ISSN 2515-8260 Volume 09, Issue 07, 2022

Title:

Granular cell tumor of the breast: An imposter of carcinoma

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Abstract:

A granular cell tumor is a rare benign tumor of neuroectodermal origin. It is derived from Schwann cells of the peripheral nerve. Granular cell tumors can originate anywhere in the body and about 5 to 15% of all granular cell tumors originate from the breast. Out of which 1 to 2% can show malignant change. Here we report a case of a 53-year-old female who came with complaints of swelling in the right nipple for 1 month associated with pain in the swelling. On examination 1X1.5cm lump in the right retro areolar region was present. The mammogram showed BI-RADS category 4(suspicious for malignancy). An excision biopsy was done for tissue diagnosis. Upon histopathological examination and the immunohistochemical study confirmed the diagnosis of a granular cell tumor.

The existence of granular cell tumors in the breast is uncommon and it can mimic carcinoma clinically and radiologically.

Introduction:

Granular cell tumor (GrCT) was first discovered by Weber in 1854 in the tongue (1). Later it was described in by Abrikossoff in 1926. Initially, it was believed to be a soft tissue neoplasm that originate from myocytes and was referred to as granular cell myoblastoma (2,3). However, in immunohistological studies, these tumor cells showed S-100 positive which displays its neurogenic origin(4).

GrCT is a benign tumor that is derived from Schwann cells of the peripheral nerves(5). They can arise from any part of the body, common sites are the tongue, head and neck, respiratory tract, gastrointestinal tract particularly the esophagus, and proximal extremities(6). Of all GrCT 5-15% of GrCT occurs in the breast(7). Though GrCT is a benign tumor, malignant changes can be seen in 1-2% of cases(4). GrCT closely mimics breast carcinoma clinically as irregular and firm mass and radiologically as poorly defined mass (8).

Case presentation:

A 53-year-old female came to OPD with complaints of swelling in the right nipple for 1 month which was slowly progressive and associated with pain in the swelling. No history of skin retraction, nipple inversion, and nipple discharge. The patient gave a family history of breast carcinoma in her mother.

ISSN 2515-8260 Volume 09, Issue 07, 2022

Local examination revealed a 1x1.5cm firm lump in the right retro areolar region of the right breasts. Tenderness present. No nipple discharges. No palpable axillary lymph nodes. The mammogram showed a 1.5cm poorly defined hypoechoic mass which was highly suspicious for malignancy, Breast Imaging Reporting And Data System (BI-RADS) category 4 (Figure 1). Clinically malignancy was suspected.

An excision biopsy was done for tissue diagnosis. Upon histopathological examination breast tissue with a lesion composed of sheets and nests of polygonal benign cells with abundant granular eosinophilic cytoplasm and round to oval hyperchromatic nuclei with intervening collagenous stroma. The tumor cells are seen focally wrap around small nerve bundles and benign ducts. No evidence of necrosis, pleomorphism, or increased mitotic activity. Immunohistochemical staining showed the tumor cells were positive for S-100 (Figure 2). Hence a final diagnosis of granular cell tumor was made.

Images:

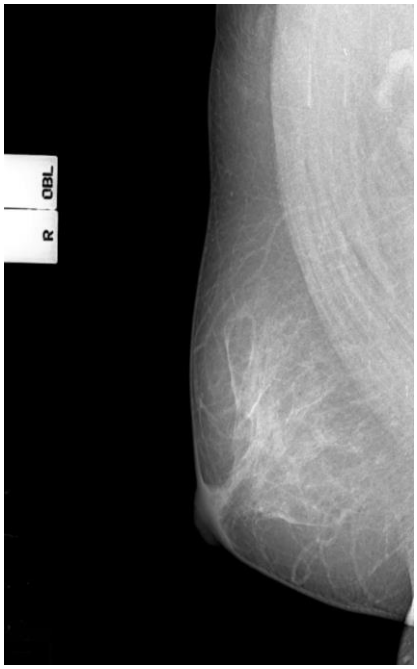

Figure 1: Mammogram image of right breast that shows a 1.5cm poorly defined hypoechoic mass.

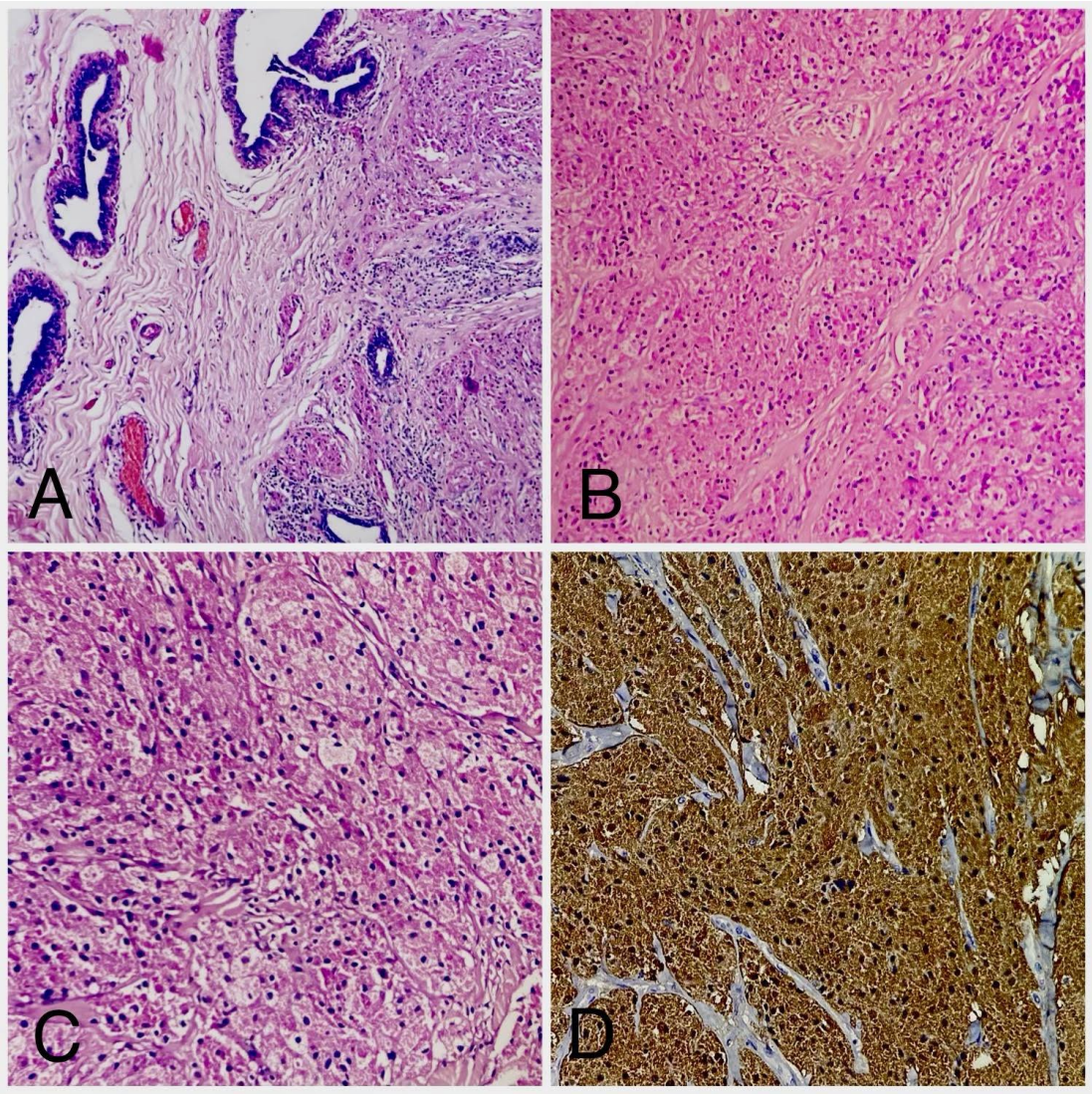

Figure 2: Breast parenchyma with tumor arranged in sheets and nests composed of benign polygonal cells (Haematoxylin and Eosin stain) (A and B). Tumor cells have abundant granular cytoplasm with round to oval hyperchromatic nuclei with intervening collagenous stroma (Haematoxylin and Eosin stain) (C). S-100 immunohistochemistry staining showing positive staining of tumor cells (D).

Discussion:

A granular cell tumor is a rare benign tumor derived from Schwann cells of the peripheral nerve(8). Among breast cancer, GnCT of the breast is seen in approximately 1 in 100 cases(9). GnCT commonly arises in women over a wide age group of 19 to 77 years and has a slightly higher incidence among premenopausal women(10). GnCT of the breast is commonly solitary lesions of the upper inner quadrant of the breast(11). Rarely multifocal lesions are also reported(3). This is in contrast to breast carcinoma which is commonly seen in the upper outer quadrant(9). GnCT can clinically present as an irregular firm, painless, slowly progressive mass that mimics carcinoma clinically(12). Skin and subcutaneous involvement are common. Radiologically they present as a poorly defined mass which also

mimics carcinoma(13). Rarely, GCT is seen in association with neurofibroma type 1, Banayan-Riley-Ruvalcaba syndrome, Noon Syndrome, and LEOPARD syndrome(14). Genetically frequently associated with loss of function mutation in ATP6AP1 and ATP6AP2 gene(5).

Macroscopically, these tumors have a regular or infiltrative border with homogenous white to tan in colour on the cut surface(12).

Microscopically, these tumors have infiltrative growth patterns with poorly defined cell borders. These tumors can be arranged in sheets, nests, clusters, cords, or trabeculae(12). The characteristic morphologic finding of GnCT is the presence of large polygonal cells with abundant granular cytoplasm(13). The nuclei are usually uniform small round to oval hyperchromatic and centrally located. This fine granular cytoplasm is due to the massive accumulation of lysosomes(14). These intracytoplasmic granules are surrounded by clear haloes known as pustule-ovoid bodies of Milian, which are PAS-positive and diastase resistant. Tumor cells are intervened by collagenous stroma(15). They usually do not show pleomorphism, atypia, or mitotic activity(16). Malignant granular cell tumor is very rare and recognized by aggressive histologic features. Perineural and perivascular involvement is common(12).

Immunohistochemical profile of tumor cells shows diffuse and strongly positive for S-100, CD63, CD68, and NSE, mostly due to non-specific reactivity with cytoplasmic lysosomes. TFE3 and MITF show strong positive nuclear expression (5). Whereas it is negative for GFAP, Keratin, and NFP. Differential diagnosis is apocrine carcinoma which is keratin positive and S100 negative, alveolar soft part sarcoma in which cells are divided in packs by thin-walled blood vessels. Their differential diagnosis is granulomatous mastitis, melanoma, and histiocytic tumor.

Conclusion:

GCT is a benign tumor that mimics carcinoma clinically and radiologically. Hence histopathologic examination is essential for diagnosis. Unlike carcinoma, GCT is treated with wide local excision with minimal local recurrences. Histopathologic diagnosis can be made with characteristic cytomorphologic features and immunohistochemical profiles.

Keywords:

Breast, granular cell tumour, S-100, carcinoma, benign tumour

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