Case Report

Red flag in granular cell tumors: Role of a pathologist

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ABSTRACT

Granular cell tumors (GCTs) are uncommon mesenchymal tumors of Schwann cell origin with malignant potential. A 50-year-old female presented with the complaints of swelling in right thigh since 1 year, associated with pain for 4 months. After clinical examination, imaging and histopathological examination diagnosis of malignant granular cell tumor (M-GCT)-Grade 1 (WHO grading of soft tissue tumors), stage-p$T_{2b}N_xM_x$ was made. On immunohistochemistry tumor cells were positive for S-100 and Ki-67 expression was increased (>10%), confirming the histopathological diagnosis. M-GCTs though rare, are associated with local recurrence and metastasis. A thorough histopathological examination, grading and immunohistochemistry analysis is crucial for differentiation from benign soft tissue tumors. Fanburg-Smith *et al*. grading may aid in differentiating benign, atypical, and malignant variants. This case is reported for its rarity and to stress upon the importance of diagnosing malignancy in GCTs.

Key words: Fanburg-Smith grading, Ki-67, malignant granular cell tumor

INTRODUCTION

Soft tissue tumors are a group of neoplasms with varied appearances and prognostic potential. Among these tumors, granular cell tumors (GCTs), first described by Abrikossoff in 1926, are uncommon mesenchymal neoplasms of Schwann cell origin.[1] The benign counterpart of these tumors (B-GCTs) are known to occur throughout the body: In the head and neck region, the most common site is the tongue. Skin, subcutaneous tissue of trunk and upper extremities, breast, and female genital tract are the other sites of the tumor.[2-6]

Granular cell tumors are known to have malignant potential, and therefore a cautious and careful approach in diagnosis is of utmost importance malignant granular cell tumors (M-GCTs) were first described by Ravich *et al*. in 1945 and they constitute 1-2% of all GCTs.[7,8]

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Though metastasis is an important criterion to differentiate between benign and M-GCTs, even high grade tumors may not metastasize, making it difficult to differentiate between the two at the time of initial diagnosis.[9]

This differentiation is important as M-GCT should be treated by wide local excision with local lymph node sampling if any.

CASE REPORT

A 50-year-old woman presented to the surgical outpatient department of our hospital with a history of a swelling in her right thigh since over a year. It was associated with pain for the past 4 months. She did not complain of any restriction of mobility or paresis.

On clinical examination, a swelling in the anterolateral aspect of the right thigh measuring 15 cm × 10 cm × 5 cm was seen. The swelling was mobile, and firm in consistency.

Magnetic resonance imaging of the right thigh revealed a well lobulated soft tissue mass arising from the vastus lateralis and vastus intermedius without involving the bone. On fine-needle aspiration of the swelling, a diagnosis of fibroma was made. On a strong clinical suspicion of soft tissue sarcoma, wide local excision of the tumor was

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done, along with a part of the vastus lateralis and vastus intermedius, and sent to us.

On gross examination, a skin covered fibrofatty mass measuring 15 × 10.5 × 6 cm was seen.

The cut section revealed a grey-white irregular tumor measuring 8.5 × 8 × 4.5 cm. The tumor borders were irregular, the closest margin being 0.5 cm away from the surgically resected margin [Figure 1a and b].

On histopathological examination, the tumor showed sheets of round to polygonal tumor cells with granular cytoplasm, round to oval vesicular nucleus with very prominent nucleoli. Mitotic index was 2-3 mitotic figures/10 high power fields. There were intracytoplasmic and extracellular eosinophilic globules. At the periphery of the tumor, infiltration into adipose tissue was seen. No necrosis/hemorrhage/lymphovascular invasion was seen [Figure 2a and b]. On immunohistochemistry, tumor cells were positive for S-100. Proliferation rate as determined by Ki-67 was over 10% [Figure 3a and b].

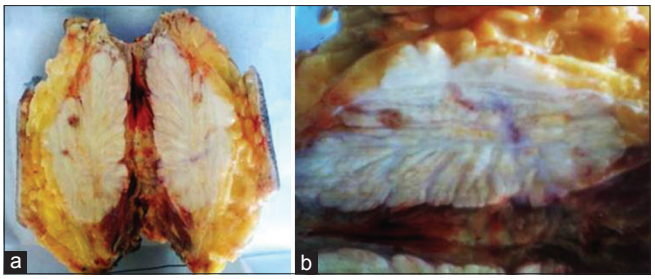

Figure 1: (a) Cut section of grey-white irregular tumor measuring 8.5 × 8 × 4.5 cm surrounded by fibrofatty tissue. (b) The tumor borders were irregular, the closest margin being 0.5 cm away from the surgically resected margin

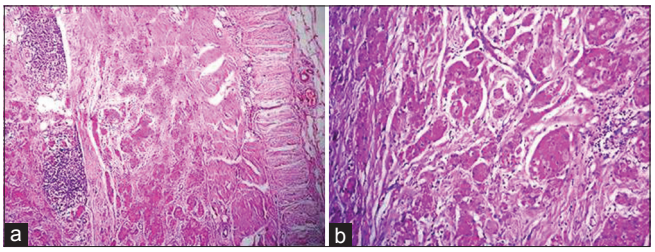

Figure 2: (a) Sheets of round to polygonal tumor cells with granular cytoplasm, round to oval vesicular nucleus with very prominent nucleoli (H and E, ×40). (b) Periphery of the tumor showing infiltration into adipose tissue (H and E, ×100)

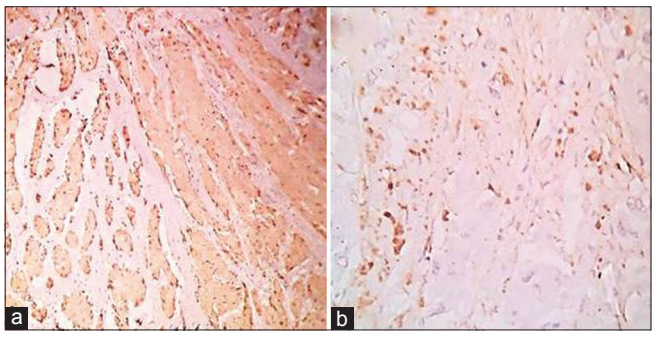

Figure 3: (a) Tumor cells positive for S-100 (immunohistochemistry [IHC], ×40). (b) Proliferation rate by Ki-67 >10% (IHC, ×40)

DISCUSSION

Though both benign and M-GCT share common epidemiological features such as being more common in females than in males, occurring at the age of 40-69 years, the malignant ones are commonly larger and are frequently localized to the lower limb while the benign tumors are smaller and occur more commonly in the head and neck region and tongue.

On histopathological examination benign granular cell tumors may show features of multicentricity, focal pleomorphism, or recurrence, thereby searching the criteria for diagnosing them as benign.[9]

In some tumors metastasis to bone, nerve, peritoneal cavity, lung, and breast has been documented. Though metastasis is a definitive feature of malignancy, sometimes even when high grade tumors may not metastasize, and it is imperious to wait for patient to develop metastasis to make a diagnosis of M-GCT.[2,10,1]

In view of all these confusion Fanburg-Smith *et al.*,[9] described six important histological features to differentiate between malignant and benign granular cell tumors which includes pleomorphism, necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity, increased nucleocytoplasmic ratio.

Sonobe *et al*. divided M-GCT into two categories: Those that are malignant both histologically and clinically, and those that are benign histologically, but are clinically malignant.

The patient in this case report was lost to follow-up and hence the metastasis of the tumor following excision could not be assessed.[12]

Initially, Abrikosoff suggested that granular cell tumors originate from skeletal muscle cells and so referred to them as myoblastomas; this suggestion probably arose from examination of tumors of the tongue in which infiltration between the striated muscle bundles gave the impression of a muscular origin. Recent studies suggest derivation from Schwann cells of the peripheral nerves, and the presence of S-100 protein supports this.[13]

All three categories of granular cell tumors display similar light microscopic, ultrastructural and immunohistochemical features. The immunoprofile showed positivity for S-100 and vimentin in almost all cases, as well as identical expression of CD57, NSE and CD68 in most cases.

Characteristic ultrastructural features included lysosomal complexes, interdigitating cytoplasmic processes, and external laminae.[9]

Statistically significant adverse prognostic features with regard to survival include local recurrences, metastasis, larger tumor size, older patient age, histological classification as malignant, presence of necrosis, increased mitotic activity, spindling of tumor cells, vesicular nuclei with large nucleoli, and Ki-67 values over 10%.[9]

Time interval between initial diagnosis and metastasis varied widely in different case reports. Crawford and de Bakey[14] have reported a patient in whom metastasis occurred 14 years after initial treatment. Mullins and Magner[15] have reported a case of a woman who first had a right flank subcutaneous mass, diagnosed as granular cell tumor, and then developing 2 years later a mass in the contralateral parotid gland. Another report was about a case of M-GCT in the popliteal cavity, which showed a metastatic focus after 2 years of initial diagnosis.

Differential diagnoses to be considered for granular cell tumors include granular cell features in carcinoma, ameloblastic lesions, leiomyoma, leiomyosarcoma, dermatofibroma, dermatofibrosarcoma protuberans, malignant fibrous histiocytoma, malignant peripheral nerve sheath tumor, angiosarcoma, melanoma as well as congenital gingival granular cell tumor. Immunohistochemistry helps in their differentiation.[15]

The treatment of choice for benign GCT is wide local excision. In the malignant variant, the treatment should additionally include wide local excision with regional lymph node dissection and radiological evaluation for metastasis. Radiotherapy and chemotherapy are used with variable success, but their effectiveness remains unproven.[16]

CONCLUSION

Malignant granular cell tumors can present as a diagnostic dilemma for pathologists, owing to the difficulties in differentiating them from other soft tissue tumors with overlapping features as well as from benign and atypical subtypes. This case is reported for its rarity and to highlight the need for cautious histopathological examination, use of Fanburg-Smith criteria and hence aid the clinicians in appropriate management and treatment.

REFERENCES

1. Abrikossoff A. Uber Myome, ausgehend von der quergestreiften willkiirlichen miiskulatur. Virchow Arch Pathol Anat Physiol 1926;26:215-33.
2. Chen J, Wang L, Xu J, Pan T, Shen J, Hu W, *et al.* Malignant granular cell tumor with breast metastasis: A case report and review of the literature. Oncol Lett 2012;4:63-6.
3. Paskin DL, Hull JD, Cookson PJ. Granular cell myoblastoma: A comprehensive review of 15-years experience. Ann Surg 1972;175:501-4.
4. Hatta J, Yanagihara M, Hasei M, Abe S, Tanabe H, Mochizuki T. Case of multiple cutaneous granular cell tumors. J Dermatol 2009;36:504-7.
5. Park JY, Hwang JJ, Lee SA, Lee WS, Kim YH, Chee HK, *et al.* Granular cell tumor occurring in the chest wall: A case report. Korean J Thorac Cardiovasc Surg 2012;45:196-8.
6. Ullmann AS, Dacso MR. Multiple granular cell myoblastoma. Can Med Assoc J 1965;92:531-3.
7. Simone J, Schneider GT, Begneaud W, Harms K. Granular cell tumor of the vulva: Literature review and case report. J La State Med Soc 1996;148:539-41.
8. Ravich A, Stout AP, Ravich RA. Malignant granular cell myoblastoma involving the urinary bladder. Ann Surg 1945;121:361-72.
9. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumor of soft tissue: Diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998;22:779-94.
10. Canacci AM, Nunez C, Getty P, Abdul-Karim F. Diagnosis of malignant granular cell tumor metastatic to bone by fine needle aspiration cytology: A case report. Acta Cytol 2010;54:190-2.
11. Curtis BV, Calcaterra TC, Coulson WF. Multiple granular cell tumor: A case report and review of the literature. Head Neck 1997;19:634-7.
12. Sonobe H, Iwata J, Furihata M, Moriki T, Ohtsuki Y. Malignant granular cell tumor: Report of a case and review of the literature. Pathol Res Pract 1998;194:507-13.
13. Weber-Chappuis K, Widmann JJ, Kapanci Y. Histologic and immunohistochemical profiles of benign granular cell tumors. Report of 41 cases. Ann Pathol 1995;15:198-202.
14. Crawford ES, de Bakey ME. Granular-cell myoblastoma; two unusual cases. Cancer 1953;6:786-9.
15. Mullins GM, Magner JW. Multiple granular cell myoblastomas - A case report. Ir Med J 1984;77:286-7.
16. Qureshi NA, Tahir M, Carmichael AR. Granular cell tumour of the soft tissues: A case report and literature review. Int Semin Surg Oncol 2006;3:21.

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