ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

ORIGINAL ARTICLE

Granular Cell Tumour – A Case Series

Amit H. Agravat[1], Vaidya Tejas H.[2], Gauravi A. Dhruva[3], Nikita A. Machhi[4]

[1]Professor, Department of Pathology, P.D.U. Government Medical College and Hospital, Rajkot, Gujarat, India.
[2]Resident Doctor, Department of Pathology, P.D.U. Government Medical College and Hospital, Rajkot, Gujarat, India.
[3]Professor and HOD, Department of Pathology, P.D.U. Government Medical College and Hospital, Rajkot, Gujarat, India.
[4]Senior Resident, Department of Pathology, P.D.U. Government Medical College and Hospital, Rajkot, Gujarat, India.

Received Date: 22/01/2023 Acceptance Date: 10/03/2023

Abstract

Background: Granular cell tumour is the soft tissue tumour with neuroectodermal differentiation composed of large cells with eosinophilic, granular cytoplasm. It is very rare, predominantly benign soft tissue tumour involving a wide variety of sites. It shows wide age range, though most common in 30 – 50 year olds but rare in children <5 years or adults >80 years and it shows slight female predominance. **Material And Methodology:** The present study was undertaken in the department of Pathology, P.D.U. Government Medical College, Rajkot. All the five specimens were fixed in 10% formalin overnight, processed, blocks were made and sectioning was done and stained with Harris haematoxylin and Eosin stain. **Result:** A series of five cases of granular cell tumours in five patients. All tumours were benign. Females were more affected than males. Common age group affected was in third decade. Most common site affected in the present study was tongue, followed by one case each at supraclavicular region, over phalanx of finger and back. **Conclusion:** Most granular cell tumours are benign and cured by simple resection. Although granular cell tumours are usually benign and slow growing, it is difficult to distinguish them from malignant lesions. Therefore, it is very important that clinicians and pathologists are aware of their clinical and histopathological features [17].

KEY WORDS: Granular, benign, rare tumour.

Corresponding Author: Dr. Nikita A. Machhi, Senior Resident, Department of Pathology, P.D.U. Government Medical College and Hospital, Rajkot, Gujarat, India.
Address: B-17, Purushottam park society, Opp, Chamunda Temple, Zadeshwar Road, Bharuch – 392011, Gujarat, India.
Email: nikita081094@gmail.com

Introduction

Granular cell tumors (GCTs), also known as Abrikossoff's tumors, are rare neoplasms first discovered in 1926 by Abrikossoff and originally thought to arise from smooth-muscle tissue [1, 2].

The dispute, over many years, as to whether granular cell tumour represents a metabolic, degenerative, or neoplastic process has been resolved in favour of the neoplastic view. However, it should be noted that, although most granular cell neoplasms are probably neuroectodermal in nature, on the basis of their immunophenotype and close association with

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

nerves, this is by no means true of all lesions showing this distinctive pattern of granular cytoplasmic change [3].

In the decades following, immunohistochemical and ultrastructural studies of the affected cells revealed that they are actually of neural-crest cell origin, derived from Schwann cells that are normally responsible for the production of myelin around neuronal axons in the peripheral nervous system [4].

GCTs are most commonly benign, with only 1–2% of cases presenting as malignant, and usually occurring in middle-aged females [5]. GCTs can be found anywhere in the body, but commonly affected areas include the tongue, head, neck, and subcutaneous tissues [6].

Granular cells in GCTs are histopathologically characterized by cytoplasmic granulation manifesting as microtubules, microvesicles, myelinic structures, and high-density regions [7]. The myelinic component of the granules, marked by the presence of sphyngomyelin and lipoproteins, is one indicator that GCTs originate from Schwann cells [5].

Granular cells have also tested positive for protein S-100, associated with neurodegeneration, and neuron-specific enolase, providing further support for GCTs' affiliation with Schwann cells [4].

There are reports of congenital lesions, most of which arise in the gingiva, but such lesions are S-100 negative and probably represent distinct entity (congenital epulis) [8].

Material And Methods

The following cases were diagnosed in Cytopathology and Histopathology laboratory, Department of Pathology, P.D.U. Government Medical College and hospital, Rajkot.

Cytopathology: First, the skin is cleaned with antiseptic solution and mass is immobilized with thumb and finger of non-aspirating hand, then 22 or 23-gauge needle, which is attached to disposable 10 ml syringe is pierced into the mass. When needle reaches the mass, the plunger of the syringe is drawn out, thus creating a negative pressure in the syringe and needle lumen. The needle is moved to and fro several times and moved in different directions so as to collect samples from different areas around. The needle is then withdrawn and pressure applied to puncture site, with sterile cotton swab.

The material obtained in the syringe is spread on many slides. Some of them are fixed immediately in methanol for Hematoxylin and Eosin stain while some are kept air dried and then fixed in methanol for May Grunewald Geimsa stain.

Histopathology: Received specimens were fixed in 10% formalin; following fixation of 12 hours, sections were passed through the steps of dehydration, clearing and impregnation and embedding in paraffin, finally block preparation, cutting done and sections were stained with Harris Haematoxylin and Eosin stain and made ready for microscopic examination.

Results

Case 1

A 30 year old female patient came to Otorhinolarynogology Outdoor Patient Department (OPD) with complain of swelling over right supraclavicular region (Figure 1). Size of the swelling was 7 x 5 cm and swelling was slow growing, non-mobile, non-tender and firm in consistency.

Radiological examination (MSCT scan of neck and thorax) showed lesion of size 52 x 47 x 52 mm which was suggestive of neoplastic lesion.

Fine Needle Aspiration Cytology was done and blood mixed material aspirated.

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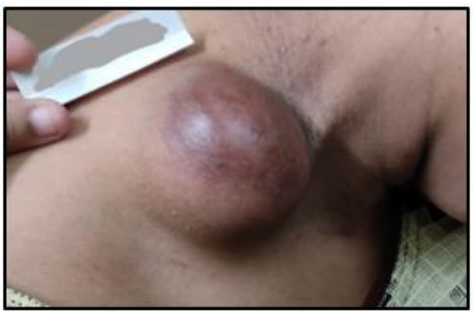

Figure 1: Shows FNAC site: Right supraclavicular region swelling

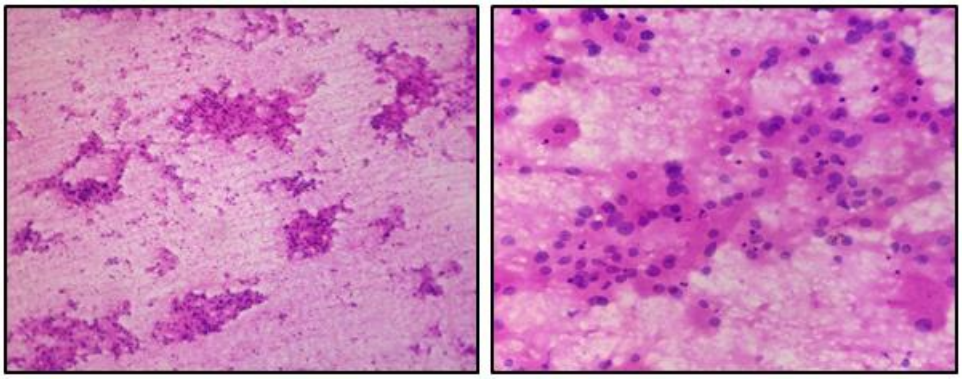

Figure 2 (10x and 40x) shows microscopic examination of fine needle aspiration cytology

Microscopic examination (Figure 2) shows high cellularity which contained tumour cells that were arranged in clusters and irregular sheets. Cells showed abundant and syncytial eosinophilic cytoplasm with mild to moderate anisonucleosis, nuclei showed fine chromatin and at places distinct small nucleoli. All tumour cells showed oncocytic material. Background was blood mixed.

Diagnosis: The lesion was diagnosed with three possibilities, first being Alveolar soft part sarcoma followed by Rhabdomyosarcoma and Rhabdomyoma.
Excisional biopsy was done and specimen was sent to histopathology laboratory.

Gross Examination (Figure 3): Skin covered tissue received size measuring 7 x 5 x 4.5 cm. On cut surface mass was uninodular, well defined, firm, yellowish white with fine granular texture.

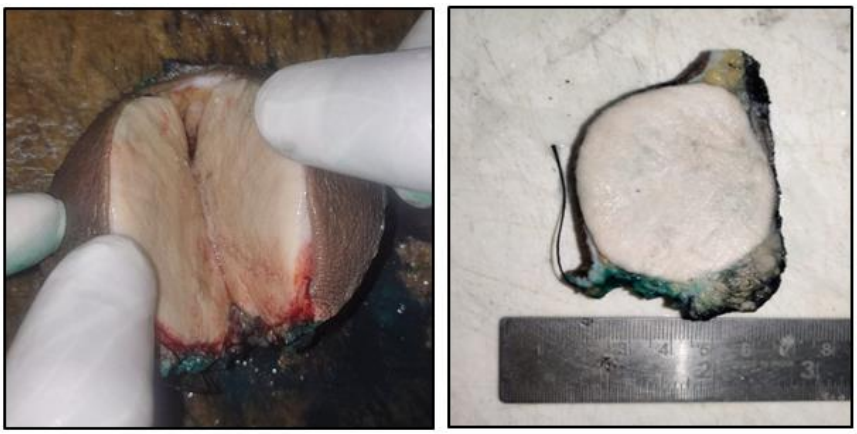

Figure 3: Shows uninodular, well defined, firm, yellowish white with fine granular cut surface

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Microscopic Examination (Figure 4 (10x) and (40x)): Studied sections from mass show tumour cells arranged in sheets and lobules. Tumour cells having eosinophilic, granular cytoplasm with hyaline bodies seen in few tumour cells with eccentric blend, homogenous nuclei seen. Margins are free from tumour cells.
Overall findings are in favour of
? Rhabdomyoma.
?? Granular Cell Tumour.

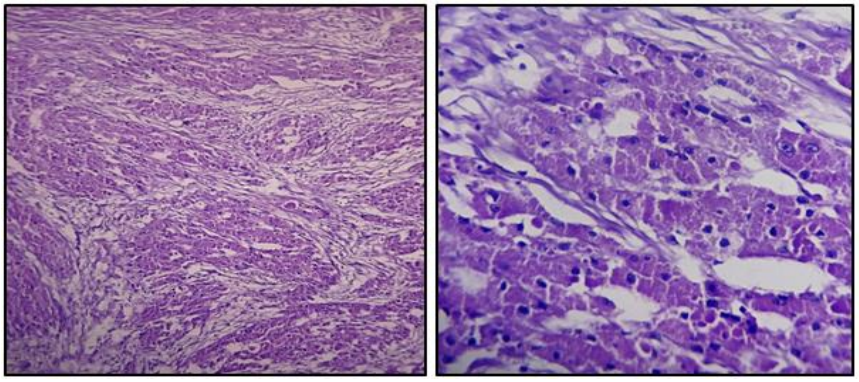

Figure 4: Low power and High power view
For confirmatory diagnosis, IHC was performed and tumour cells are immunopositive for **S100** and **SOX10** and are immunonegative for Desmin, CD34 and Pancytokeratin.

Final Diagnosis: Granular Cell Tumour.
Case 2
A 28 year old male patient came to Otorhinolaryngology Outdoor Patient Department (OPD) with complain of small painless nodule over mucosal surface of tongue. Size of the swelling was 2 x 1.5 cm and swelling was slow growing, non-mobile, non-tender and firm in consistency.
Excisional biopsy was done and specimen was sent to histopathology laboratory.
Gross examination (Figure 5): Tissue received size measuring 1.5 x 1 cm. Uninodular, well defined mass received. Cut surface is yellowish, firm. Whole tissue is passed for histopathological examination.

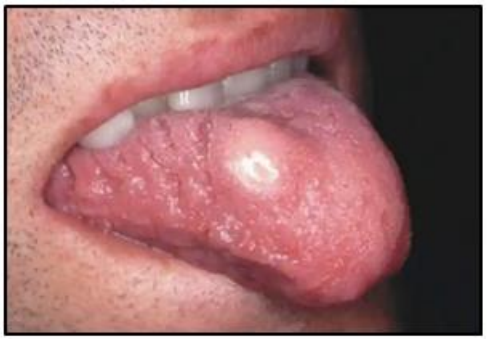

Figure 5
Microscopic examination (Figure 6): Tumour cells arranged in sheets, nests or ribbons separated by thin collagenous band. Cells are round and polygonal to slightly spindle shaped. Cells show small and dense to large, vesicular nuclei and abundant granular eosinophilic cytoplasm.
Overall findings are suggestive of **GRANULAR CELL TUMOUR**.

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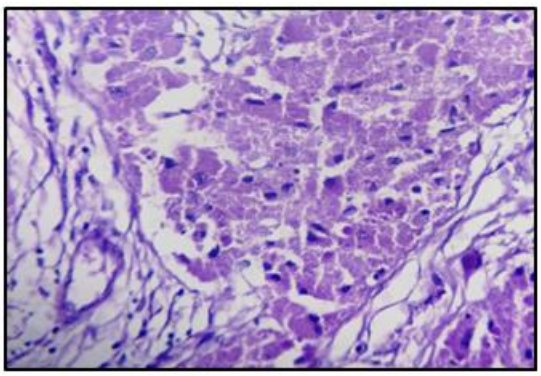

Figure 6

Case 3

A 21 year old female patient came to Surgical Outdoor Patient Department (OPD) with complain of swelling over 3rd phalanx of left hand. Size of the swelling was 1.5 x 1.5 cm and swelling was slow growing, non-mobile, non-tender and firm in consistency.

Excisional biopsy was done and specimen was sent to histopathology laboratory.

On gross examination (Figure 7): Tissue received size measuring 1.3 x 1.1 x 0.6 cm. Greyish white to brown, firm. Whole tissue is passed for histopathological examination.

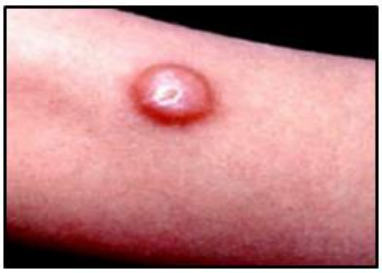

Figure 7

Microscopic examination (Figure 8): Studied section shows proliferation of clusters of large polygonal cells with abundant granular eosinophilic cytoplasm and uniform small nuclei separated by fibrovascular stromal tissue. At places, cells are oval to spindle in shape. No nuclear atypia seen.

Overall findings are in favour of **BENIGN SOFT TISSUE NEOPLASTIC LESION-GRANULAR CELL TUMOUR**.

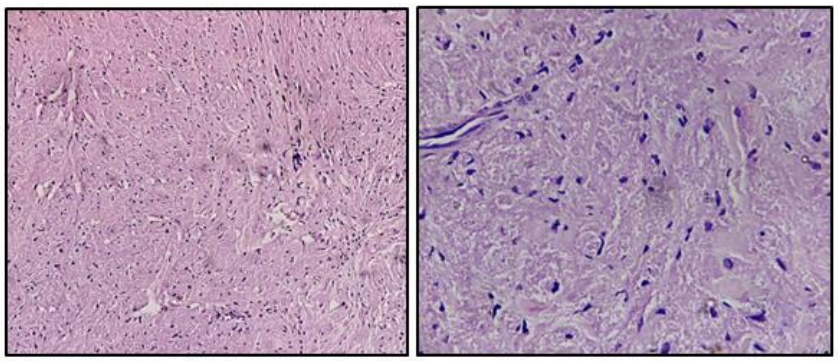

Figure 8

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Case 4

A 36 year old female patient came to Otorhinolarynogology Outdoor Patient Department (OPD) with complain of small painless nodule over dorsal surface of tongue. Size of the swelling was 1 x 1 cm and non-tender, firm in consistency.

Excisional biopsy was done and specimen was sent to histopathology laboratory.

Gross examination (Figure 9): Tissue received size measuring 1 x 0.8 cm, greyish white, firm. Whole tissue is passed for histopathological examination.

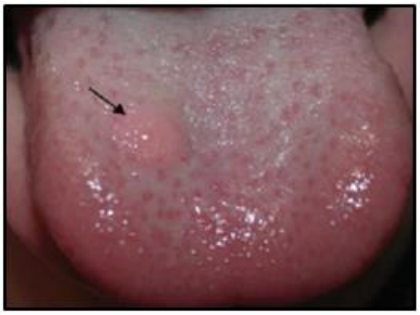

Figure 9

Microscopic examination (Figure 10): Tumour cells arranged in sheets and nests separated by collagenous band. Cells are round to slightly spindle shaped. Cells shows small, vesicular nuclei and abundant granular eosinophilic cytoplasm.

Overall findings are suggestive of **GRANULAR CELL TUMOUR**.

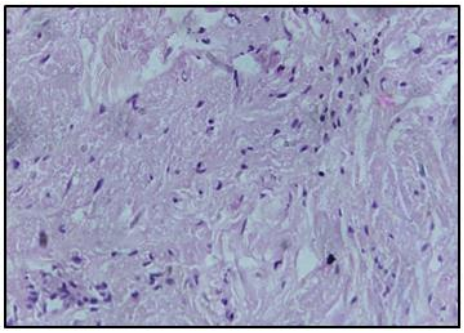

Figure 10

Case 5

A 42-year-old female patient came to Surgical Outdoor Patient Department (OPD) with complain of slow growing mass on back. Size of the swelling was 3 x 2 cm and swelling was non-mobile, non-tender and firm in consistency.

Excisional biopsy was done and specimen was sent to histopathology laboratory.

Gross examination (Figure 11): Well defined skin covered tissue received size measuring 2.5 x 1.6 cm. Cut surface was yellowish and firm in consistency.

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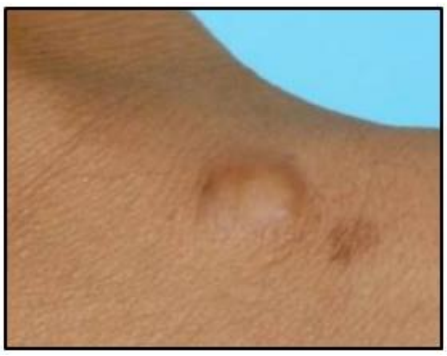

Figure 11

Microscopic examination (Figure 12): Studied sections show diffuse infiltration of the dermis with tumour nests. Cells shows small, round to oval nuclei and abundant granular eosinophilic cytoplasm.
Overall findings are suggestive of **GRANULAR CELL TUMOUR**.

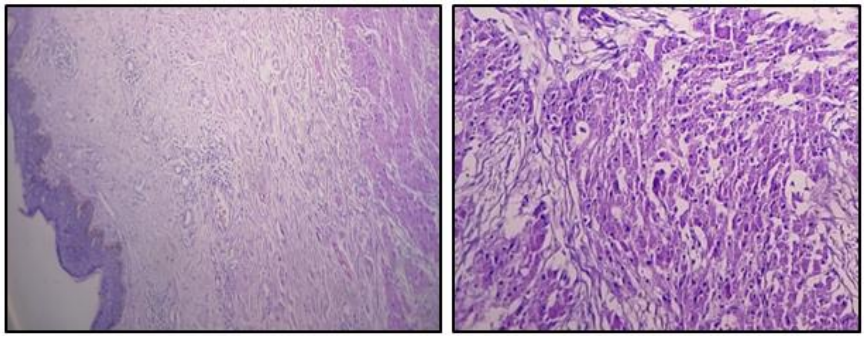

Figure 12

Discussion

Granular cell tumour was originally named granular cell myoblastoma, but currently, granular cell tumour is considered to be neural in origin according to immunohistochemical studies [9]. Granular cell tumour accounts for 0.5% of all soft-tissue tumors [10].
In the literature, there is a female preponderance, and usually, the reported cases occurred between the fourth and fifth decades [11].
These tumors mostly present as a painless mass in the subcutaneous tissue; however, they may rarely be multicentric at the time of diagnosis. Familial cases and cases of congenital granular cell tumour have been reported to be associated with multiple lesions [12].
The tumour can be localized on the skin or submucosa of various locations. In 30-45% of cases, granular cell tumour affects the skin, followed by the area of the head and neck, where the most common location is the tongue and oral cavity [13].
Granular cell tumour of the skin mostly presents with asymptomatic slow growing solitary nodule with overlying normal skin. Since the clinical presentation of cutaneous granular cell tumour does not have any specific features, it is not always considered in the differential diagnosis.
The diagnosis of granular cell tumour is mostly reached by a histopathological examination with immunohistochemical staining. Histopathologically, granular cell tumour is composed of large cells with an eosinophilic granular cytoplasm. This granular appearance is the result of secondary dense cytoplasmic lysosomes. These cells contain a large amount of dense cytoplasmic lysosomes which yield a granular image under the microscope. These granules are Periodic acid-Schiff positive and diastase resistant.

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In granular cell tumour, immunohistochemical stains are positive for S100, neuron-specific enolase, and vimentin, whereas tumoral cells are not stained with epithelial, melanocytic, muscle, endothelial, and glial cell markers. This staining pattern is also suggestive of a Schwann cell origin [12].

The clinical differential diagnosis of granular cell tumour in the subcutaneous tissue includes dermatofibroma (fibrous histiocytoma), lipoma, adnexal tumors, neurofibroma, and schwannoma, all of which could be differentiated by histopathological and immunohistochemical features [14].

Granular cell tumour mostly behaves in a benign fashion, but malignant transformation can be recognized in 1-2% of cases. The most common metastatic sites are regional lymph nodes, lungs, and bones. It is a challenge to predict the malignant behavior at the time of diagnosis. When the tumor size is >4 cm, the risk of malignancy is increased.

Fanburg-Smith criteria [15]:

Necrosis, tumour cell spindling, vesicular nuclei with large nucleoli, >2 mitosis/10 high power fields, high nuclear to cytoplasmic ratio and pleomorphism.

Grade 0: Benign

Grade 1-2: Atypical

Grade >= 3: Malignant

Nasser-Ahmed-Kowalski criteria [16]:

Necrosis and > 2 mitosis/10 high power fields

Grade 0: Benign

Grade >= 1: Granular cell tumour with uncertain malignant potential

Metastasis was the only criteria to diagnose malignant granular cell tumour.

The treatment of choice in granular cell tumour is a local wide excision with clear margins. Radiotherapy and chemotherapy have not shown to be effective in the clinical course of recurrent or malignant disease [10].

Conclusion

The outcomes of granular cell tumors depend in part on whether the lesions are malignant or benign. Benign tumors have excellent outcomes with wide local excision and rarely recur or metastasize.

We present a series of five cases of granular cell tumours in five patients. All tumours were benign. Females were more affected than males. Common age group affected was in third decade. Most common site affected in the present study was tongue, followed by one case each at supraclavicular region, over phalanx of finger and back.

Although oral neural neoplasms are uncommon, they should be included in the differential diagnoses for oral soft tissue lesions. Additionally, if diagnosed, the clinician should be mindful of the associated syndromes as this may play an important role in the early diagnosis, prognosis and improved long-term patient outcome. Significant variation exists in demographics, clinical appearance, and histologic findings with regards to these neoplasms therefore both clinicians and pathologists should be sentient in order to best refer and if required manage their patients.

Although granular cell tumours are usually benign and slow growing, it is difficult to distinguish them from malignant lesions. Therefore, it is very important that clinicians and pathologists are aware of their clinical and histopathological features [17].

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