



## Case Report

# Granular Cell Tumors are Very Rare but Important Vulvar Masses that should not be Overlooked

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### Abstract

Granular cell tumors are uncommon neoplasms of neural origins affecting the submucosal and subcutaneous tissue in the tongue, neck, head, and genitals. Vulvar tumors represent about 15% of the cases and present as solitary painless swellings with or without accompanying local manifestations. It is more common in Afro-American women in their fourth to fifth decade.

They are predominantly benign tumors with malignant variants in 1-3% of cases. Malignant forms are aggressive, therapy-resistant, and can metastasize. Wide excision with clear margins is the recommended curative treatment. More than 33% of excisions have positive margins, increasing the risk for local recurrence from 2% to about 20%. The combined risk of recurrence and malignant transformation is a reason for recommending wide re-excision in cases with positive margins. We recommend a preoperative biopsy for every solid vulvar lump in order not to miss such a rare diagnosis and to correctly plan treatment.

### Keywords

Case report; Granular cell tumor; Vulva; Vulvar masses; Vulvar neoplasm; Vulvar tumor

## Introduction

Abrikossoff first described a granular cell tumor (GCT), which was originally reported by Virchow [1], as granular cell myoblastoma of the tongue back in 1926 [2]. The immunohistochemical characteristics of GCTs illustrated their derivation from Schwann cells, thus their origin from the neural sheath [3].

GCTs are rare, usually benign tumors affecting the submucosal and subcutaneous tissue throughout the body, but mainly of the tongue, neck, breast and vulva [4]. GCTs predominantly affect Afro-American women with a peak incidence in the fourth to fifth decade [5].

Vulvar involvement is described in 7-16% of GCT cases, mainly as solitary benign tumors with malignancy in only 2% and multiple lesions in 25% [6]. We report a new case of vulvar GCT to add to the fewer than 200 cases in published literature.

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## Case Report

A 64-years old white female presented with a one-year history of a painless growth on her vulva. Examination revealed a 2 cm × 2 cm, smooth, solid, mobile, indolent tumor in the upper third of the labia majora, located at 10 o'clock of the vulva with echogenicity on ultrasound examination. The mass was not associated with regional lymphadenopathy, discoloration or ulceration. The patient had a known history of postmenopausal recurrent lipomas throughout the entire body with several surgical excisions, positive family history for malignant tumors with more than 9 individuals with stomach-, breast-, prostate- and lung-cancer, and two siblings with lipomas.

Due to suspicion of vulvar lipoma a local excision was performed. The histological findings showed 1.2 cm GCT with irregular margins of proliferating cells with small nuclei and abundant eosinophilic granular cytoplasm. Immunohistochemically, the cells showed a very strong S100 protein staining, negative MNF116, negative estrogen- and progesterone-receptors, weak Ki67 of less than 5%, and weak p53 in less than half of the tumor cells. The microscopic findings of GCT with different strains are shown in Figure 1.

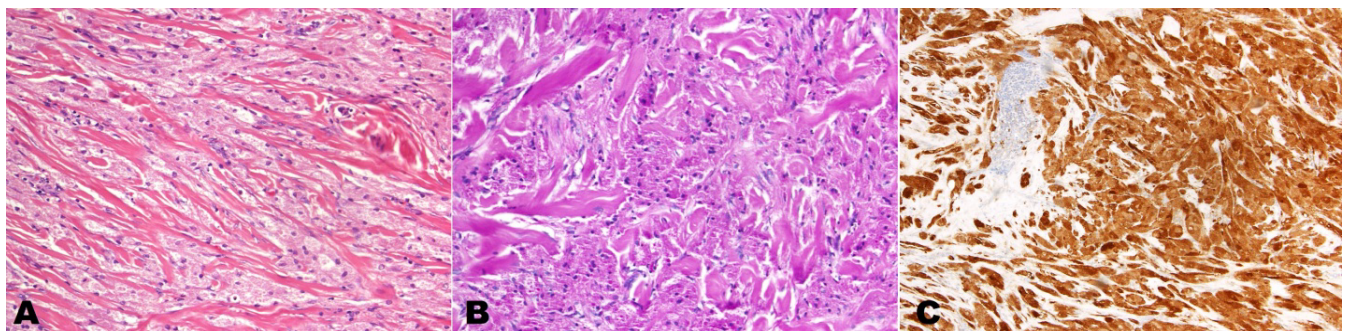
Due to involvement of the specimen's margins, wide re-excision was performed to achieve a complete removal of the tumor. CT-scan showed normal results with no signs of metastasis, lymphadenopathy, or other tumors in the body. Bone scintigraphy excluded skeletal involvement. Regular annual follow-up is planned for ongoing surveillance.

## Discussion

GCTs are rare, soft tissue neoplasms of neural origins with involvement of variety of sites, but predominantly affecting the tongue (30%), neck, head, breast and vulva (15%) [5,7]. GCTs have male to female ratio of 1:4 [8], and have higher incidence in the fourth to fifth decade [5] even though a case in the neonatal period has been reported [8]. GCTs are usually solitary painless tumors with multiple lesions described in 7-29% of cases and mainly affecting the oral regions of Afro-American women [7]. Therefore, our case of a 64-year-old Caucasian female is an atypical GCT presentation.

Multiple GCTs or GCTs in younger age are reported to be associated with syndromes such as Noonan and LEOPARD syndromes [7]. A familial link for GCT has also been suggested in families with soft tissue tumors [4]. Our case here shows positive family history for malignant tumors as well as soft tissue tumors (lipomas), thus supports the suggestion of investigating further familial and genetic predisposition.

The differential diagnosis of vulvar GCT includes Bartholin's cysts, fibromas, lipomas, epidermal cysts and papillomas and the definitive diagnosis is based on the typical histological findings [5]. GCTs are almost always misdiagnosed based on clinical presentation [8]. The fact that our patient had multiple lipomas



**Figure 1:** The microscopic findings under 20x magnification for GCT with a) hematoxylin & Eosin stain b) Periodic acid-Schiff stain c) S100 protein stain.

already as well as the similarity in clinical presentation was the reason why we preoperatively misdiagnosed the tumor for a vulvar lipoma. This misdiagnosis was also the reason why wide excision was not initially performed and consequently the specimen's margins were involved. Incomplete initial resection is associated with a 2-10% local recurrence [5]. A preoperative biopsy would have provided a definitive histological diagnosis. This in turn would have helped in planning the correct initial management with wide excision.

Even though GCTs are usually benign tumors, malignant forms are present in 1-3%. Necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity, high nuclear to cytoplasmic ratio, and pleomorphism are six criteria, that can be used to classify GCTs. Neoplasms meeting three or more of these criteria are considered histologically malignant and those that display focal pleomorphism without meeting any of the other criteria are classified as benign [9].

Malignant GCTs can show local recurrence, lymphatic and hematogenous metastasis and resistance to both radio- and chemotherapy. There is no successful treatment for the metastasized malignant variants and regimens with paclitaxel, carboplatin, cisplatin, and 5-fluoro-uracil have shown no effect. Therefore, aggressive surgical removal is recommended for all GCTs [10].

Tumors larger than 4-5cm, rapid growth, invasion of the adjacent tissues, older age at presentation, and local recurrence are suggested as prognostic factors for anticipating malignant changes in GCTs [11]. High Ki67 and p53 overexpression are also two indicators for atypical malignant GCT with worse prognosis [3]. Our patient had a benign tumor and only one poor-prognosis factor, which was her age at presentation.

The irregular margins of GCTs are due to the extension of the tumor cells beyond the macroscopic limits of the mass. This is one of the reasons why more than 33% of excisions have positive margins. Positive excision margins increase the risk for local recurrence from 2% to about 20% [5]. The combined risk for recurrence and malignant transformation is a reason for recommending wide re-excision in cases with primarily positive margins. Based on this recommendation, we performed a curative re-excision in our case.

## Conclusion

Even though GCTs are rare, they represent an important differential diagnosis in vulvar tumors that should not be missed. Wide excision with clear margins is the recommended curative treatment with annual follow up. The 1-3 % risk for malignant transformation is small, but must be considered and discussed when counseling a patient with GCT given the aggressive and resistant pathophysiology. We recommend a preoperative biopsy for every solid vulvar lump in order to correctly plan initial treatment.

## Acknowledgments

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## Disclosure

We declare that we have no conflict of interest. Informed consent was obtained from the patient reported in this manuscript.

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