Granular cell tumor of the breast

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Introduction

In 1906, granular cell tumor (GCT) was first described by Abrikosoff as a granular cell myohistoma that originated from striated muscle cells in the tongue. Subsequent immunohistochemical and ultrastructural studies, however, have elucidated that these tumors are most likely derived from Schwann cells of peripheral nerves. GCTs occur frequently in the head and neck area such as the oral cavity, but, these tumors are able to develop throughout the body including the skin, soft tissue, and gastrointestinal and respiratory tracts.

GCT of the breast is usually a benign tumor and constitutes approximately 5–8% of all GCT cases, however, it is often diagnosed as a malignant breast tumor clinically or radiologically. We experienced a case of GCT diagnosed using core needle biopsy and immunohistochemistry (IHC) in a patient with a right orbital inflammatory pseudotumor and hyperthyroidism.

Case Report

A 54-year-old woman presented with a nonpalpable lump in her right breast found by screening mammography. She had a history of benign breast tumor excision in the right upper central quadrant 30 years ago, and was taking antihypertensive and antipsclerotic medications for transient ischemic attack. Eight months ago, she complained of right exophthalmos and diplopia. Postcontrast T1-weighted MRI with fat suppression showed increased thickness of the right superior rectus muscle with contrast enhancement (Fig. 1A). She was on prednisolone therapy for a right orbital inflammatory pseudotumor. She did not manifest thyroid goiter. Thyroid function tests revealed a T3 level of 137.86 ng/dL (normal, 60–200 ng/dL), free T4 of 1.10 ng/dL (normal, 0.73–1.85 ng/dL), TSH of 0.71 mU/L (normal, 0.4–3.1 mU/L), and TBI of 14.55% (positive reference, ≥10%).

According to a thyroid uptake scan using 123I–99m pertechnetate, the size of the thyroid gland was within normal limits and uniform distribution of the nodotracers without focal lesions was noted. The values for thyroid...
uptake were calculated to be 5.88% at 2 hours and 12.74% at 24 hours. After a follow-up period of 6 months, thyroid function tests revealed a T3 level of 161.70 ng/dL, free T4 of 1.78 ng/dL, TSH of 0.08 μU/mL, and TSH of 27.78%. She was taking methimazole for Graves’ disease since then.

Physical examination showed a previous operative scar in the upper central quadrant of the right breast and there was no skin change, palpable mass, or tenderness. Mammography revealed a 2-cm dense mass with ill-defined borders in the right upper inner quadrant and no microcalcifications or skin changes were noted (Fig. 1B). Ultrasound examination demonstrated a 13-mm hypoechoic lump with an irregular border, heterogeneous interior, and posterior shadowing at the 10 o’clock position, at a 5-cm distance from the nipple (Fig. 1C). The lump was categorized as 5 by Breast Imaging Reporting and Data System (BI-RADS), and core needle biopsy was performed using a 14-gauge needle. Histologic examination showed haphazard infiltration of solid cell nest composed of epithelial cells with eosinophilic cytoplasmic granules and prominent nuclei (Fig. 2A, H&E stain, x100). IHC demonstrated that tumor cells were negative for cytokeratin (AE1/AE3, DAKO, Glostrup, Denmark) and positive for 8–100 protein (DAKO) and CD68 (PG-MD, DAKO) (Fig. 3A→3C, x100). Based on these results, a diagnosis of OCT was made and wide excision without sentinel lymph node biopsy was performed with sonographic wire localization.

On gross examination, the surgically excised tumor revealed a spiculated, white-pink, firm, and solid mass measuring 13x12 mm (Fig. 2B). Microscopically, the tumor was composed of compact sheets of polygonal cells that contained coarse cytoplasmic granules and round nuclei. At the margins, the tumor cells showed an infiltrative growth pattern mimicking breast carcinoma (Fig. 2C, x40). These findings were consistent with OCT, and the patient remains well 3 months after operation.
Fig. 2. Histopathologic findings of granular cell tumor
A. H&E stain, x100
B. Gross findings of excised tumor
C. x40

Fig. 3. Immunohistochemical staining of granular cell tumor
A. cytokeratin (AE1/AE3) (H&E stain, x100)
B. S-100 protein (x100)
C. CD68 (PG-M1) (x100)
Discussion

OCT of the breast is a rare disease and often encountered in middle-aged, premenopausal black women. Its prevalence in premenopausal women has led to the hypothesis of implications of hormonal factors in the pathogenesis of these tumors, however, no estrogen or progesterone receptors are expressed. In our case, there was no expression of estrogen receptor (NeoMarkers for Lab Vision Corp., CA, USA), progesterone receptor (DAKO), and human epidermal growth factor receptor type 2 (HER-2) (DAKO) (Fig. 3D–3F, x200). The patient was diagnosed with Graves’ disease only 2 months before surgery. To date, there is no report of OCT of the breast in a patient with Graves’ disease. Therefore, these findings may suggest that there are no effects of thyroid hormones on the pathogenesis of this tumor. OCT of the breast occurs frequently in the upper inner quadrant in contrast to breast cancer, which is presented commonly in the upper outer quadrant. Usually, this tumor presents as a firm and painless lump. In cases of a palpable mass or superficial location, however, ulceration, nipple retraction, or fixation to the pectoral muscle may be demonstrated and clinically, it is often misdiagnosed as a malignant tumor.

Radiologic findings are also variable from a benign-appearing lump to suggestive of malignancy. Mammographic features of these tumors are often suspicious of malignancy, which are irregular spiculated lumps or retraction of surrounding tissue and skin invoked by desmoplastic reactions, and there are usually no microcalcifications. On ultrasound examination, there are frequently demonstrated as ill-defined hypoechic masses with posterior shadowing and vascularity of the tumor may range from no vascularity to prominent arterial flow by doppler sonography.

Gross examination shows a firm, grayish–white to yellow mass with infiltrative borders. Microscopically, these tumors are characterized by clusters or sheets of polygonal cells with small, round, and centrally–located nuclei, and abundant eosinophilic cytoplasmic granules that are diastase
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resistant and periodic acid–Schiff (PAS) positive. Occasionally, there is mild nuclear pleomorphism, and rare mitoses. IHC studies reveal that these tumors are positive for S-100 protein, CD68, vimentin, and neuron–specific enolase (NSE) and negative for cytokeratin, epithelial membrane antigen (EMA), desmin, α-smooth muscle actin (SMA), carcinoembryonic antigen (CEA), and estrogen and progesterone receptors. These findings suggest that GCTs are derived from mesenchymal cells with features of neurogen origin and Schwann cells. Preoperative diagnosis of GCT of the breast can be made by fine-needle aspiration cytology. In most cases, however, histologic examination is necessary to establish a definite diagnosis and true nature of the lesion. If it is histologically proven to be benign, close observation might be an acceptable management guideline, however, wide excision is recommended as the gold standard in the treatment of benign GCT. As incomplete resection may lead to local recurrence, complete excision with histologically clear resection margins is important and sentinel lymph node biopsy or axillary sampling is not indicated. Features of malignant GCT of the breast have been described as large tumor size of greater than 5 cm, cellular pleomorphism, prominent nuclei, increased mitotic activity, presence of necrosis, and local recurrence.

Clinical or radiological features of GCT of the breast may lead to misdiagnosis as breast carcinoma, and accurate histologic examination is necessary to avoid overtreatment such as mastectomy or sentinel lymph node biopsy. We experienced 1 case of GCT of the breast accurately diagnosed using core needle biopsy and immunohistochemical staining in a patient with Graves’ disease and report the case with a review of the literature.

Acknowledgements
A major part of this study was presented at the 23th Annual Meeting of Korean Breast Cancer Society, Poster exhibition, June 19–20, 2009 in Jeju, Korea.

REFERENCES
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Abstract

Granular cell tumor (GCT) of the breast is an uncommon, usually benign tumor originating from Schwann cells of peripheral nerves. Clinical and radiological findings of GCTs are similar to those of malignant tumors, and GCTs of the breast are often confused with breast cancer clinically or radiologically. We experienced 1 case of GCT diagnosed by core needle biopsy and immunohistochemical staining in the right breast of 54-year-old woman with Graves’s disease and report the case with a review of the literature.

Key Words: Granular cell tumor, Breast

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Received: November 20, 2010 : Accepted: December 23, 2010