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(CASE REPORT)

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A rare case malignant granular cell tumor of the thigh with radiological imaging likely rhabdomyosarcoma: A case report

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Abstract

Granular cell tumors (GCTs) are uncommon soft tissue tumors characterized by the cytoplasmic granular appearance of the neoplastic cells. Malignant GCTs are rare neural tumors, intensely aggressive. Both the rare occurrence of malignant GCTs and its similarities in features with their benign lesions make the diagnosis of this malignancy difficult. Malignant GCTs comprise less than 2% of GCTs and are mostly found in the subcutaneous soft tissues of the lower extremities, especially the thighs. This article presents a case of a large malignant GCTs in the left thigh of a 46-year-old woman. Plain radiograph of the left thigh demonstrated a soft tissue mass without bone involvement. MRI images showed a malignant solid mass 7.8 x 5.2 x 21.6 cm, with ill-defined border, irregular edges, and suspected rhabdomyosarcoma. Incisional biopsy of the mass lesion revealed mixed epithelioid and spindle tumors, suspected malignant GCTs. Histological examination performed by a musculoskeletal pathologist, demonstrated nests and sheets of epithelioid to polygonal cells with hyperchromatic, intensely eosinophilic granular cytoplasm, prominent nucleoli, increased mitotic activity, necrosis, areas of spindling with significant atypia, and positive for S100 by immunohistochemistry. In conclusion, this patient with malignant soft tissue tumor demonstrated polygonal and spindle cells with eosinophilic granular cytoplasm, which need to be considered diagnosed as Malignant GCTs. This case stresses the importance of thorough histological examination in the diagnosis of malignant GCTs.

Keywords: Granular cell tumors; Thigh; Neural tumor; Malignant soft tissue tumor

1. Introduction

Granular cell tumors (GCTs) were first described in 1926 by Abrikossoff [1]. GCTs is a rare tumor with the incidence of 0.019%-0.03%. The presence of S100 protein, a Schwann cell marker, suggested its neurogenic origin [2]. By convention, granular cell tumors are considered malignant when a morphologically benign granular cell tumor metastasizes to regional lymph nodes or to distant sites or causes death. Fanburg-Smith et al. further characterized malignant granular cell tumors histologically from their benign counterparts when their constituent cells met three out of six histopathologic criteria: necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity, high nuclear to cytoplasmic ratio, and pleomorphism [3,4].

Although most GCTs had excellent outcomes after surgical resection, less than 2% of GCTs were malignant [5]. Malignant GCTs have been found in a wide variety of locations, including lower extremities [6], breast [7], thyroid [8], abdominal

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wall [9], and bronchus [10]. Here we report a case of malignant GCTs showing an uncommon localization in the left thigh with complete imaging data, histopathologic findings and reviewing the literature.

2. Case presentation

A 46-year-old woman came to the dr. Saiful Anwar Malang hospital with a 2 year history of mass in the left thigh, with no pain history. There were no fevers, chills or weight loss. On physical examination, there was a fixed mass, firm, with an uncircumscribed margin involving the left thigh. Range of movement was within normal limits, with a normal thigh circumference of 60 cm and a left thigh with mass circumference of 66 cm. Plain radiographs of the left thigh (Figure 1) demonstrated a soft tissue mass without bone involvement. Magnetic resonance imaging (MRI) scan of the left thigh region was performed with contrast. MRI images (Figure 1) showed a malignant solid mass intra-left vastus lateralis muscle 7.8 x 5.2 x 21.6 cm, ill-defined border, irregular edge, with feeder vascularisation from the branch of the left deep femoral artery, suspected rhabdomyosarcoma.

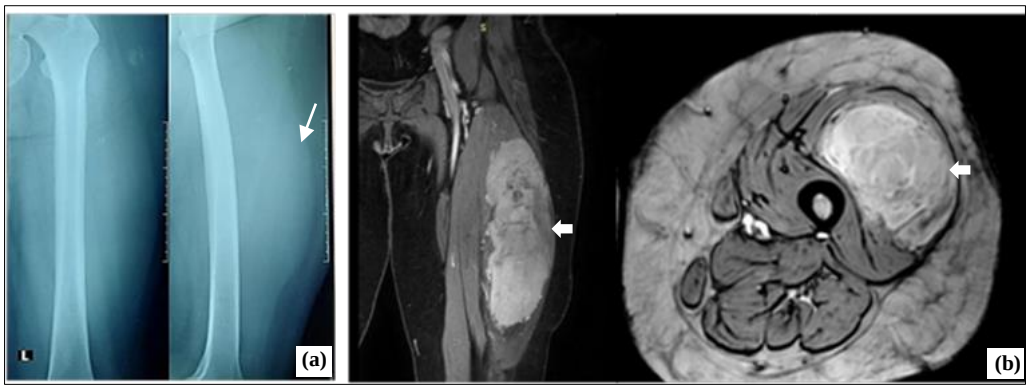

Figure 1 (a) Plain radiograph of the left thigh demonstrated a soft tissue mass (white arrow) without bone involvement. (b) MRI images showed a malignant solid mass intra-vastus lateralis muscle (open white arrow) with an irregular edge and ill-defined border

An incisional biopsy was performed in March 2023 (Figure 2) and reported a diagnose of mixed epithelioid and spindle tumor, suspected malignant GCTs. The tumor was composed of nest, polygonal and spindle cells with intensely eosinophilic, granular cytoplasm. The nuclei were vesicular and contained prominent nucleoli; mitoses were numerous with 9 mitoses per high-power field (Figure 3). Immunohistochemistry was positive diffuse for Vimentin in the cytoplasm and positive for S100 both in the cytoplasm and nucleus. (Figure 3).

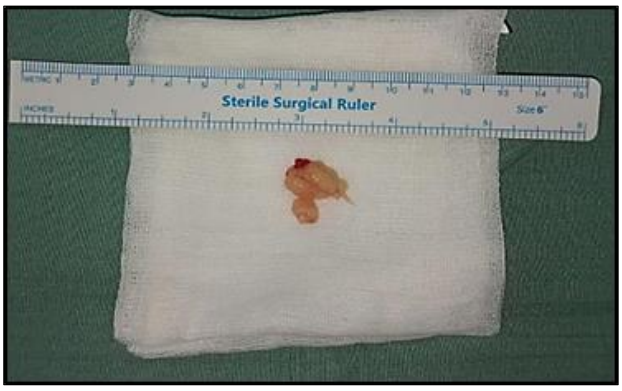

Figure 2 Incisional biopsy of the left thigh mass

In April 2023, the patient underwent widely excision of the primary tumor, which was interpreted as malignant GCTs. The surgical specimen measured 24 x 10 x 12 cm, containing a homogeneous white tumor 23 x 7 x 6 cm. Histological examination performed by a musculoskeletal pathologist, demonstrated nests and sheets of epithelioid to polygonal cells with hyperchromatic, intensely eosinophilic granular cytoplasm, prominent nucleoli, increased mitotic activity, necrosis, areas of spindling with significant atypia (Figure 4). The cells are arranged in nests, divided by connective tissue septae and infiltrated within the muscle. Immunohistochemistry was negative for Desmin and Myogenin to

distinguish with skeletal muscle tumor (Figure 3). These findings met the histologic criteria for malignant granular cell tumor. The large size and relatively rapid growth of the neoplasm supported this diagnosis.

After the reconstructive surgery, the patient was started on radiotherapy. The patient was seen six months after surgery with no evidence of local recurrence. In September 2023, a plain radiograph of the left thigh was performed and no soft tissue mass was detected. It was indicated the improvement of the patient's condition.

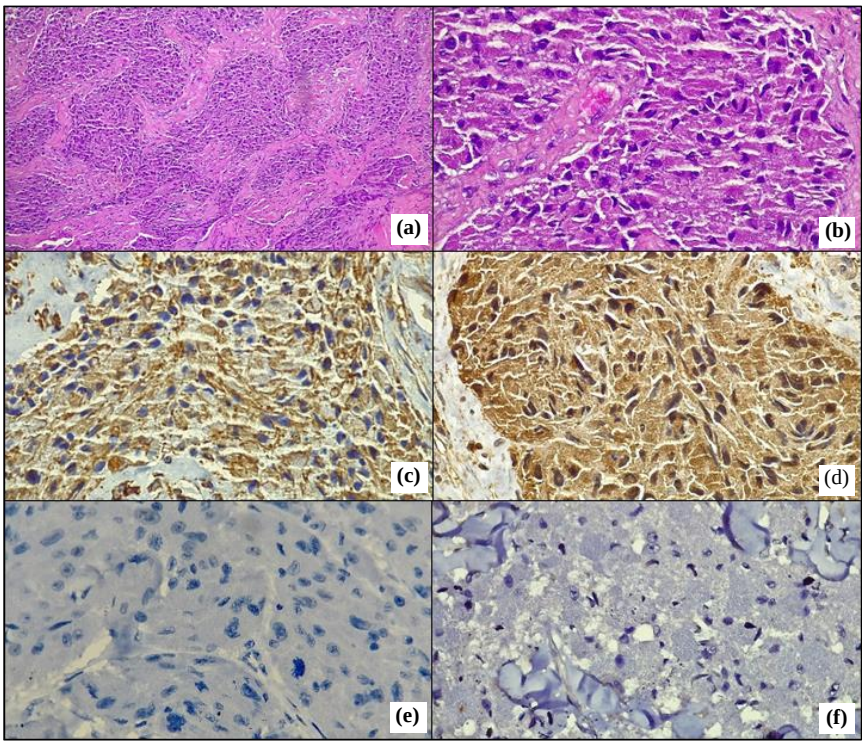

Figure 3 (a) (Hematoxylin and eosin original magnification, 100x). The malignant granular cell tumor was composed of nest, polygonal and spindle cells with intensely eosinophilic, granular cytoplasm, (b) (Hematoxylin and eosin original magnification, 400x). The nuclei were vesicular, hyperchromatic pleomorphic nuclei and contained prominent nucleoli, including mitotic figures, and necrosis, (c) Vimentin immunohistochemistry stain of biopsy specimen, (d) S-100 immunohistochemistry stain of biopsy specimen, (e) Desmin from resection specimen was negative, and (f) Myogenin from resection specimen was negative

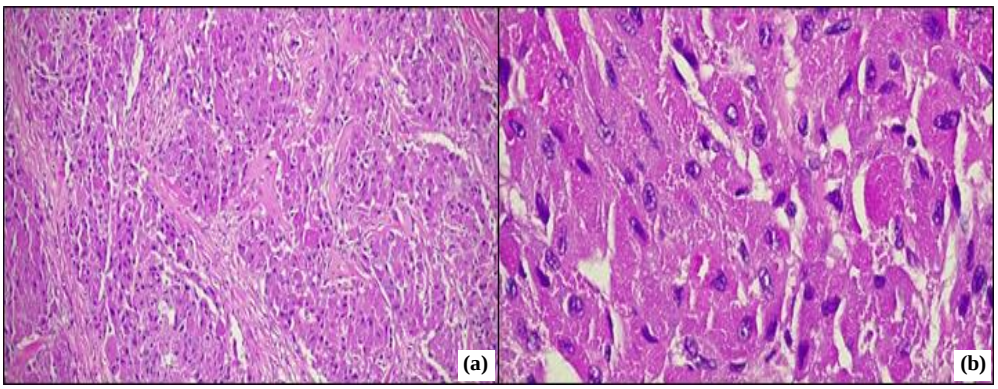

Figure 4 From Resection specimen (a) (Hematoxylin and eosin original magnification, 100x). The malignant granular cell tumor was composed of nest, polygonal and spindle cells with intensely eosinophilic, granular cytoplasm, (b) (Hematoxylin and eosin original magnification, 400x). The malignant granular cell tumor was composed of multiple large spindle cells with abundant granular cytoplasm and pleomorphic, hyperchromatic nuclei with prominent nucleoli, scattered mitotic figures and necrosis

3. Discussion

Granular cell tumors can appear in all age groups but are thought to arise most commonly in the 4th to 6th decades [11]. These tumors are most often seen in women (ranging from 1.8 to 2.4 females: male) [12]. Both factors above were shown in this patient as a 46-year-old woman.

Regardless of benign and malignant status, GCT is a very rare tumor. Malignant GCTs are rare, aggressive neural tumors that were first reported by Ravich et al [13] in 1945. The 2 distinct clinical characteristics of malignant granular cell tumors were larger average size as a median size of 4.0 to 5.0 cm and frequent localization to the lower limbs [14]. Thus, the following factors in patients were highly indicative of the malignancy of tumor: a tumor that was large (diameter more than 5.0 cm), deep location (intramuscular) at the lower extremities.

Furthermore, the scarcity of cases and related studies make the diagnosis of malignant GCT difficult. In 1998, Fanburg-Smith et al. reported a large series of GCTs and proposed histologic criteria for the diagnosis of malignant GCT [3], in which GCTs were categorized as malignant, atypical, or benign according to the following six histologic features: 1) nuclear pleomorphism, 2) tumor cell spindling, 3) vesicular nuclei with large nucleoli, 4) increased N:C ratio, 5) necrosis, and 6) increased mitotic rate (>2 mitoses/10 HPF). Tumors with more than three of these features were classified as malignant GCT. Tumors with only one or two features were classified as atypical, while tumors with none of these features or with only focal nuclear pleomorphism were considered benign [3]. Despite the worldwide use of the Fanburg-Smith classification, other criteria for the diagnosis of malignancy have also been proposed. Nasser et al. [15] reclassified GCTs according to the presence of necrosis and/or mitotic activity (>2 mitoses/10 HPF). Tumors with at least one of these features were defined as GCTs with uncertain malignant potential. Additionally, the presence of metastasis was the only factor required for the diagnosis of malignant cases [15]. In the present case, the GCTs tissue showed histological evidence of nuclear pleomorphism, tumor cell spindling, and vesicular nuclei with large nucleoli. The tumor cells also had the presence of necrosis area, an increased N:C ratio, and increased mitotic rate (>2 mitoses/10 HPF). Thus, the tumor met six criteria in the Fanburg-Smith classification and two cirteria in the Nasser classification. Furthermore, in this case, the neoplastic cells are strongly immunoreactive with Vimentin and S-100 protein, while negative immunoreactive with Desmin and Myogenin. By combining these findings, the patient could be definitively diagnosed with malignant GCT.

Once diagnosed with a malignant granular cell tumor, patients should undergo a full physical examination geared to localization of metastatic disease. To exclude metastases to more commonly involved sites, some advocate screening of patients with malignant granular cell tumor with lymphatic and hepatic sonography, chest, abdominal, and pelvic computed tomography, thoracic X-ray, and bone scintigraphy [16].

In all malignant and benign GCTs, the best treatment was complete resection of the mass. Although this was not always possible because of lacking a surrounding capsule or proximity to structures such as nerves or vessels, surgical excision with a safe and clean margin was the first choice of treatment for this tumor [17,18]. If the resection margins were involved, the wider local excision might be recommended to decrease the risk of recurrence [19]. The role of adjuvant chemotherapy and radiotherapy is uncertain, but should be considered in patients with recurrent malignant GCTs or metastatic disease [20]. So, long-term follow-up was necessary for GCTs.

4. Conclusion

In conclusion, malignant GCTs should be considered in the differential diagnosis of deep and large intramuscular tumors with diameter greater than 5 cm, and had the histological appearance of polygonal and spindle cells, eosinophilic granular cytoplasm, necrosis, and increased mitotic rate.

Compliance with ethical standards

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Data availability

The image data used to support the findings of this study are available from the corresponding author upon request.

Disclosure of conflict of interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work. There is no professional or other personal interest of any nature or kind in any product, service, and/or company that could be construed as influencing the position presented in, or the review of the manuscript entitled.

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Statement of informed consent

We have obtained informed consent from the patient for the publication of this case report.

References

[1] Abrikossoff A I. Über Myome[J]. Virchows Archiv Für Pathologische Anatomie Und Physiologie Und Für Klinische Medizin 1926;260(1):215–33.

[2] Vigier S, Traverse-Glehen A, Durbec M, Tringali S, Dubreuil C, Ceruse P, et al. Deep cervical granular cell tumor: An atypic location suggestive of neurogenic origin[J]. European Annals of Otorhinolaryngology, Head and Neck Diseases, 2014;131(1):65–7.

[3] J. C. Fanburg-Smith, J. M. Meis-Kindblom, R. Fante et al., "Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation," American Journal of Surgical Pathology, vol. 22, no. 7, pp. 779–794, 1998.

[4] J. C. Fanburg-Smith, J. M. Meis-Kindblom, R. Fante et al., "Erratum: malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation," The American Journal of Surgical Pathology, vol. 23, no. 1, p. 136, 1999.

[5] Elkousy H, Harrelson J, Dodd L, Martinez S, Scully S. Granular cell tumors of the extremities.[J]. Clinical Orthopaedics and Related Research 2000;380:191–8.

[6] Hwang JS, Beebe KS, Rojas J, Peters SR. Malignant granular cell tumor of the thigh. Orthopedics (2011) 34(8):e428–31. doi: 10.3928/01477447-20110627-31

[7] Akahane K, Kato K, Ogiso S, Sakaguchi K, Hashimoto M, Ishikawa A, et al. Malignant granular cell tumor of the breast: Case report and literature review. Breast Cancer (2015) 22(3):317–23. doi: 10.1007/s12282-012-0362-1

[8] He YQ, Lu HZ, Li DZ, Chen MQ, Wang K, Xu ZG, et al. Recurrent granular cell tumor of the thyroid: A case report and literature review. BMC Surg (2020) 20 (1):154. doi: 10.1186/s12893-020-00814-8

[9] Rehan S, Paracha H, Masood R, Wang R. Granular cell tumor of the abdominal wall, a case report and review of literature. AME Case Rep (2021) 5:28. doi: 10.21037/acr-20-160

[10] Ishaq M, Arabi E, Yousef AF, Almedbal H. Granular cell tumor of the bronchus: A case report. Int J Surg Case Rep (2022) 90:106704. doi: 10.1016/j.ijscr.2021.106704

[11] Machado I, Cruz J, Lavernia J, Llombart-Bosch A. Solitary, multiple, benign, atypical, or malignant: the "Granular Cell Tumor" puzzle. Virchows Arch. 2016 May;468(5):527-38

[12] Becelli R, Perugini M, Gasparini G, Cassoni A, Fabiani F. Abrikossoff's tumor. J Craniofac Surg. 2001 Jan;12(1):78-81.

[13] Ravich A, Stout AP, Ravich RA. Malignant granular cell myoblastoma involving the urinary bladder. Ann Surg 1945;121(3):361–72

[14] Tsuchida T, Okada K, Itoi E, Sato T, Sato K. Intramuscular malignant granular cell tumor. Skeletal Radiol 1997;26(2):116–21.

[15] H. Nasser, Y. Ahmed, S.M. Szpunar, P.J. Kowalski, Malignant granular cell tumor: a look into the diagnostic criteria, Pathol. Res. Pract. 207 (2011) 164–168.

[16] O. Schmidt, G. H. Fleckenstein, B. Gunawan, L. Fuzesi, and ¨G. Emons, "Recurrence and rapid metastasis formation of a granular cell tumor of the vulva," European Journal of Obstetrics, Gynecology and Reproductive Biology, vol. 106, no. 2, pp. 219–221, 2003.

[17] Porta N, Mazzitelli R, Cacciotti J, Cirenza M, Labate A, Schiavo M G L, et al. A case report of a rare intramuscular granular cell tumor[J]. Diagnostic Pathology 2015;10(1):162.

[18] Park SJ, Chang YH, Yang NR, Seo E K. Granular cell tumor in the pituitary stalk: a case report. Brain Tumor Res Treat 2015;3:60–3.

[19] Deskoulidi P, Koufopoulos N, Diamantopoulos P, Basagiannis E, Maltzaris N, Nikolaidou T et al. Intramuscular granular cell tumor of the gluteal region. J Surg Case Rep 2018;2:1–3.

[20] Singh V, Gunasagaran J, Pailoor J. Granular cell tumour: malignant or benign? Singapore medical journal 2015;56(09):513