

Granular Cell Tumour of the Chest Wall: FNA Diagnosis with a Review of Literature and Elaboration of Cytological Mimickers

ZEBA CHOUDHARY¹, PRAJWALA GUPTA², PURNIMA MALHOTRA³, MINAKSHI BHARDWAJ⁴, PRAFULL KUMAR SHARMA⁵

ABSTRACT

Granular Cell Tumours (GCTs) are uncommon tumours which can be confused with other benign soft tissue tumours on clinical examination. Fine Needle Aspiration Cytology (FNAC) plays a significant role in their diagnosis. There are certain cytological mimickers of GCTs so a cytopathologist must be aware of its characteristic cytomorphology. These tumours can be present anywhere on the body; however, chest wall is one of the uncommon sites. We present a case of GCT present on the chest wall in an elderly male as a subcutaneous nodule. We have discussed the common cytological differential of GCTs, features of malignant GCTs along with cytomorphological and immunohistochemical features.

Keywords: Lymphadenopathy, Pleomorphism, Subcutaneous nodule

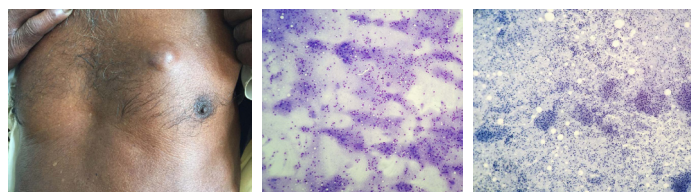
CASE REPORT

A 70-year-old male patient presented to the Dermatology OPD with a complaint of left sided anterior chest wall swelling which was gradually increasing in size since two years. On examination, the swelling was present over the anterior 5th and 6th thoracic segment. The swelling was subcutaneous, non-tender, nodular, measuring approximately 2 x 2 cm in size and was fixed to the overlying skin [Table/Fig-1]. There was no ulceration or pigmentation of the overlying skin. There was no palpable peripheral lymphadenopathy. The patient had no systemic complaint. Routine haematological and biochemical investigations were normal. A clinical diagnosis of dermatofibroma was kept. Ultrasonographic evaluation of the swelling revealed a well defined, heteroechoic lesion measuring 2.2 x 1.7 x 1.8 cm, present in the subcutaneous plane. The swelling was causing indentation of the underlying muscle; however, no direct invasion was seen in the muscle or overlying skin. FNAC of the swelling was done which yielded thick cellular aspirate. Smears were prepared and fixed in 95% ethyl alcohol and air dried and was subsequently stained with Papanicolaou and Giemsa stains respectively.

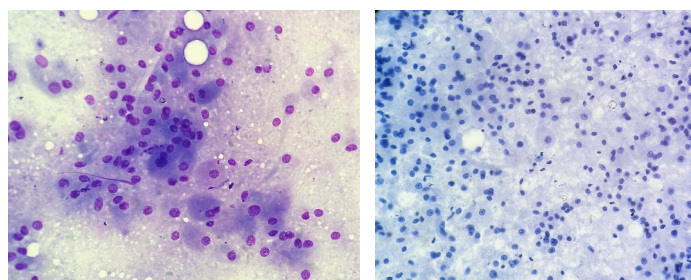
Smears were moderately cellular comprising large, polygonal cells seen as loosely dispersed clusters, sheets, syncytium and singly scattered. The cells revealed eccentric nuclei with fine nuclear chromatin, inconspicuous to prominent nucleoli and abundant granular cytoplasm and many cells showed indistinct cytoplasmic border [Table/Fig-2, 3]. No intranuclear inclusion or pseudoinclusion was seen. Few binucleate and occasional spindle shaped cells were also noted. Background revealed dispersed granular material [Table/Fig-2, 3]. No nuclear atypia, mitosis or necrosis was seen. Periodic Acid-Schiff stain with Diastase Digestion (PAS- D) was done and showed PAS positive, diastase resistant cytoplasmic granules [Table/Fig-4]. A diagnosis of benign GCT was given on FNAC and excision was advised. The excised tumour was sent for the histopathological examination.

A single, circular, skin covered soft tissue piece measuring 5 x 2 x 2 cm was received in the Histopathology Department. Cut section showed a circumscribed, greyish yellow, subcutaneous nodule measuring 2.5 cm in diameter. Microscopic examination revealed a well circumscribed tumour comprising of nests and sheets of cells.

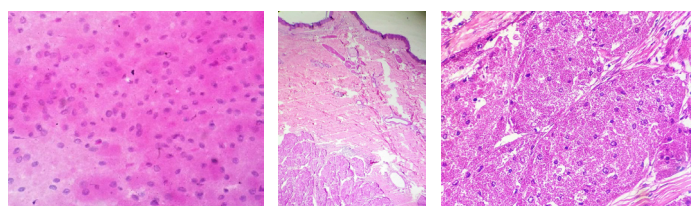
The cells were polygonal with abundant eosinophilic cytoplasm and showed round small central nuclei and vesicular chromatin. No necrosis, pleomorphism or mitosis was noted. A diagnosis of Benign GCT on the basis of histomorphology was given. Immunohistochemistry for confirmation was not performed as both the cytomorphology and histomorphology were strongly suggestive of GCT [Table/Fig-5a, b]. The patient was followed-up after a month



[Table/Fig-1]: Well defined subcutaneous lesion on chest wall. **[Table/Fig-2 a and b]:** Moderately cellular smears comprising of loosely dispersed, round to polygonal cells in a granular background (a-Giemsa stain, 10X, b-papanicolaou stain 10X. (Images from left to right)



[Table/Fig-3 a and b]: Polygonal cells with eccentric nuclei, fine nuclear chromatin and granular cytoplasm arranged in loose clusters (a-Giemsa 40X, b-pap, 40X). (Images from left to right)



[Table/Fig-4]: PAS positive and diastase resistant granules of granular cell tumour with PAS positive background (PAS-D, 40X). **[Table/Fig-5 a and b]:** Granular cell tumour present in the lower dermis, comprising of benign looking tumour cells with prominent granular cytoplasm arranged in nests (H&E 10X & 40X).

Differential diagnosis	Cytomorphological features	Special stain/IHC
Granular cell tumour [6]	Cells with granular cytoplasm, indistinct cell borders, and eccentric nuclei arranged in syncytium, clusters or singly scattered.	PAS + diastase resistant cytoplasmic granules S-100 + CD 68+ NSE+ CK negative
Rhabdomyoma [11]	Cells with well defined cell borders and 'cross striations' intense eosinophilic fibrillary cytoplasm	PAS + diastase sensitive Desmin+ Myoglobin+ MSA+ CK negative CD 68 negative
Alveolar Soft Part Sarcoma (ASPS) [12]	Frequent bi-, multi-nucleate cells with granular cytoplasm showing prominent nucleoli and characteristic needle like rhomboid crystals	PAS+ diastase resistant TFE3+ {transcriptional factor E3(strong nuclear)} S-100 negative CK negative
Xanthogranuloma/histiocytes rich lesions [13]	Bean shaped nuclei of histiocytes Foamy rather than granular cytoplasm Background inflammation	PAS negative CD 68 +
Oncocytic tumours [14]	Central nucleus with distinct cell border, prominent nucleoli	CK+ PTAH+ (mitochondrial) PAS-D negative
Hibernoma [15]	Distinct cell borders with cytoplasmic multivacuolations and fatty background	S-100 + Fat stains+ CK negative

[Table/Fig-6]: Common cytological mimickers of GCTs with cytomorphological and immunohistochemical features.

and was found to be stable and without any recurrence of the tumour.

DISCUSSION

GCTs are rare tumours first reported by Abrikossoff A [1]. They account for 0.5% among soft tissue tumours and only 2% of all GCTs are malignant [2]. Most common site of this tumour is the head and neck region. Other common sites for GCT are tongue (40%), breast (15%), respiratory tract (10%) and oesophagus (2%) [3]. The aetiology of GCT is still controversial, however, the most accepted hypothesis is that it arises from Schwann cells or their precursors. Finding supporting this hypothesis is the strong and consistent positivity for S-100 [4].

These tumours primarily affect adults with a predilection for females between second to the sixth decade with a male:female ratio of 1:1.8-2.4. GCTs have characteristic cytological features which are well described in the literature; however, it often becomes difficult to differentiate it from the similar tumours with eosinophilic granular cytoplasm [5]. The GCT cells are round to polygonal with abundant amount of finely granular, eosinophilic cytoplasm, round to oval, eccentric nuclei with fine chromatin and occasionally small to inconspicuous nucleoli. These cells usually have indistinct cell membranes and often a granular background. The characteristic feature which is the cytoplasmic granularity is due to the accumulation of lysosomes. These accumulated lysosomes/autophagosomes are noted on electron microscopy along with replicated basal lamina and these granules give positive reaction to the Periodic acid-Schiff stain and CD 68 [6,7].

GCTs are usually benign tumours with malignant GCT being quite rare. Malignant GCTs present as rapidly growing tumours with size usually measuring more than 5 cm. Studies like Wieczorek TJ et al., Fanburg-Smith JS et al., and Wang J et al., have evaluated diagnostic criteria for malignant GCTs [8-10]. Three out of six features should be present to label it as malignant GCT which include necrosis, the presence of spindle cells, mitosis (>2/10 HPF), the presence of a vesicular nucleus and large nucleolus, high N:C

ratio and pleomorphism. The tumour is labeled as 'atypical GCT' if two out of these six features are present.

The common differential diagnosis of GCT includes rhabdomyoma, Alveolar Soft Part Sarcoma (ASPS), xanthogranuloma or histiocytes rich lesions, oncocytic tumours and hibernoma. FNAC with ancillary investigations helps to resolve the diagnosis [Table/Fig-6] [6,11-15].

Further, Rhabdomyoma may have characteristic radiological feature [12]. ASPS occur in children and young adults with a predilection for lower extremities, trunk, genitals and pharynx [12].

Other tumours like Extra Gastrointestinal Stromal Tumours (EGIST), Melanoma, epithelioid sarcoma and metastatic carcinoma may also come under the differential diagnosis of malignant GIST and in these cases the immunohistochemistry becomes obligatory. Epithelioid variant of EGIST may resemble GCT but these tumours are positive for CD-117(c-kit), vimentin, CD 34 and negative for CD 68, NSE and PAS. Similarly, GCT is negative for HMB-45, Melan-A/MART-1, desmin, myogenin, Myo-D 1 and cytokeratins AE1/AE3 [11-14]. In our case, the characteristic cytomorphology on FNA smears as well as the use of special stain PAS with diastase helped in reaching the correct diagnosis of GCT.

Our case is a rare case as our patient is an elderly male and the site of the tumour is chest wall which is a rare site for the Granular cell tumours and this site has been rarely reported in the literature [16].

CONCLUSION

The Granular cell tumours are rare tumours which can arise anywhere on the body and has a wide spectrum of cytological mimickers. A simple procedure like FNAC can accurately diagnose the lesion if the cytopathologist is aware of its characteristic cytomorphology and a simple stain like Periodic acid-Schiff can help in arriving at a correct diagnosis.

REFERENCES

- Abrikossoff A. About fibroids, emanating from the cross-strained wilful musculature. *Virchows Arch Pathol Anat.* 1926;260:215-33. (Translated from German to English language).
- Khansur T, Balducci L, Tavassoli M. Granular cell tumour. Clinical spectrum of the benign and malignant entity. *Cancer.* 1987;60:220-22.
- Liu Z, Mira JL, Vu H. Diagnosis of malignant granular cell tumour by fine needle aspiration cytology. A case report. *Acta Cytol.* 2001;45:1011-21.
- Le BH, Boyer PJ, Lewis JE, Kapadia SB. Granular cell tumour: Immunohistochemical assessment of inhibin-alpha, protein gene product 9.5, S100 protein, CD68, and Ki-67 proliferative index with clinical correlation. *Arch Pathol Lab Med.* 2004;128:771-75.
- Liu K, Madden JF, Olatidoye BA, Dodd LG. Features of benign granular cell tumour on fine needle aspiration. *Acta Cytol.* 1999;43:552-57.
- Agarwal A, Sinha A, Rijal A, Karki S, Nizamani SM. Cytology diagnosis of granular cell tumour of umbilicus mimicking metastatic skin nodule and review of literature. *Medical Channel.* 2010;16:103-05.
- Toi P, Siddharaju N, Basu D. Fine needle aspiration cytology of granular cell tumour: A report of two cases. *J Cytol.* 2013;30(3):195-97.
- Wieczorek TJ, Krane JF, Domanski HA, Akerman M. Cytologic findings in granular cell tumours, with emphasis on the diagnosis of malignant granular cell tumour by fine needle aspiration biopsy. *Cancer.* 2001;93(6):398-408.
- Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumour of soft tissue: Diagnostic criteria and clinicopathologic correlation. *Am J Surg Pathol.* 1998;22:779-94.
- Wang J, Zhu XZ, Zhang RY. Malignant granular cell tumour: A clinicopathologic analysis of 10 cases with review of literature. *Zhonghua Bing Li Xue Za Zhi.* 2004;33:497-502.
- Limbach AL, Goyal A. Adult rhabdomyoma: A challenging diagnosis on cytology. *Cytojournal.* 2012;9:20.
- Folpe AL, Deyrup AT. Alveolar soft part sarcoma: A review and update. *J Clin Pathol.* 2006;59:1127-32.
- Nareesh KN, Soman CS. Granular cell tumour of the mammary skin. *Acta Cytol.* 1996;40:610-12.
- McCluggage WG, Sloan S, Kenny BD, Alderdice JM, Kirk SJ, Anderson NH. Fine needle aspiration cytology (FNAC) of mammary granular cell tumour: A report of three cases. *Cytopathology.* 1999;10:383-89.

- [15] Lemos MM, Kindblom LG, Meis-Kindblom JM, Remotti F, Ryd W, Gunterberg B, et al. Fine needle aspiration characteristics of hibernoma. *Cancer*. 2001;93:206–10.
- [16] Park JY, Hwang JJ, Lee SA, Lee WS, Kim YH, Chee HK, et al. Granular cell tumour occurring in the chest wall: A case report. *Korean J Thorac Cardiovasc Surg*. 2012;45(3):196–98.

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