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CASE REPORT

Giant Granular Cell Tumor of the Left Thigh, a Rare Case Report and Literature Review

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Background: Granular cell tumor (GCT) is a rare soft tissue tumor characterized by Schwann cell differentiation. While GCT can occur in any part of the body, it is less common in the lower limbs. We report a case of a giant atypical GCT located in the left thigh, the tumor was initially small and painless at the time of discovery but gradually grew to 17 cm over a two-year period.

Case Presentation: A 60-year-old male patient presented to our hospital two years ago with a painless mass measuring 39×22 mm on the left thigh. He refused treatment due to the absence of discomfort. Over the following two years, the painless mass gradually enlarged. Magnetic resonance imaging (MRI) upon admission revealed a mixed signal, spindle-shaped shadow measuring approximately 170 mm × 50 mm × 55 mm in the left femur's subcutaneous soft tissue, accompanied by mild surrounding swelling. Surgical resection was performed. Microscopic examination revealed round or polygonal tumor cells distributed in sheets or nests, with no evident atypical cells or signs of nuclear division. Immunohistochemistry demonstrated positive staining for S100, SOX-10, Vimentin, NSE, CD56, and H3K27Me3 in the tumor cells, with a Ki-67 labeling index of approximately 15%. The postoperative pathological diagnosis confirmed giant GCT.

Conclusion: We report a case of a benign giant GCT in the left thigh. Early diagnosis and treatment of painless lower-limb masses are essential to prevent their enlargement or malignant transformation. Surgery remains the primary treatment for this condition. Pathological assessment is crucial for definitive diagnosis and for distinguishing between benign and malignant forms.

Keywords: granular cell tumor (GCT), lower limb, soft tissue tumor, histopathology, surgery

Introduction

The granular cell tumor (GCT), also known as Abrikossoff tumor, was first described by Russian pathologist Alexei Ivanovich Abrikossoff in 1926. GCT is an extremely rare soft tissue tumor, accounting for only 0.02% to 0.03% of all neoplasms.[1] The disease can occur in all populations, but it is most prevalent among African Americans and has a higher incidence in women aged 40 to 60.[2]

Most GCTs are typically solitary and painless benign tumors, only 5–10% are multiple lesions, and 1–2% are malignant.[3] GCT was first discovered in the tongue, most cases are found in the head and neck region, particularly in the oral cavity.[4] Sporadic case reports of GCT have also been documented in other areas, including the respiratory tract, digestive tract, nervous system, reproductive system, skin or subcutaneous soft tissue, and upper extremities.[5–9] Recently, some articles have reported chest wall and even myocardial GCTs; however, these are isolated case reports.[10–12] GCTs in the lower limbs are extremely rare. GCTs may pose diagnostic challenges when they occur in atypical locations or grow to larger sizes.[2] Furthermore, GCTs typically present no symptoms due to their small size (average diameter of 2.1 cm) and slow growth. When the mass gradually increases in size, it is often misclassified as a malignant tumor, which can increase patient anxiety. Insufficient awareness of the disease often leads to overtreatment. In this study, we report a rare

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benign GCT arising in the left thigh that gradually reached 17 cm in size within two years and was successfully treated with surgical resection.

Case Presentation

A 60-year-old male patient presented to our hospital in November 2022 with a painless mass in the left thigh. The patient had no significant chronic medical history. Physical examination revealed a 32 mm × 20 mm mass located behind the left thigh, characterized by a hard texture, good range of motion, no tenderness, and no abnormal sensations or activity in the left lower limb. Ultrasound examination revealed a 39 mm × 22 mm mass with indistinct borders, a regular shape, uneven internal echoes, and detectable blood flow signals (Figure 1A). The patient declined Magnetic Resonance Imaging (MRI) and biopsy for further diagnostic confirmation; therefore, no specific treatment was provided at that time.

On April 26, 2024, the patient was readmitted due to progressive enlargement of the left thigh mass. Physical examination revealed a flexible, spindle-shaped mass measuring approximately 100 mm × 60 mm within the left thigh. MRI of the left thigh suggested a long spindle-shaped abnormal signal within the fascicle of the posterior medial gracilis muscle, measuring approximately 140 mm × 50 mm × 55 mm. T1-weighted imaging showed an equal signal, while PD-weighted imaging revealed a slightly higher and non-uniform signal. The laminar demarcation is clear, and the laminar

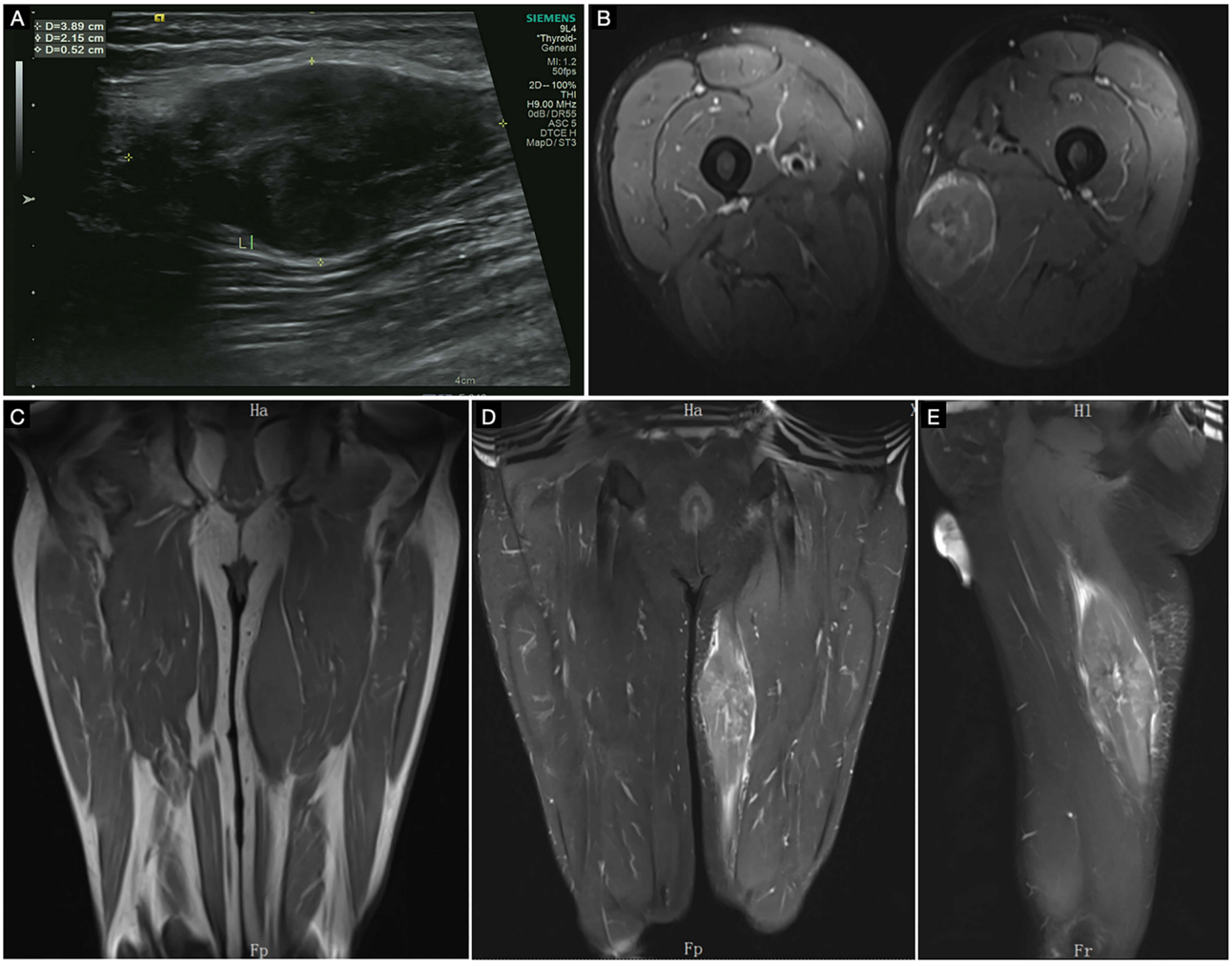

Figure 1 Imaging examinations revealed a mass in the right thigh. (**A**) Ultrasound examination revealed a mass measuring 39×22 mm. (**B-E**). MRI revealed a mass measuring 140 mm × 50 mm × 55 mm. (**B**) Axial fat-suppressed PDWI exhibited a slightly higher signal. (**C**) Coronal T1WI displayed an equal signal. (**D**) Coronal PDWI exhibited a slightly higher signal, although the signal is not uniform. (**E**) Sagittal PDWI exhibited a slightly higher signal.

bundles are intact, though adjacent muscle groups are compressed (Figure 1B-E). As no evidence of malignancy or additional lesions was detected, neoadjuvant therapy was not considered.

The patient underwent surgical resection of the left thigh mass, followed by muscle suturing and vacuum-assisted closure therapy for wound management. Postoperative specimens revealed grayish-red nodules measuring 170 mm × 110 mm × 30 mm, with partial muscle involvement on the surface; the cut surface was gray. The nodules had moderate solidity, and focal areas exhibited mucous degeneration. Under microscopic examination, the tumor was poorly demarcated and comprised round or polygonal cells arranged in nests, sheets, or broad bands, with fibrous connective tissue intervals of varying widths between the tumor cells (Figure 2A). At high magnification, most tumor cell nuclei were small and round, located centrally, with no clear pathological mitosis observed. The chromatin was either compact or vacuolar, and the cytoplasm was abundant, exhibiting eosinophilic fine granularity; eosinophilic globules were occasionally observed. Some local tumor cells exhibited mild to moderate atypia (Figure 2B). Immunohistochemical analysis revealed positive staining for S100, SOX-10, Vimentin, NSE, CD56, and H3K27Me3 in the tumor cells, with a Ki-67 labeling index of approximately 15% (Figure 2C-I). The pathological diagnosis was GCT of left thigh with atypical hyperplasia. The patient recovered well without complications. The patient was followed up via phone on October 21, 2024, and reported no significant discomfort.

Discussion

GCTs in the thigh, particularly giant variants, are extremely rare. These tumors are usually firm and non-tender. Patients often remain asymptomatic until the tumor grows large enough to compress nearby structures, causing discomfort or

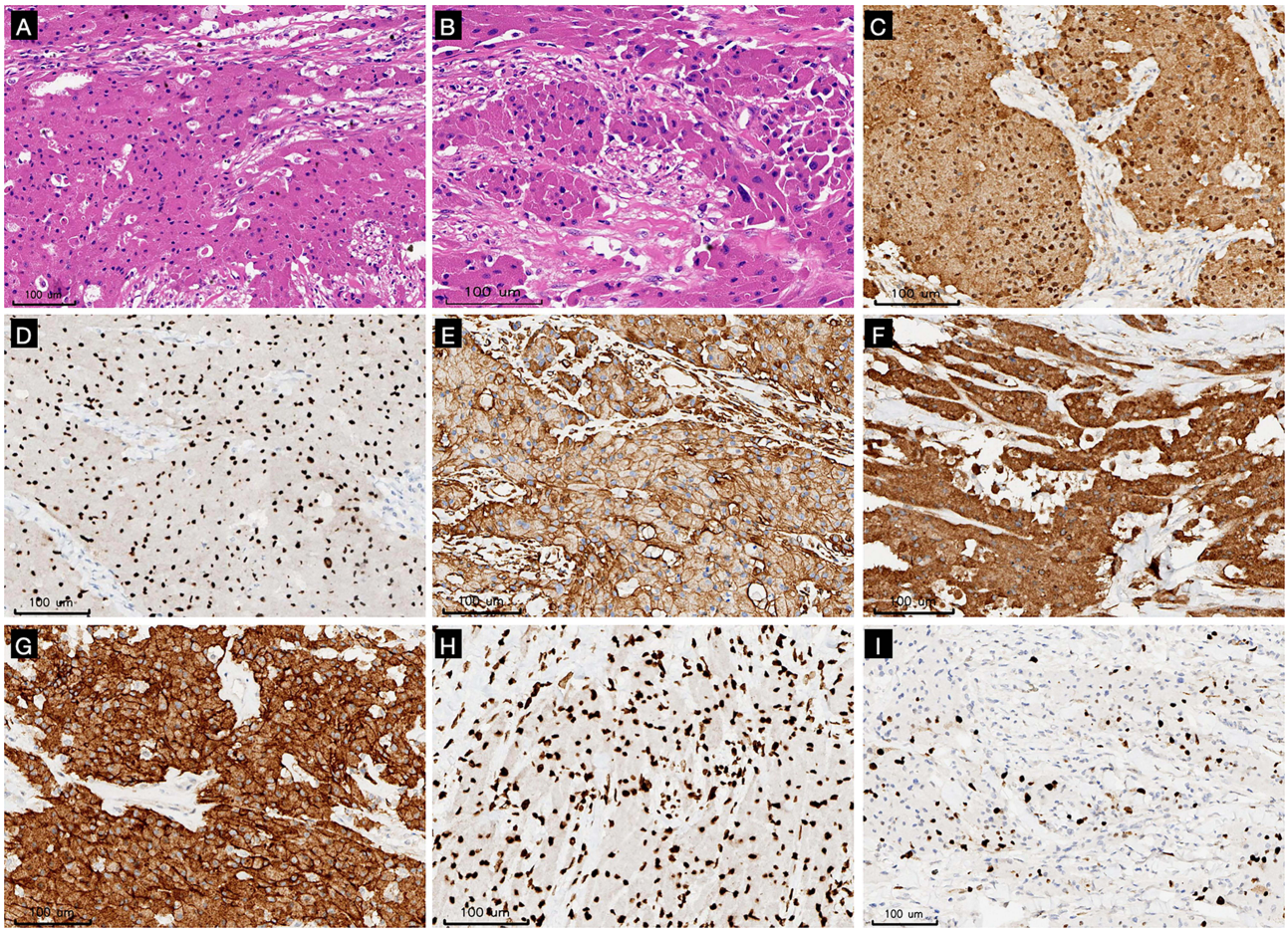

Figure 2 Pathological and histochemical staining findings of GCT. (**A**) The tumor was not well-defined and consisted of round or polygonal cells arranged in nests, sheets, or wide bands at 100× magnification. (**B**) The nuclei of most tumor cells are small and round, located in the center of the cells; the chromatin is compact or vacuolar, and the cytoplasm is abundant, eosinophilic, and finely granular at 200× magnification. (**C-I**). Immunohistochemistry revealed that the tumor cells tested positive for S100 (**C**), SOX-10 (**D**), Vimentin (**E**), NSE (**F**), CD56 (**G**), and H3K27Me3 (**H**) at 200× magnification. The Ki-67 labeling index is 15% (×200) (**I**).

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functional impairment.[13] In this report, the patient presented with a large mass in the left lower limb but without obvious discomfort. To our knowledge, this is the largest GCT involving the lower limb reported in contemporary literature[14–19] (Table 1).

GCTs of the thigh may be mistaken for other soft tissue lesions, such as lipomas or neurofibromas.[21] Imaging tests, including ultrasound and MRI, provide critical information on tumor size and extent, playing a crucial role in preoperative evaluation.[22–24] On ultrasonography, GCTs typically appear as well-defined, hypoechoic masses but may exhibit variable echogenicity based on the degree of fibrosis and cellularity. The lesions are usually homogeneous with posterior acoustic enhancement.[24] MRI is the preferred modality for detailed characterization of GCTs. On MRI, GCTs typically present as well-circumscribed lesions, isointense or slightly hypointense to muscle on T1-weighted images. On T2-weighted images, these tumors often show intermediate or high signal intensity, which can vary based on the amount of collagen and cellularity within the lesion.[22] Infiltration into surrounding tissues, if present, is a critical feature to assess, as it may indicate malignancy or aggressive behavior. These imaging features are important for preoperative planning and differentiation from other soft tissue tumors.

The pathological diagnosis of GCTs primarily relies on histological and immunohistochemical analysis. Histologically, GCTs consist of large, polygonal cells with abundant eosinophilic granular cytoplasm.[25] The granularity, a hallmark of GCTs, results from the accumulation of lysosomes within the cytoplasm. These cells typically exhibit indistinct borders and are arranged in nests, sheets, or occasionally in a trabecular pattern. In addition to histological characteristics, Immunohistochemistry is crucial for the definitive diagnosis as GCTS are known to express various markers.[26] These tumors show strong positivity for S-100 protein and neuron-specific enolase.[27,28] This supports the widely accepted theory that GCTs originate from Schwann cells.

Distinguishing between benign and malignant GCTs is challenging due to their similar epidemiology and morphology, excepting poor prognosis.[21] While most GCTs are benign, about 1–2% of cases exhibit malignant transformation.[29] Malignant GCTs exhibit key histopathological features, including increased mitotic activity, nuclear pleomorphism, necrosis, and spindling of tumor cells.[13] Additionally, malignant GCTs are usually larger, typically exceeding 5 cm in diameter.[30,31] The Fanburg-Smith criteria, consisting of six parameters (necrosis, spindling of cells, increased mitotic rate, high nuclear-to-cytoplasmic ratio, vesicular nuclei with prominent nucleoli, and pleomorphism), are commonly used to differentiate benign from malignant GCTs.[13] Molecular studies have identified potential malignancy markers, including p53 overexpression and loss of E-cadherin expression, which may aid in differential diagnosis and predicting malignant potential.[32,33] Some experts argue that metastasis is the only unequivocal sign of malignancy. However, diagnosing a tumor as malignant after metastasis provides no clinical benefit (5). Therefore, incorporating the tumor's clinical behavior into the diagnostic criteria is essential.

Wide surgical resection is typically the best treatment option for GCTs. Benign lesions rarely recur after complete resection, while malignant GCTs often recur or metastasize within one year (4). Malignant GCTs may exhibit local recurrence and metastases to lymph nodes, lungs, and bones, which typically require active antitumor treatment,

Table 1 Review of the Literature on GCT of the Thigh

References	Age/sex	Nature	Size (cm)	Duration	Symptoms	Treatment	Follow-up (months)
Present case	60/male	Benign	17×11 ×3	2 years	Mass	Excision	6
A. Andalib[14]	30/male	Benign	11×7×5	4 years	Mass, not painful	Excision	12
L. K. Hobbs[15]	14/male	Benign	3×3	Several weeks	Erythematous nodule with prominent hemorrhagic	Excision	ND
K. Haghayeghi[20]	26/male	Benign	5	8 years	Local pain and discomfort	Excision	ND
J. Lee[16]	12/female	Benign	2.3×1.5	8 months	Quite painful if pumped	Excision	4
J. Moon[17]	43/male	Malignant	2.9	ND	Mass	Wide excision	17
J. S. Hwang[18]	69/female	Malignant	18.2×7.6	3 months	Non tender firm mass, pain	Excision	1
K. Shah[19]	14/male	Malignant	4×5	2 years	Mass, not painful	Wide excision	6

Abbreviation: ND, not described.

including surgery, radiation, chemotherapy, and pazopanib.[29,34] Nasser et al believe that necrosis indicates poor prognosis, while tumor size > 10 cm suggests rapid progression and poor prognosis.[33] Moten et al suggest that tumor size > 5 cm and distant metastasis may predict worse survival, while these patients may benefit from radiotherapy or chemotherapy.[34] Although the cure rate after local resection of benign GCTs is high, there remains a risk of local recurrence.[35] In our case, despite the tumor's benign nature, its considerable size necessitates regular follow-ups after surgery. Postoperative follow-up involves clinical and imaging evaluations every 3–6 months during the first year, every 6–12 months in the second and third years, and annually from the third to the fifth year. The goal of follow-up is to detect local recurrence, residual lesions, or the appearance of new lesions.

Our study has several limitations, including its single-case nature, lack of long-term follow-up, and absence of molecular analysis, which limit insights into recurrence risks and tumor pathogenesis. Although histopathological confirmation is reliable, it carries a risk of misdiagnosis in similar cases. Future studies should emphasize larger case series, extended follow-ups, and advanced molecular analyses to identify biomarkers, refine management strategies, and improve understanding and treatment outcomes for large granular cell tumors.

In conclusion, we report a case of a giant GCT in the left thigh that gradually enlarged over two years and was initially misdiagnosed as a malignant lesion. Early diagnosis and treatment are essential to prevent tumor enlargement, mitigate the risk of malignant transformation, and enhance patient outcomes. Extensive resection remains the primary treatment for this condition, with postoperative pathology playing a key role in ensuring diagnostic accuracy and avoiding overtreatment.

Ethics Approval

This study was approved by the Ethics and Scientific Committee of Hubei University of Medicine with approval number 2022PR-H002. Written informed consent was obtained from the individual for the publication of any potentially identifiable images included in this article. Institutional approval was obtained from Xiangyang No.1 hospital for the publication of the case detail.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors report no conflicts of interest in this work.

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