



Case report

Case report of a breast granular cell tumor in a young transgender man

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ABSTRACT

Introduction and importance: Granular cell tumors (GCTs) can be diagnostically challenging due to their rarity, diverse anatomic locations, and clinical and radiologic similarities to other more common entities. GCTs involving the breast are rare and are most commonly encountered in premenopausal cisgender women. We report an unusual case of a breast GCT in a young transgender man.

Case presentation: A 20-year-old transgender man who was on testosterone therapy for about 1 year presented with a painless, palpable mass in the right breast which radiologically resembled a lymph node. A fine needle aspiration showed morphology and immunohistochemistry consistent with a GCT. The tumor was excised by a mastectomy for therapeutic and gender-affirming purposes which confirmed the diagnosis of a breast GCT.

Clinical discussion: Breast GCTs are most commonly found in cisgender women, however the mechanisms behind this relationship and whether transgender persons have an altered risk profile are not well understood. Breast GCTs are typically benign lesions with a low chance of recurrence following excision.

Conclusion: GCTs are rare and poorly understood entities which have not been previously documented in transgender patients and can resemble other benign or malignant lesions.

1. Introduction

Granular cell tumors (GCTs) are rare neoplasms which are thought to arise from Schwann cells although the exact histogenesis remains unclear [1]. GCTs are most commonly found in the tongue but can arise in nearly any anatomic location [2]. GCTs of the breast are rare and comprise between 5 and 15% of all GCT and 0.1 and 0.7% of all breast tumors [3–5]. GCTs in any anatomic location are slightly more common in cisgender women [6]; however, GCTs of the breast are much more common in cisgender women with only 6.6% occurring in cisgender men [3]. GCTs of the breast typically present as solitary, palpable, painless masses and are most often located in the upper-inner quadrant along the distribution of the supraclavicular nerve [7,8]. Breast GCTs have a wide age range with the mean age of diagnosis between 45 and 55 years old. Radiologic features of breast GCTs are often non-specific and can resemble other benign or malignant entities [9]. Histologically, GCTs are characterized by sheets or clusters of large, round to

polygonal cells with eosinophilic granular cytoplasm and are positive for staining with S100 and CD68 [7]. GCTs are a diagnostic challenge due to their rarity and similar clinical and radiologic findings to other breast neoplasms [10]. In this case report, we discuss a case of a GCT in a young transgender man who was treated at several academic hospitals (Women's College Hospital, University Health Network, and Mount Sinai) in Toronto, Ontario, Canada. This work has been reported in line with the SCARE 2020 criteria [11].

2. Presentation of case

We report the case of a 20-year-old transgender male patient with a 3-month history of a painless, palpable hard mass in the upper-inner quadrant of the right breast. The patient underwent menarche at age 12, had previously been on oral contraceptives for 1 year, and had been on testosterone for approximately 1 year prior to presentation. The patient had no other significant personal or family medical history.

Abbreviations: GCT, granular cell tumor; FNA, fine needle aspiration; IHC, immunohistochemistry.

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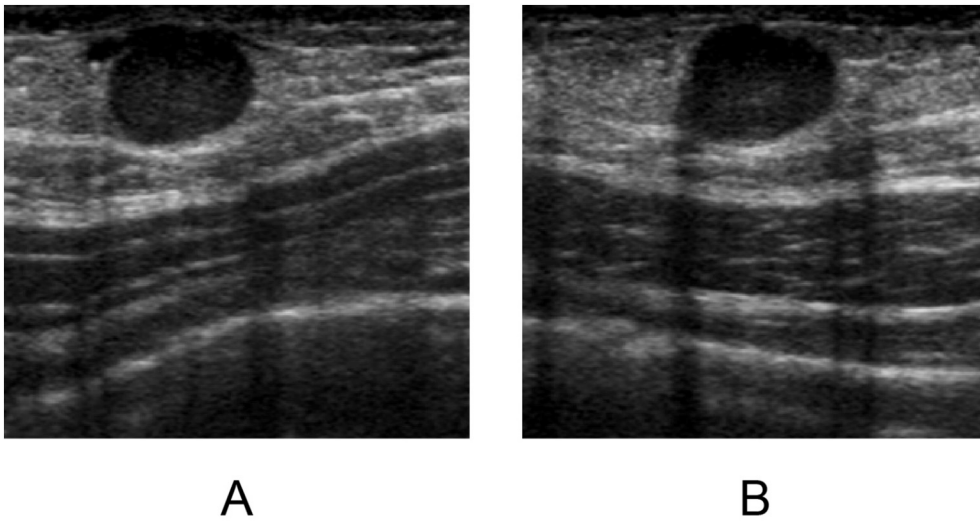


Fig. 1. Representative transverse (A) and sagittal (B) ultrasound images of the tumor showing a 7 mm hypoechoic oval-shaped mass with mildly irregular margins.

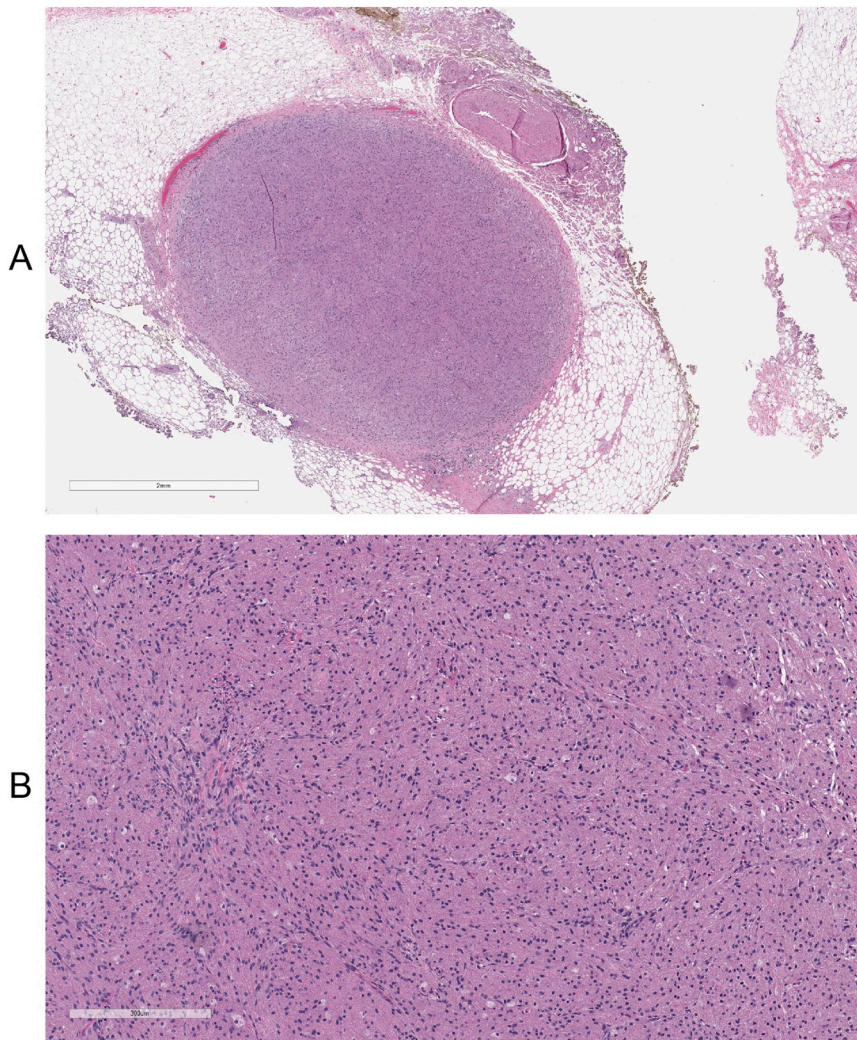


Fig. 2. Representative H&E-stained images from the resected tumor taken at 2× (A) and 20× (B) objective power. The tumor is well-circumscribed and composed of sheets of polygonal cells with granular eosinophilic cytoplasm.

Physical examination revealed a small firm, mobile mass located 10 cm away from the nipple at the 1 o'clock position. There were no overlying skin changes. A targeted ultrasound revealed a hypoechoic oval-shaped mass measuring $7 \times 7 \times 6$ mm with mildly irregular margins, with internal vascularity resembling a lymph node (Fig. 1).

A fine needle aspiration (FNA) biopsy was submitted in CytoLyt fixed specimen. ThinPrep® showed numerous epithelioid cells with abundant granular cytoplasm arranged in single cells with a few cohesive clusters. The cells were relatively uniform with round to oval nuclei, fine chromatin, and indistinct nucleoli. Neither mitoses nor necrosis were identified. Immunohistochemical (IHC) stainings were performed on cell block prepared from residual Preservcvt. Tumor cells were positive for S100 protein, CD68, SOX10, inhibin, and CD56 (weak cytoplasmic and membranous) and negative for staining with calretinin, AE1/AE3, CAM5.2, and ER. Based on cytomorphological and IHC findings, a diagnosis of granular cell tumor was rendered.

A bilateral, double-incision mastectomy was performed for therapeutic as well as gender-affirming purposes by an experienced plastic surgeon who performs around 250 top surgeries per year. Grossly, the resected tumor was composed of a single solid nodule measuring $9 \times 8 \times 5$ mm with a homogenous white cut surface. On histology, the tumor was well-circumscribed and composed of sheets of polygonal granular cells consistent with the prior FNA (Fig. 2). No features of malignant GCTs, such as areas of necrosis, increased mitotic activity, or pleomorphism, were identified. There was no significant pathology identified in the left breast. The patient tolerated the procedure well and was discharged home the same day and was seen for follow up at 1 day, 1 week, and 4 weeks post-procedure. The patient was satisfied with the cosmetic and therapeutic outcomes of the procedure, and no further follow up is planned unless there are patient concerns.

3. Discussion

While the clinical, radiologic, histologic, and IHC findings were otherwise consistent with a typical breast GCT, this case is unusual as the patient is young and breast GCTs have not previously been documented in transgender individuals. Although breast GCTs are much more common in cisgender women compared to cisgender men, the mechanism that underlies this relationship is not well understood. GCTs generally do not express estrogen, progesterone, or androgen receptors, which suggests that sex hormones do not directly influence tumor growth unlike other breast malignancies [7,12]. Another speculated explanation for the increased risk of GCTs in women is that the putative molecular drivers of GCTs, mutations in *ATP6AP1* or *ATP6AP2*, are located on the X-chromosome [13]. However, in women mutations in these genes occur only in the active, unmethylated allele which appears to be sufficient to drive GCT tumorigenesis. This suggests that men and women should have a similar risk of acquiring this driver mutation. While there is no data specific to GCT in transgender patients, transgender men have been found to have a reduced risk of developing breast cancer overall compared to cisgender women [14]. It remains an open question as to why cisgender women are more susceptible to breast GCTs and whether there is any additional risk to their development in transgender individuals.

The vast majority of GCTs, including this case, are benign and are treated with surgical excision. Recurrence of benign GCTs is rare although there are a small number of reports of recurrence within several years of resection [8]. Approximately 2% of GCTs are classified as malignant and there remains some debate as to which histologic features are needed to classify tumors as malignant GCTs [15]. GCTs remain a diagnostic challenge and require histopathology for proper diagnosis.

4. Conclusion

Breast GCTs are a diagnostic challenge due to their rarity and non-

specific clinical and radiologic features which overlap with many benign and malignant breast lesions. While GCTs are typically benign, their pathophysiology, predisposition to cisgender women, and prevalence among transgender individuals remains poorly understood. This case highlights how GCTs can present in unusual clinical circumstances.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

Alexander Oberc: wrote the paper.
 Kathleen Armstrong: provided information on clinical details, surgical techniques, and follow-up; obtained patient consent.
 Hyang-Mi Ko: reviewed cytology findings.
 Allison Grant: reviewed radiologic findings.
 Phillip Williams: reviewed pathological findings.
 J Brendan M Mullen: reviewed pathological findings.

All authors edited and reviewed the manuscript.

Declaration of competing interest

The authors have no conflicts of interests to declare.

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