Case Report

Recurrent metastatic malignant granular cell tumor of the back presenting with axillary mass: A rare case report and review of the literature

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Abstract

Malignant granular cell tumor (MGCT) is a rare aggressive tumor that comprises 0.5%–2% of all granular cell tumors. They most commonly occur on lower extremity, nuchal region, chest wall, gastrointestinal tract, and head and neck. We report fine needle aspiration and histopathological findings of a rare case of recurrent MGCT presenting with axillary mass along with a tumor on the right back in a 56-year-old female. Tumor cells with abundant granular eosinophilic cytoplasm showing pleomorphism, enlarged vesicular nuclei, prominent nucleoli, 4–5 mitotic figures/10 high-power field, periodic acid–Schiff-positive diastase-resistant cytoplasmic granules, and metastasis in the axillary lymph node were also suggestive of MGCT. Immunohistochemically, the tumor cells were positive for S-100 confirming the diagnosis.

Keywords: Fine needle aspiration cytology, granular cell tumor, malignant

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INTRODUCTION

The malignant granular cell tumors (MGCTs) are extremely rare, representing less than 0.5%–2% of all GCTs.[1] Both benign GCT and MGCT have been found in a wide variety of locations, including lung, heart, pelvis, bladder, vulva, abdominal wall, and esophagus.[2-10,11] They occur most commonly on lower extremities. The diagnostic histological criteria have been proposed by Fanburg-Smith *et al.*[12] although these criteria for malignancy are still debated among pathologists. We present cytological and histopathological findings of a rare case of MGCT presenting as recurrent axillary mass in a 56-year-old female.

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CASE REPORT

The patient noted the swelling for the first time in the right axillary region, 3 years back. Excision of the swelling was done, but the patient did not follow up and did not collect the report. The swelling recurred in the right axillary region after 3 years along with a mass below the inferior angle of the right scapula. The right axillary mass was of size 3 × cm 2 × cm 1 cm, nontender, firm, mobile. A similar nontender, firm mass of size 1 cm × 1 cm was also noted below the right inferior angle of the scapula. Computed tomography of the thorax and abdomen with contrast showed enhancing enlarged nodes in the right axilla measuring 4 cm × 1.8 cm

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with few small subcentimeter-sized nodules in both lung fields. Positron emission tomography scan revealed a primary tumor in the right inferior scapular region with metastasis in the axillary lymph nodes and bilateral lungs. Fine needle aspiration (FNA) of the axillary mass revealed clusters of tumor cells revealing pleomorphism, enlarged, irregular nuclei with fine nuclear chromatin, variably prominent nucleoli, and abundant granular basophilic cytoplasm in a lymphoid background [Figure 1]. These cytological findings were suggestive of metastatic deposits from an MGCT. Right axillary mass as well as mass over the right side of upper back was excised and sent to us for histopathological examination.

On microscopic examination of the axillary mass, there were nests and sheets of tumor cells diffusely relaxing the lymph node parenchyma with focal residual lymphoid follicles. Similar tumor was found in scapular mass also. The tumor cells in both sites were revealing large polyhedral to spindled tumor cells with moderate pleomorphism, irregular vesicular nuclei, prominent one to multiple nucleoli, occasional intranuclear cytoplasmic inclusions, and moderate-to-abundant granular eosinophilic cytoplasm and 4–5 mitotic figures/10 high-power field (HPF) [Figure 2]. Periodic acid–Schiff (PAS) stain with diastase revealed PAS-positive diastase-resistant granules in the cytoplasm of tumor cells [Figure 3]. Immunohistochemistry (IHC) revealed S-100 positivity in the tumor cells [Figure 4]. The case was diagnosed as MGCT of the back with metastatic deposits in the axillary lymph nodes.

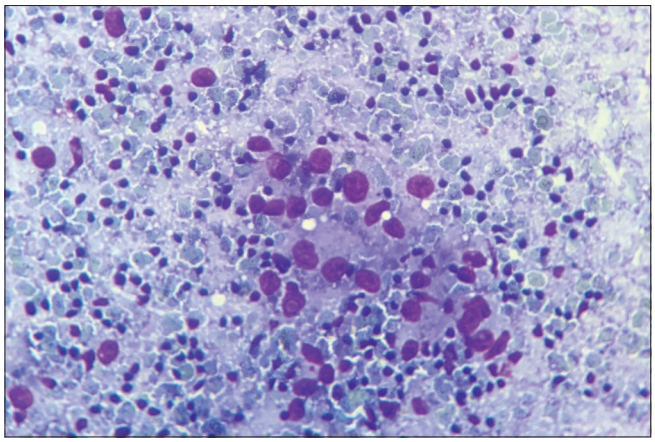

Figure 1: Fine needle aspiration smears of axillary mass revealing clusters of pleomorphic tumor cells with abundant granular basophilic cytoplasm (Giemsa, ×400)

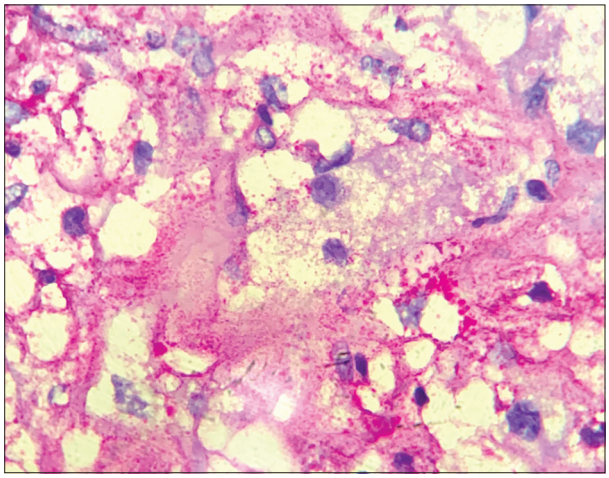

Figure 3: Tumor cells showing periodic acid–Schiff-positive diastase-resistant granules in the cytoplasm (PAS, ×400)

DISCUSSION

MGCTs are extremely rare neural tumor which was first reported by Ravich *et al*. in 1945. Since then, less than 100 cases have been reported so far. Among the reported cases, they are most commonly seen in lower extremities, nuchal region, chest wall, gastrointestinal tract, and head and neck. However, isolated cases have been reported in

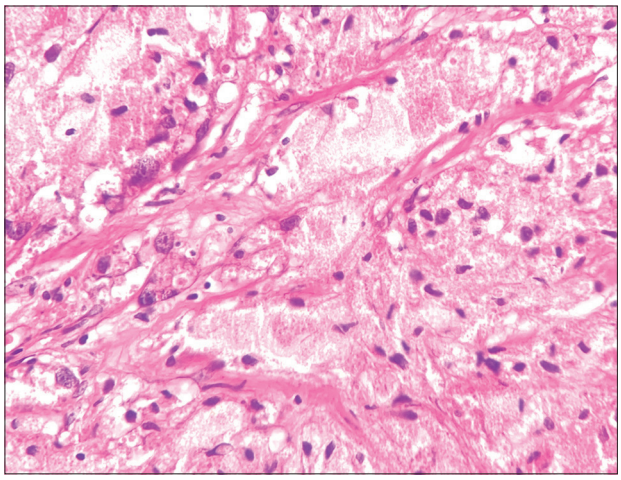

Figure 2: Sheets of pleomorphic tumor cells with abundant granular eosinophilic cytoplasm (H and E, ×400)

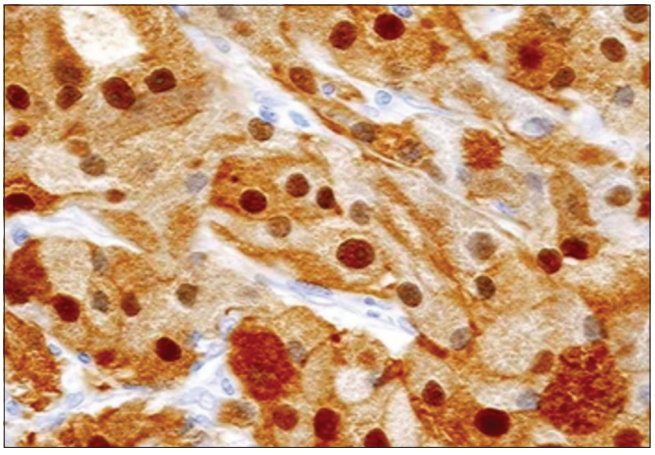

Figure 4: Tumor cells showing positivity for S-100 (IHC, ×400)

various sites, including lung, heart, pelvis, bladder, vulva, abdominal wall, and esophagus.[2-10]

The origin of GCTs is uncertain. Initially, it was thought that they arise from skeletal muscle, fibroblastic, histiocytic, or undifferentiated mesenchymal cell origin. More recently, based on the evidence that monoclonal antibody KP-1, which recognizes the lysosome-associated glycoprotein, CD68, reacts positively with schwannomas and GCTs, it is believed that these tumors arise from Schwann's cells. Furthermore, GCTs cytoplasmically stain for S-100 protein are closely associated with nerves and are often present in distal nerve trunks. All these features support Schwann's cell origin.

MGCT differs from benign counterpart by longer clinical duration with sudden rapid growth and larger size on presentation (median size of 4–5.0 cm, as compared to benign tumors, which in most cases are <3 cm) with frequent history of local recurrence. These tumors more commonly occur in lower limbs, unlike benign GCTs, which commonly occur in the head, neck, and tongue. MGCT-like benign tumors show female predominance (70%), with presentation usually in the fifth decade of life.

Most cases present as a large mass varying in size from 4 to 20 cm, slightly fleshy, firm, yellowish to tan brownish in color with foci of hemorrhage and degeneration. Microscopically, tumor shows sheets of polygonal cells with round hyperchromatic nuclei and abundant PAS-positive diastase-resistant granules in the cytoplasm. The tumor cells display features of malignancy.

Histological criteria of malignancy were first proposed by Fanburg-Smith *et al*.[12] They proposed six histologic criteria for the diagnosis of atypical GCTs and MGCTs, including necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 HPF at ×200), 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.

Nasser–Ahmed–Kowalski[13] criteria refined the above criteria and proposed that necrosis and >2 mitoses/10 HPF are the most important criteria and score 0 indicates benign granular tumor and score ≥1 indicates GCT of uncertain malignant potential. They proposed that metastasis is the only criterion to diagnose MGCT. Our case showed spindling, pleomorphism, high nuclear-to-cytoplasmic ratio, vesicular nuclei with large nucleoli, 4–5 mitotic figures/10 HPF including atypical mitotic figures, as well as metastatic deposits in the axillary lymph nodes. Thus, our case meets all the criteria to be classified as MGCT.

Diagnosis and prognostication from preoperative FNA cytology are hampered by the fact that only a few case reports on cytological features of MGCT have been published.[14] The FNA of metastatic GCT may lack cytological features of malignancy. The diagnosis necessitates clinical correlation and an understanding of the spectrum of histopathological changes in GCT and MGCT.

IHC tumor cells are positive for S-100, Ki-67, and p53 and negative for ER, PR, Her2neu, GCDFP, and PanCK. Electron micrograph shows intracytoplasmic, dense, membrane-bound lysosomes typical of GCT. Features are not helpful in distinguishing between benign and malignant lesions.

Wide local excision with regional lymph node dissection remains the main modality of treatment. However, the role of systemic chemotherapy is still debated. Ordóñez[15] reviewed 41 cases of MGCT in the literature, most of which were treated with wide local excision and found a 59% recurrence rate.[15] It is advisable to follow up these patients annually to rule out late recurrences. Radiation and chemotherapy are not advised because of the tumor's high degree of resistance.[16] Tumors typically spread via lymphatic and hematogenous routes to the lungs, liver, lymph nodes, and bones. Prognosis is poor in patients with MGCT, with frequent metastasis (>50% overall) and 30%–50% mortality over 3 years in two case series.[17]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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