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Imprint Cytology of Granular Cell Tumor
-A Case Report-

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Granular cell tumor is a rare tumor of the soft tissue and this is characterized by proliferation of large cells with granular appearing eosinophilic cytoplasm. We report the imprint cytologic features of a case of granular cell tumor in the left calf of a 52-year-old woman. Microscopic examination showed moderate cellularity. The tumor cells were arranged both as single cells and in clusters. The cells were large polygonal-shaped and they had small round nuclei with finely granular chromatin and occasionally conspicuous nucleoli. The cytoplasm was abundant eosinophilic and granular. Naked nuclei and spindle-shaped tumor cells were occasionally noted. No mitosis and necrosis were present. The background showed cytoplasmic granular materials. The tumor cells showed positivity for S-100 protein. Ultrastructurally, abundant lysosomes were present in the cytoplasm of the tumor cells.

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Key Words: Granular cell tumor, Soft tissue, Cytology, Imprint

INTRODUCTION

Granular cell tumor is a rare tumor of the soft tissue, and this tumor was first described in 1926 by Abrikossoff.[1] It affects in all age groups, but it is most common in middle-aged people. It mainly occurs the skin and subcutaneous tissue, particularly that of the head, neck, trunk, and extremities. However, visceral involvement can also occur.[2] Granular cell tumor is composed of large polygonal cells with eosinophilic granular cytoplasm and these cells often are positive for periodic acid-Schiff (PAS), immunoreactive for S-100 protein; ultrastructurally, they contain large numbers of secondary lysosomes.[3] Although the cytologic features have been described in several reports,[4-7] the cytologic diagnosis of granular cell tumor may be difficult due to the overlapping cytomorphology with other tumors. We describe here the imprint cytologic features of a case of granular cell tumor that arose in the left calf of a 52-year-old woman.

CASE

A 52-year-old woman presented with a mass in her left calf for three years. On physical examination, an irregularly marginated, hard mass was palpated in the left calf. The mass was slowly growing. Plain radiographs showed no bony lesion. Magnetic resonance images demonstrated a tumor located in the medial aspect of the posterior compartment of the left calf. The tumor showed signal isointense to muscle on the T1-weighted images and there was a peripherally increased signal and a central intermediate signal on the T2-weighted images. The axial fat-saturated T1-weighted contrast enhanced images showed high signal intensity (Fig. 1). The wide excision of the mass was done. The imprint cytologic smears were obtained.

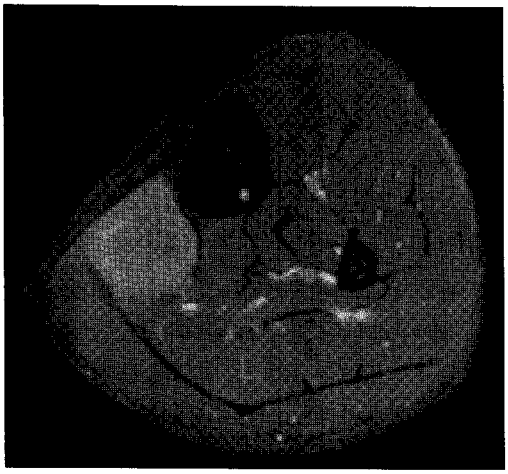

Fig. 1. Magnetic resonance imaging. The tumor shows high signal intensity on axial fat-saturated T1-weighted contrast enhanced image.

Cytologic Findings

The alcohol-fixed smears were stained with Hematoxylin-eosin and with the Papanicolaou method. The smears were moderately cellular. The tumor cells were arranged in loose clusters or single cells (Fig. 2A). The background showed cytoplasmic granular materials and occasionally red blood cells and lymphocytes. The tumor cells were large in size and polygonal shaped (Fig. 2B). The tumor cells had relatively uniform small round nuclei, with finely granular chromatin. The nuclei were eccentrically located. The nuclear/cytoplasmic ratio was low. The tumor cells had abundant amounts of granular eosinophilic cytoplasm in hematoxylin-eosin stain. The cell borders were indistinct. The tumor cells had vesicular nuclei with conspicuous nucleoli. Some of the tumor cells were arranged in vaguely microfollicular pattern. Naked nuclei were also noted and spindle-shaped tumor cells were occasionally found (Fig. 2C). Neither mitosis or necrosis were seen. Immunohistochemical staining for S-100 protein was performed on the smears. Tumor cells revealed positivity for S-100 protein (Fig. 2D).

Gross and Histologic Findings

The tumor measured 5.0 × 3.0 × 3.0 cm for its dimensions. The cut surface of the tumor was grayish yellow and rubbery, with an ill-defined margin (Fig. 3). Histologic examination showed sheets or nests of granular tumor cells (Fig. 4). The tumor cells had round nuclei with abundant granular cytoplasm. The cytoplasmic granules were PAS positive and diastase resistant. No tumor necrosis was found. On the immunohistochemical staining of the tissue sections, the tumor cells were positive for S-100 protein and neuron specific enolase, and they were negative for smooth muscle actin, desmin and cytokeratin (AE1/AE3). Electron microscopic examination was performed. The tumor cells showed abundant lysosomes (Fig. 5). The resection margin was free from tumor. Ten months after surgery, the patient has remained alive and well, with no evidence of recurrence or metastasis.

DISCUSSION

Granular cell tumor is a rare tumor of soft tissue and this tumor is composed of nests of large cells with granular, eosinophilic cytoplasm. There is a mild female

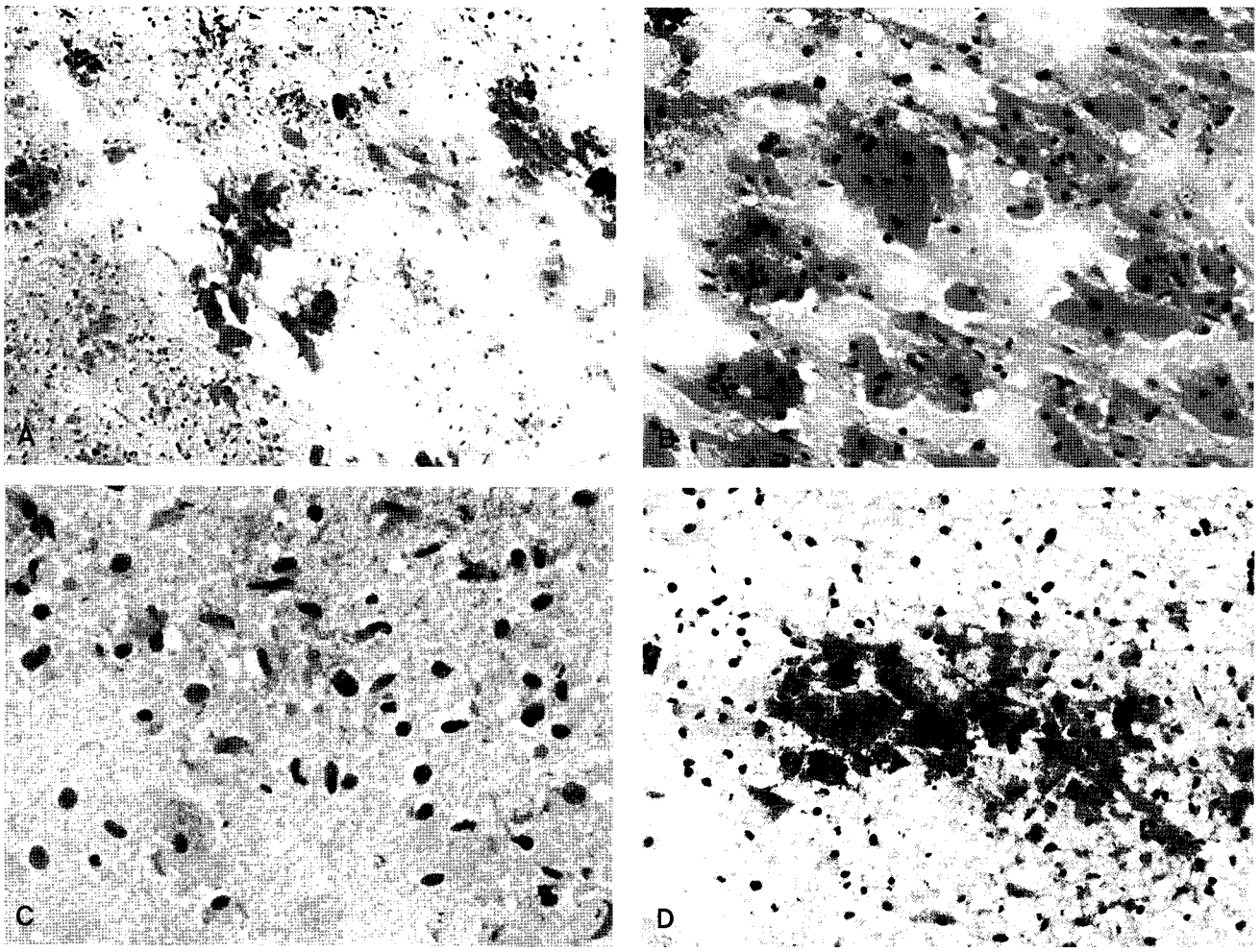

Fig. 2. Cytologic finding. (A) Tumor cells are arranged in loose clusters and single cells. (H&E). (B) Tumor cells are large polygonal shaped and have small round nuclei with abundant granular cytoplasm and indistinct cell membrane. (H&E). (C) Naked nuclei and spindle-shaped tumor cells are present. The background shows cytoplasmic granular materials. (Papanicolaou). (D) Tumor cells reveal cytoplasmic staining for S-100 protein. (Immuohistochemical stain).

predominance. The tumor usually present in superficial soft tissues and less commonly in the respiratory and gastrointestinal tract. Grossly, the tumor varies from sharply circumscribed to an ill-defined mass, typically with a yellow cut surface. The cytologic findings of granular cell tumor show polygonal cells with abundant granular cytoplasm and indistinct cell borders.[4-7] The nuclei are usually small and round with finely dispersed chromatin. Cytologic atypia may occur, but mitoses are rare. The cytologic features of the present case are similar to those of the previously reported cases. Naked nuclei were present in our case. It is probably the result of fragility of the cell cytoplasm.

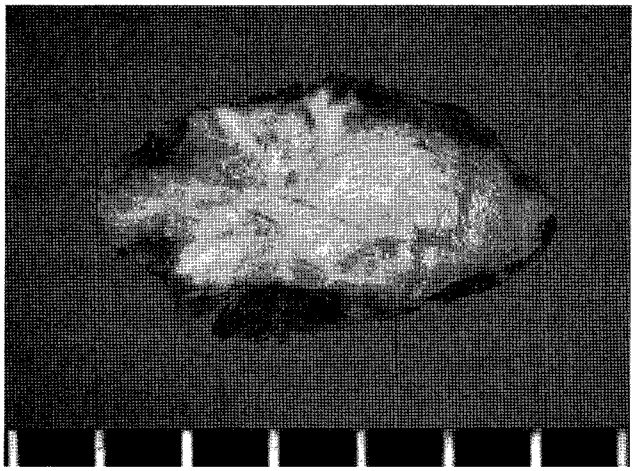

Fig. 3. Gross finding. Tumor shows a yellowish gray solid cut surface with an ill-defined margin.

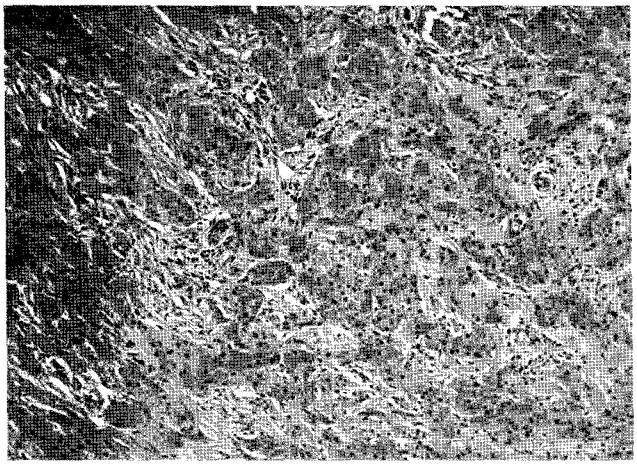

Fig. 4. Histologic finding. Histologic section of the tumor shows sheets of polygonal cells with small round nuclei, abundant granular cytoplasm and indistinct cell membrane. (H&E).

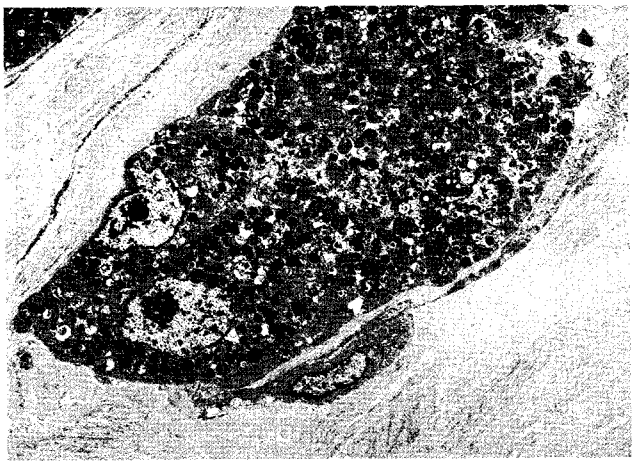

Fig. 5. Electron microscopic finding. Tumor cells show abundant lysosomes. (magnification x1,500).

The histogenesis of granular cell tumor is a matter of ongoing debate and the derivation from Schwann cells, myofibroblasts and macrophages has been postulated.8 The Schwann cell derivation is more favored on the basis of the immunohistochemical and electron microscopic findings.[9,10] The tumor cells are positive for S-100 protein and neuron specific enolase and negative for muscle cell markers and epithelial markers. In the present case, the tumor cells were positive for S-100 protein, which supports the Schwann cell differentiation. The granularity of the cytoplasm is caused by a massive accumulation of lysosomes. The present case showed abundant lysosomes in the cytoplasm.

Granular cell tumor should be differentiated on the cytologic smears from the other polygonal cell tumors such as smooth muscle tumors, hibernoma, paraganglioma, malignant granular cell tumor, epithelioid sarcoma, rhabdomyosarcoma, alveolar soft part sarcoma, and metastatic renal cell carcinoma.[11,12] Smooth muscle tumors may have a granular cell appearance. Smooth muscle tumors show as blunted-ended, cigar-shaped nuclei and eosinophilic fibrillary cytoplasm. The immunohistochemical demonstration of the smooth muscle phenotype can establish the diagnosis since granular cell tumor does not express muscle markers. Unlike hibernoma, the cells of granular cell tumor do not have vacuolated cytoplasm.[3] Paraganglioma may resemble granular cell tumor. However, paraganglioma shows moderate nuclear pleomorphism and occasionally a gland-like or follicle-like pattern. Paraganglioma is positive for chromogranin and synaptophysin. Clinically, paraganglioma does not occur as a primary soft tissue rumor in the extremities. Compared with granular cell tumor, malignant granular cell tumor shows hyperchromasia, pleomorphism, a spindle cell morphology, a necrotic background and mitoses.[13] 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. Rhabdomyosarcoma reveals hyperchromatic and pleomorphic nuclei and characteristic rhabdomyoblasts. Rhabdomyosarcoma shows positivity for muscle markers such as desmin and myogenin, whereas granular cell tumor shows positivity for S-100 protein and neuron specific enolase. Alveolar soft part sarcoma shows marked nuclear pleomorphism and prominent nucleoli, with an alveolar arrangement. Metastatic clear cell renal cell carcinoma may mimic granular cell tumor. However, metastatic clear cell renal cell carcinoma is negative for S-100 protein. Finally, reactive granular cell histiocytic reaction that complicates previous trauma

may simulate granular cell tumor.[14] The granular cells in the reactive lesions tend to be associated with inflammatory elements and areas of necrosis.

Most granular cell tumors are benign. Because of the potential for local recurrence, complete excision is recommended.[2] In the present case, the patient has remained alive ten months after surgery, with no evidence of recurrence or metastasis.

In conclusion, granular cell tumor should be considered in the differential diagnosis when the cytologic findings include large polygonal cells with abundant granular cytoplasm. A combination of the characteristic cytomorphology and the use of ancillary techniques such as immunohistochemistry and electron microscopy are important for establishing a correct diagnosis of granular cell tumor.

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