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Recurrent benign granular cell tumor of breast with malignancy: does it exist?

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Summary. A granular cell tumor of the breast parenchyma is a rare tumor accounting for 5-6% of the breast carcinomas and is mostly benign in nature. The rarer malignant granular cell tumor comprises 1-2% of all granular cell tumors. This is a case of a 35-year woman who presented with a palpable mass in the right breast. On wide local excision, a diagnosis of benign granular cell carcinoma was made. On follow up, with a disease-free interval of one year, she developed local recurrence and she underwent simple mastectomy with adjuvant radiation therapy. Histopathological examination confirmed benign granular carcinoma. This is one such case where histologically confirmed to be benign, but the clinical behavior of a tumor favored malignant variety. Hence adjuvant therapy should be considered for this benign appearing, malignant tumor.

Key words: breast, granular cell tumor, benign, malignant

Introduction

Granular cell tumor (GCT) or Granular Cell Schwannoma of the breast is a rare benign tumor of the neural cells. It is commonly noticed in the oral cavity and other soft tissues (1). About 5-8% of GCTs occur in breast (2). Most of the GCT in the breast is benign, and occurrence of malignant GCT is even rarer. This case of GCT in the breast of pre-menopausal women which morphologically did not show any conventional features of malignancy, but it acted in an aggressive fashion. This case report emphasis the existence of a rare benign looking variant of GCT with clinical aggression.

Case report

A 35-year woman presented with a lump in the right breast of two years duration and she developed pain in the lump for the past 2 weeks. She did not give any history of nipple discharges or any other swelling in the body. On evaluation, the mammogram showed a BI-RADS score of 4 in the right breast. Clinically examination revealed a mobile lump in the upper outer quadrant of right breast measuring 2x2 cm with no axillary nodes. Biopsy of the lump showed tumor tissue arranged in a diffuse sheet, composed of polygonal cells with abundant eosinophilic cytoplasm and round nuclei with inconspicuous nucleoli. Nuclear pleomorphism, mitosis or necrosis was not seen. These cells were immunopositive for S100, CD 68 while immunonegative for cytokeratin with Ki-67 of 0-1%. So come to the diagnosis of benign granular cell tumor of the breast.

She underwent wide local excision of the lump on 15.01.2013. Post-op specimen showed a well circumscribed tumor, which measured 3x3x2 cm, confirming the diagnosis of benign granular cell tumor. The resection margins were free of tumor.

She was kept on follow-up. In January 2014 she developed a lump in the upper outer quadrant of the right breast. With clinical suspicion of recurrence, biopsy of the lump showed benign granular cell tumor.

She underwent completion mastectomy and axillary nodal sampling on 05.02.2014. Postop Histopathology showed a tumor measuring 4x3 cm with histomorphology similar to the previous excision. Features of malignancy like spindling, nuclear pleomorphism, prominent nucleoli, necrosis, and mitosis were not seen. This tumor had Ki-67 of 6%. These cells were immunopositive for S100, calretinin while immunonegative for cytokeratin as shown in Figure 1. Margins were free of tumor and all the 13 nodes are negative for metastasis.

She received post-op radiotherapy to the right chest wall of 45Gy in 25 fractions. She was kept on follow-up. After 16 months of follow-up, she is disease free.

Discussion

GCT is an uncommon tumor of the breast with a good prognosis. These tumors most commonly occur in women between 30 and 50 years of age i.e. in the pre and perimenopausal age group (3). GCT of the breast is commonly located in the inner quadrant of the breast due to the close association with supraclavicular nerves. Most of the GCT of the breast is benign with less than 1% is malignant (4). Tumor transformation from benign to malignant variety is rare.

In 1998 by Fanburg-Smith *et al.* established the histological criteria of a malignant granular cell. (5) Which included necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10HPF at 200×magnification), high nuclear to cytoplasmic ratio and pleomorphism. However, these criteria may not hold value of every case and the histological diagnosis of the malignant lesion can be challenging on the present case which closely resembled its benign counterpart. In addition to this features of local recurrence, metastasis, large tumor size, older patient age and Ki 67 values greater than 10% were regarded as statistically significant adverse prognostic factors. Tumor lesions which met three or more of these criteria were classified as histologically

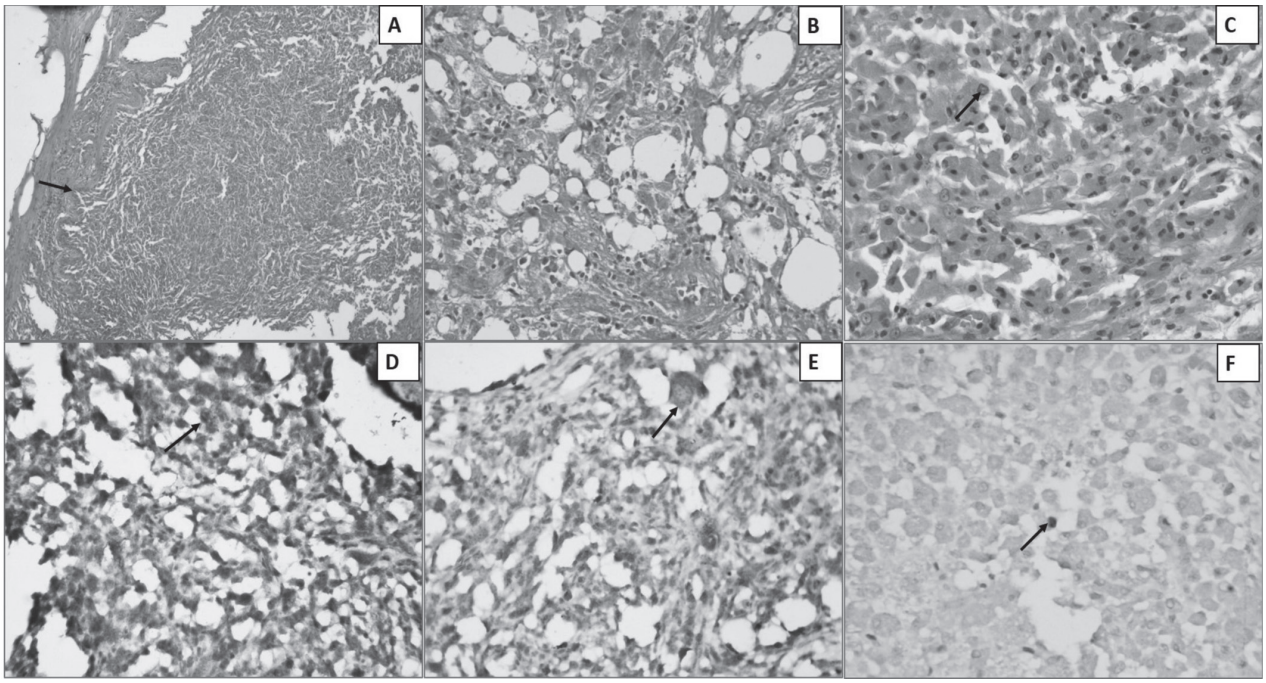

Figure 1. Mastectomy specimen showing a partially encapsulated tumor (capsule marked with arrow) (A) (H&E, 10x); Focal infiltration into adipose tissue of adjacent breast parenchyma (B) (H&E,20x); The tumour cells are arranged in diffuse sheets, composed of polygonal cells with abundant eosinophilic cytoplasm and round nuclei with inconspicuous nucleoli (arrow) (C) (H&E, 40x). These cells show predominant cytoplasmic positivity (arrow) and focal nuclear immunopositivity for S100 (D) (IHC, 20x) and Calretinin (E) (IHC, 20x); Ki67 labelling index is low, with occasional nuclear staining (arrow) (F) (IHC,40x).

malignant; those of atypical variety have one or two of the features, and those that displayed only focal pleomorphism but fulfilled none of the above-mentioned criteria was classified as benign.

In this patient, the tumor had all the features of benign tumor except the size of the lesion, which was around 4 cm and developed recurrence of a year span.

There are only a few such cases reported in the literature which is histologically benign but with clinical malignant features. Simsir A *et al.* (6) reported a GCT of the orbit which was histologically benign based on fanburg definition but termed malignant based on the locally advanced lesion. Jardines L *et al.* (7) reported soft tissue GCT with uncertain malignant potential histologically but had regional nodal metastasis radiologically. Akahane K *et al.* (8) reported an atypical GCT of the breast with clinical features of malignancy. This report concluded that high-level Ki-67 alone was considered as a proof of malignancy. Chen J *et al.* (9) reported the simultaneous appearance of two benign lesions namely in the breast and abdominal wall. Due to multiple recurrences, this case of benign GCT was classified as malignant. It was presumed that malignant GCT results from the transformation of benign GCT.

In considering the above-reported cases and the present case, classifying GCT as malignant based only on histological features is debatable. In this patient, the tumor recurred after a disease-free interval of one year. There are some reports on the transformation of benign GCT to malignant nature, so considering all the facts radiation therapy was given to the chest wall. She is disease free on follow-up of more than 16 months.

Conclusion

GCT of the breast is a rare neoplasm. The physician must be vigilant of this benign GCT with the malignant potential tumor. The patient must have a close follow up especially in the first 2 years.

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