Granular cell tumor of hand presenting as subcutaneous nodule mimicking dermal adnexal tumor: A diagnosis by cytology

Jitendra G. Nasit, Sanjaykumar Chauhan[1], Gauravi Dhruva

Department of Pathology, P. D. U. Government Medical College and Hospital, Rajkot, [1]Department of Pathology, GMERS Medical College-Gotri, Vadodara, Gujarat, India

ABSTRACT

Granular cell tumor (GCT) is an uncommon tumor and is believed to be of schwannian origin. GCT is benign but rare malignant cases are recorded. GCT occurs in almost any part of the body. The common sites are the tongue, skin, and subcutaneous tissue. GCT of hand is an extremely rare. Till date only 17 cases are reported in the literature. Preoperative diagnosis of GCT is important, because GCT mimics dermal adnexal tumor in subcutaneous tissue, other soft tissue tumor or inflammatory lesions. GCT is composed of large polygonal cells with eosinophilic granular cytoplasm and these cells are often immunoreactive for the S-100 protein. Fine-needle aspiration cytology has been suggested to be diagnostic modality of choice and this would undoubtedly aid the correct diagnosis. Excision with wide surgical margins is curative for benign GCT. Recurrence and malignant transformation requires regular follow-up. Here, this communication documents a case of cytological diagnosis of the granular cell tumor of hand in a 21-year-old female, clinically suspected to be a dermal adnexal tumor.

Key words: Fine-needle aspiration cytology, granular cell tumor, hand, histology, immunohistochemistry

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Address for correspondence:
Dr. Jitendra G. Nasit, C/4, Suryadeep Society, Near Nutan School, Behiend Chankyapuri society, New Sama Road, Vadodara, Gujarat, India.
E-mail: eagleeyenasit@gmail.com

INTRODUCTION

A granular cell tumor (GCT) is an uncommon tumor with an incidence of 0.017-0.029% in general surgical specimen.[1-4] It was first described in 1926 as granular cell myoblastoma by Abrikossoff.[4-8] Though the most common site of involvement is the tongue, it can occur anywhere in the body.[3-5,9] A GCT usually presents as a small solitary painless firm nodule affecting the middle-aged people.[3-5,6,8,10,11] The GCT of hand is exceedingly rare with only 17 cases bieng reported in the literature till date.[1-3,5,9-15] A GCT usually has a distinctive cytological appearance.[4,6-8] Here, a rare benign GCT of hand is diagnosed by fine-needle aspiration cytology (FNAC). The aim of presenting this case is to emphasize the importance of cytology in identifying this rare neoplasm in an uncommon cutaneous area of hand which closely simulates the dermal adnexal tumor. FNAC also helps to rule out other mimickers of GCT.[4,6,7] A GCT generally follows a benign clinical course; however recurrence and malignant transformation are rarely reported.[3,6,5,9,11,12]

CASE REPORT

A 21-year-old female presented with a slow growing, dome-shaped, painless nodule on left index finger for 15 months. She had no history of pain or fever. She had a history of thorn injury at this site before 2 years. Clinically, a single, soft-to-firm, slightly mobile, nontender swelling was noted without significant changes of the surface of the skin. Swelling measured 2.0 × 2.3 cm in size [Figure 1]. No other masses were found. Clinical diagnosis of the primary dermal adnexal tumor was considered and FNAC was requested. Plain radiographs showed no bony lesion. Laboratory evaluations were unremarkable.

The tumor was sampled by a 22 G needle. The smears were prepared, fixed immediately in 95% ethanol and air dried. Smears were stained with Hematoxylin-eosin (H and E) and May-Grunwald-Giemsa (MGG) stain. Smears were highly cellular, composed of syncytial clusters and many scattered single tumor cells. The cells were fairly uniform, round to polygonal with

abundant, finely granular cytoplasm, eccentric round to slightly oval nuclei, evenly distributed chromatin, and occasional small nucleoli. Cytoplasmic borders were poorly defined. The cells were fragile, with many stripped nuclei in a background of finely granular material. Nuclear atypia, mitosis, and necrosis were not observed [Figure 2]. A cytologic diagnosis of benign GCT was made and excision was advised.

At surgery, the tumor was located in the dermis and subcutaneous area without continuity with any structures. The tumor was completely excised with wide margins. The tumor was ill-defined, firm with a homogenous gray white cut surface. The tumor measured 1.9 × 2.0 cm in size. Histopathological examination revealed sheets of tumor cells. Tumor cells were large, round to polygonal with ill-defined borders. The cells had abundant granular eosinophilic cytoplasm, round to oval centrally or eccentrically located nuclei with mild variation in size, and occasional small nucleoli. Few larger, brightly eosinophilic ovoid bodies surrounded by a clear halo were identified. Mitoses and necrosis were not evident. On immunohistochemistry, the tumor cells show strong cytoplasmic reaction for the S-100 protein. Tumor cells were also positive for neuron-specific enolase and vimentin. CD68 was negative in tumor cells [Figure 3]. The cells were negative for cytokeratin, desmin, alpha smooth muscle actin, and HMB-45. The diagnosis of benign GCT was confirmed. Postoperatively the hand incision healed uneventfully, and the patient is well after 15 months without recurrence.

DISCUSSION

The granular cell tumor (GCT) of hand is very rare. The incidence of the GCT of hand is less than 0.1%.[11] The origin of GCT is an ongoing debate and includes muscle, fibroblast, histiocyte, neural crest, and nerve sheath.[4,6,8,11]

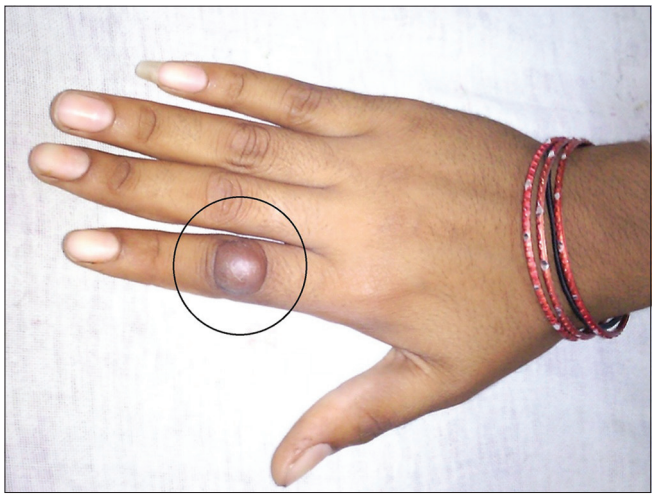

Figure 1: A single, dome-shaped, swelling is seen at the left index figure without significant changes of the overlying skin. Tumor nodule measures 2.0 × 2.3 cm in size

The cell of origin is now accepted to be the schwann cell due to strong S-100 protein expression on immunohistochemistry and granular cells contains lysosomal vacuoles with myelin figures, prominent basal lamina, and intracytoplasmic filaments ultrastructurally.[1,4,6-8,11]

GCT may occur at any age, but common in the third to fifth decade of life.[6,8,10,11] Two-third of cases are reported in women and in black population.[3,4] The common sites are the tongue, skin, and subcutaneous tissue. It can also been found in the soft tissue, nerve, breast, scalp, abdominal wall, head and neck, back, extremities, lymphnode, mediastinum, soft palate, orbit, salivary glands, respiratory tract, vulva, gastrointestinal tract, brain.[1-9,11,13] GCT commonly presents as an asymptomatic slow growing, solitary, painless nodule that may have either smooth or hyperkeratotic overlying skin.[3-6] The lesions are usually less than 3.0 cm in size and may undergo partial regression.[4,5] Multiple GCTs have only been reported in less than 10% of cases, especially in children and teenagers.[16] Multiple GCTs are reported in association with neurofibromatosis, Watson's syndrome, Lentiginosis profusa, Noonan syndrome, facial and ocular alterations, cardiovascular abnormalities, muscle and bones malformations, and neurologic deficits.[16] Clinically this may give an impression of malignancy; however a careful

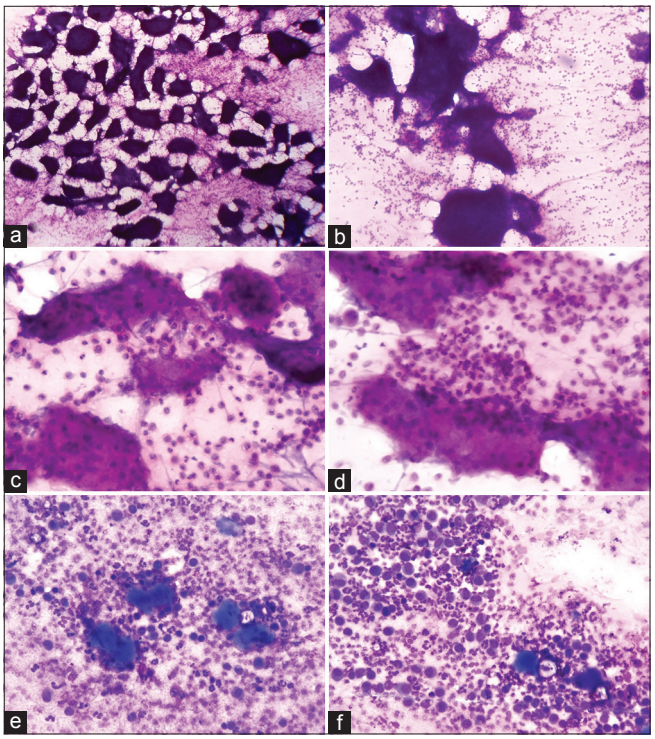

Figure 2: (a and b) Scanner and low-power view showing highly cellular smear composed of syncytial clusters and many scattered cells (H and E stain); (c and d) syncytial cluster showing round to polygonal cells with abundant, finely granular cytoplasm with an ill-defined border, eccentric round to oval nuclei, evenly distributed chromatin and occasional small conspicuous nucleoli. Many fragile cells with stripped nuclei are evident in the background of finely granular material (H and E, ×40); (e and f) MGG stain highlights the dispersed as well as clusters of tumor cells in finely granular material (H and E, ×40)

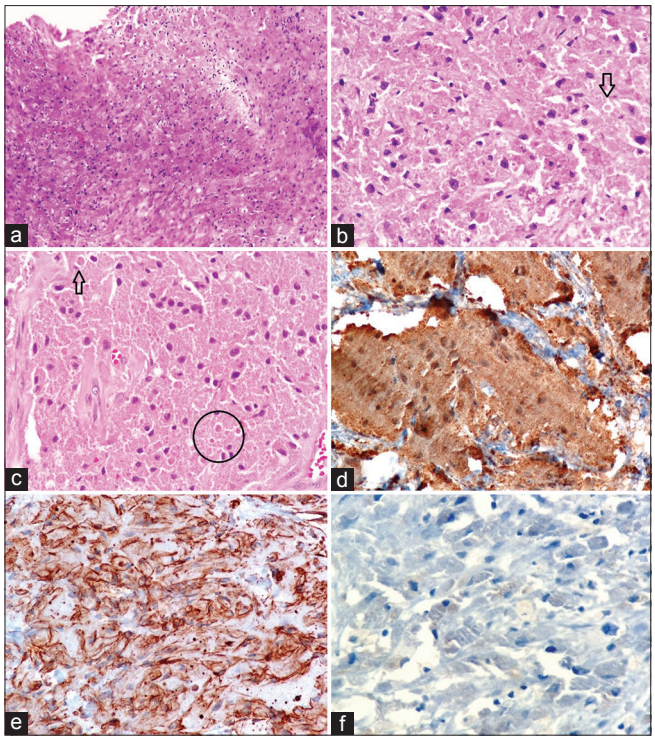

Figure 3: (a) A tumor composed of sheets of large, round to polygonal cells with ill-defined cytoplasmic borders (H and E, × 10); (b and c) the tumor cells have abundant granular eosinophilic cytoplasm, round to oval centrally or eccentrically located nuclei with occasional small nucleoli. Eosinophilic ovoid bodies are surrounded by a clear halo (arrow and circle) (H and E, ×40). On immunohistochemistry, (d) the tumor cells show strong cytoplasmic positivity for the S-100 protein (H and E, ×40); (e) the tumor cells show positivity for vimentin (H and E, ×40); (f) the tumor cells are negative for CD68 (H and E, ×40)

microscopic evaluation with attention to size of the lesion should resolve the question.[4] Very rarely, multifocal GCTs are reported in association with malignancy. Squamous carcinoma of the esophagus, adenocarcinoma of the prostate, and small cell lung cancer are among the reported cases of this association.[4,16] The common preoperative clinical diagnoses of GCT are dermatofibroma, fibromatosis, keloid or lipoma.[4,6]

GCT is sharply circumscribed to an ill-defined mass with hard consistency and yellowish cut surface.[7,8] Microscopic features of benign GCT are remarkably uniform regardless of the site.[6] Few reports describe the cytologic features of GCT.[4,6-8] The GCT of hand is probably not diagnosed by cytology in all previously described 17 cases.[1-3,5,9-15] The cytological findings of GCT in our case are identical to those described by previous authors.[4,6-8] A granular cell is large, round to polygonal with abundant eosinophilic, finely granular cytoplasm with indistinct cell borders, eccentrically located oval to round nuclei with fine nuclear chromatin, and occasional small or inconspicuous nucleoli. Pustulo-ovoid bodies of Milian are larger granules surrounded by a clear halo. They appear to represent the heterogeneity of the lysosomes, giving the appearance of large granules that have partially detached from the adjacent cytoplasm. The granularity of the cytoplasm is caused by a massive accumulation of lysosomes which gives positive reaction to CD68 and periodic acid--Schiff stain.[3,4,6-8,11] However, CD68 reaction is negative in our case. Cytologic atypia may occur, but mitoses are rare. Liu *et al.* cautioned that occasional nuclear polymorphisms and prominent nucleoli were compatible with benignancy.[6,8] In the present case, the tumor cells were positive for S-100 protein and NSE, which supports the schwann cell differentiation.[4] Vimentin is usually expressed in GCTs.[4] The GCT is associated with downward proliferation of adjacent squamous epithelium which mimics squamous cell carcinoma.[11] Most GCTs are benign.[7,5,9,11] Malignant GCTs comprise fewer than 2% of all GCTs. Malignant GCTs are usually large and deep seated.[4,6] Fanburg-Smith *et al.* classified atypical, malignant, and benign granular cell tumors on the basis of six histologic criteria: Necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 high power fields at ×200 magnification), high nuclear to cytoplasmic ratio, and pleomorphism. Neoplasms that met three or more of these criteria were classified as histologically malignant, those that met one or two criteria were classified as atypical, and those that displayed only focal pleomorphism, but fulfilled none of the other criteria, were classified as benign.[4]

In our case reactive granular cell histiocytic reaction closely mimics GCT as the patient has past history of thorn injury.[8] The granular cells in reactive lesions tend to be associated with inflammatory elements and areas of necrosis which are not seen in our case. The inflammatory cells mimicking granular cells are macrophages, foam cells, fat necrosis, and numerous histiocytes.[4,6-8] Macrophages show ingested debris with ill-defined cytoplasmic border, eccentrically located irregular to reniform in shaped nucleus with small nucleolus.[4] Foam cells of xanthoma are large pale cells with foamy cytoplasm and take up fat stains.[4] The differential diagnosis of GCT include rhabdonyoma, rhabdomyosarcoma, alveolar soft part sarcoma, hibernoma, fibroxanthoma, fibrous histiocytoma, dermatofibroma, dermatofibrosarcoma protuberans, schwannoma, neurofibroma, paraganglioma, oncocytic neoplasms, leiomyosarcoma, melanoma, and metastatic renal cell carcinoma.[3,6-8] Rhabdomyosarcoma reveals characteristic rhabdomyoblasts with positivity for muscle markers such as desmin and myogenin, whereas the granular cell tumor shows positivity for the S-100 protein.[7,8] Alveolar soft part sarcoma shows marked nuclear pleomorphism and prominent nucleoli, with an alveolar arrangement. Unlike hibernoma, the cells of the granular cell tumor do not have vacuolated cytoplasm.[8] Clinically, paraganglioma does not occur as a primary soft tissue tumor in the extremities. Paraganglioma shows moderate nuclear pleomorphism, occasionally follicle-like pattern with positivity for chromogranin and synaptophysin.[8] Epithelioid sarcoma displays vesicular nuclei with large nucleoli in the background of necrosis and inflammatory cells. Epithelioid sarcoma shows positivity for epithelial markers such as

cytokeratins and EMA.[8] Metastatic renal cell carcinoma is negative for the S-100 protein.[8]

Surgical excision with safe margins is recommended due to ill-defined margins and risk of recurrence.[2-4,6,8] This emphasizes the need of recognizing this lesion on FNAC, so that an adequate curative resection may be planned. Further follow-up is necessary due to the possibility of recurrence and malignant transformation.[3,4,5,12] The malignant variant is aggressive and metastasized to bones, lungs, liver, and regional lymphnodes.[4] Wide *en bloc* excision is recommended for malignant lesions.[3,9,12,13] Chemotherapy, alone or in association with radiotherapy, is not given unless the tumor is malignant.[3]

CONCLUSION

The GCT of hand is rare. It can be diagnosed by a simple FNAC procedure as cytopathology features of GCT are distinctive enough to allow a correct diagnosis even at an unusual site like index finger. Preoperative cytologic diagnosis helps to avoid confusion with other tumors of dermal adnexal origin, soft tissues origin, and other inflammatory mimickers. Complete resection with disease free margins is usually curative for benign GCT. Follow-up is required due to recurrence and malignant transformation .

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