or recurrence in a musculoskeletal GCT case series. Despite limited data, one review noted that two of seven patients with positive margins underwent re-excision after 14 and eight years of observation with negative margins and a stable outcome [19]. Whilst this is a small series, it must be noted that, with re-excision, five of seven or 70 percent of patients may have had unnecessary surgery if re-excised. In addition, even if negative margins are achieved, they will still experience the aforementioned 2 to 8 percent risk of recurrence [13].

There is currently no study comparing expectant versus active management given the rarity of vulvar GCTs. Follow up management and observation needs to be decided based on cases published in literature and the clinical needs of the patient. In two cases, re-excision was recommended but the patient declined [3, 20] with no recurrences detected after 18 months in one case and seven months in the other. In one case with positive margins, follow up continued for eight years with no recurrence [21]. Indeed, Trojano *et al* [20], noted that in some patients that did not accept re-excision, they experienced no recurrence in their follow up. One aspect to note in these cases that differs from ours is that all these tumours were less than 4 cm in size which is noted to be a prognostic marker [12]. The tumour in our case measured 5 by 3 by 2 cm.

In this case, surgical margins were positive and therefore, re-excision would be the most uncomplicated course. However, the aforementioned data needs to be considered. Some women will be saved surgical complications by observation and there is no evidence of adverse outcome if excision is performed after recurrence in benign cases [19]. A more radical excision would potentially have involved the underlying pubis, adjacent clitoris and may have resulted in a poor cosmetic and sexual function outcome which would have been unsatisfactory especially given her age. In this particular case after MDT discussion and review of literature, the decision for observation was advised given the limited data and clinical considerations.

This was an unusual case for two reasons: firstly, the patient was younger than average and secondly, recently postpartum with no lump having been noted during her obstetric care. It serves to highlight the importance of considering gynaecological pathology at time of obstetric visits and consideration of this rare pathology when vulvar lumps are found. The GCT diagnosis is often a retrospective histological one, emphasizing the need for clinical suspicion and always aiming for clear margins. This will directly impact the recurrence risk of the patient which is high if margins are involved. However, nuanced decision making is still required with limited data for re-excision especially in the context of difficult operative location which may result in a poor functional, psychosexual and cosmetic outcome for a young woman.

4. Conclusion

GCTs are gynaecologically rare, benign neuroectodermal tumours which are most commonly vulvar. It is important to emphasise that they are challenging to diagnose due to numerous differential diagnoses. They have a limited malignant potential but it is important to consider malignancy and extra vulvar involvement carefully, especially when planning for surgical management. Excision is the mainstay of treatment with an emphasis on clear margins due to its high recurrence rate and re-excision is recommended in involved margins. However, current literature, if sparse, and this case highlight the need to individualised care. Re-excision is preferable but this needs to be weighed in cases where this is not straightforward. Surgical morbidity and the psychosexual and cosmetic impact this may have must be considered. A nuanced approach is needed and immediate re-excision may not always be the best course of action.

AUTHOR CONTRIBUTIONS

JS—reviewed the case, associated literature and wrote the case report; LA—provided histopathological images and descriptions; LA, MB and JC—reviewed the manuscript and provided guidance on content.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The patient provided consent for the case report to be written and published. Ethics approval was not sought as per local guidelines given the patient had consented and the de-identified information was felt to not pose a risk to patient privacy.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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