Granular Cell Tumour of Breast : A Mimic of Carcinoma

Maj K Pathania*, Lt Col S Bhargava⁺

MJAFI 2010; 66 : 292-294

Key Words : Granular cell tumour; Breast

Introduction

Granular cell tumour (GCT) is a relatively uncommon lesion, which most often affects the tongue, skin and subcutaneous tissue, although it may occur at any body site [1]. Six percent of GCTs affect breast. GCT was first described by Abrikossoff in 1926 as granular cell myoblastoma, assuming a myogenic origin. On clinical breast examination, it can simulate a carcinoma with fixation to the skin and firm to hard on palpation. The lesion is painless but may cause skin puckering or nipple retraction. The controversy regarding whether the formation of a GCT is a metabolic, degenerative or neoplastic process is now resolved. It is a neoplastic process of neural derivation, as supported by immunophenotypic and ultrastructural evidence [2,3].

The tumour cells have a very granular cytoplasm due to accumulation of secondary lysosomes which gives a characteristic appearance on microscopy and thus the name. Most of these tumours behave in benign fashion, but malignant variant, which can occur de novo or from conversion of benign counterpart, is also known. We present a case of GCT of breast which clinically mimicked a carcinoma.

Case Report

A 58 years old lady presented to surgical out patient department (OPD) with a lump in the upper-outer quadrant of right breast of six weeks duration. The lump measured 2 cm in greatest dimension and was firm to hard, non-tender and adherent to overlying skin (Fig. 1). The overlying skin had reddish hue and appeared inflamed. However, there was no history of pain and local temperature was not raised. No axillary lymph nodes could be palpated. Patient did not have any systemic symptoms or signs. The patient was subjected to fine needle aspiration cytology (FNAC) which revealed a cellular aspirate of a benign spindle cell tumour, composed of cells arranged singly as well as in syncytia, along with few striped nuclei. Cells were short and spindly, with small nuclei and abundant dense cytoplasm with prominent granularity

(Fig. 2). These granules were visible on Leishman stain but became more prominent on Periodic acid-Schiff (PAS) stain, before and after diastase digestion. Depending on cytological features, diagnosis of benign GCT of breast was offered.

After one week, patient underwent wide local excision. A skin covered excised lump was received in the laboratory in which skin measured 3 cm x 2 cm x 2 cm. Cut surface of tumour was firm and white in colour (Fig. 3). On histopathology, a benign tumour was seen, which showed tumour cells in cords, sheets and nests, in a dense fibrous stroma. Cells were plump with eosinophilic granular cytoplasm and a small nucleus and inconspicuous nucleoli (Fig. 4). Granular cytoplasm became more prominent on PAS stain, before and after diastase digestion. No mitosis or necrosis was seen. All the margins of submitted tissue were free from tumour. Based on histopathological features, a diagnosis of benign GCT of breast was made which was confirmed by S-100 stain.

Discussion

GCT of breast commonly affects middle aged women with an average size of 2 cm. Lump is usually firm and non-tender. These tumours are typically solitary and located in the dermis or subcutis and less frequently in the submucosa, smooth muscle or striated muscle. They are usually free from the skin but attached to underlying fascia. They are more common in blacks. Upto 10% of GCT are multiple.

Granularity of tumour cells is due to the accumulation of secondary lysosomes in the cytoplasm which is rather nonspecific and can be observed in many non-neural tumours, including those arising from smooth muscle, connective tissue, neuralgia, endothelial and epithelial cells. Granules show PAS positivity, before and after diastase digestion which is employed for establishing diagnosis [4]. It is further confirmed by demonstration of S 100 protein. GCT also shows immunoreactivity for valentine, NSE, CD68, CD57 and nestin. Electron microscopy shows granules resembling autophagosomes and angulate bodies [5].

*Graded Specialist (Pathology), *Classified Specialist (Surgery), Military Hospital, Trivandrum-06.

Fig. 1 : Firm, indurated, lump involving right breast, upper-outer quadrant.

Fig. 2 : FNAC revealed spindle cell tumour with abundant granular cytoplasm and oval nuclei with small nucleoli. (10X, Leishman stain).

Breast lesions should be differentiated from apocrine carcinoma, fat necrosis and tumours of histiocytic origin. Subcutaneous GCT should also be differentiated from alveolar soft part sarcoma, rhabdomyoma, melanoma, histiocytic tumours and granular variant of squamous cell carcinoma [6]. They may also be found in the internal organs, particularly in the upper aerodigestive tract. Visceral involvement is encountered as mucosal or submucosal nodules in the esophagus, stomach, small and large intestines, larynx, bronchi, gallbladder, and biliary tract. Lesions can be incidental findings, or they may give rise to obstructive or pressure symptoms when large enough and in a critical location.

Benign and malignant counterparts are known, the latter are rare, comprising fewer than 2% of all GCT. Benign lesions manifest as nonulcerated and usually painless nodules with an insidious onset and slow growth rate. Necrosis, nuclear pleomorphism, spindling and increased mitosis (>2 mitoses per 10 high power fields) suggest aggressive tumour. The nuclei are sometimes hyperchromatic, irregular and contain prominent nucleoli. With these features, lesions are often termed

Fig. 3 : Gross specimen of the tumour (a) Along with overlying skin. (b) Cut surface shows a pearly white tumour.

Fig. 4 : Photomicrograph showing solid nests of large tumour cells with abundant granular cytoplasm. (10X, Haematoxylin and Eosin (H & E) stain). Inset upper shows PAS positive granules. Lower Inset shows S 100 positivity.

as GCT with undetermined malignant potential. Malignancy can be proven by metastasis only. Because of these findings, GCT may be misdiagnosed as apocrine carcinoma, especially on frozen sections. However, mitotic figures are absent or rare.

By convention, GCT is classified as malignant when it metastasizes to regional lymph nodes or distant sites or otherwise causes death [7]. Malignancy is encountered more often in deep-seated lesions in adults, with a mean patient age of 50 years, suggesting a possibility of malignant transformation from a pre-existing benign GCT. Some malignancies may be identical to their benign counterparts (small size, no local destruction, no infiltrative activity at the edge, bland histomorphology) and yet exhibit malignant potential by setting up metastases. Therefore, all lesions should undergo a careful and thorough examination. Treatment of choice is wide local excision. Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are being increasingly used in visceral lesions [8].

GCT mimics carcinoma, clinically, radiologically as well as grossly. The case has been presented for the

readers to be aware of such an entity.

Conflicts of Interest

None identified

References

1. Williams HK, Williams DM. Oral granular cell tumour: a histological and immunocytochemical study. *J Oral Pathol Med* 1997; 26:164-9.
2. Mukai M. Immunohistochemical localization of S-100 protein and peripheral nerve myelin proteins (P2 protein, PO protein) in granular cell tumors. *Am J Pathol* 1983; 122: 139-46.
3. Kurtin PJ, Bonin DM. Immunohistochemical demonstration of the lysosome-associated glycoprotein CD 68 (KP-1) in GCT and schwannomas. *Hum Pathol* 1994; 25: 1172-8.
4. Liu K, Madden JF, Olatidoye BA. Features of benign granular cell tumor on fine needle aspiration. *Acta Cytol* 1999; 43: 552-7.
5. Ciatto S, Del Turco MR, Bravetti P. Nonpalpable breast lesions: Stereotaxic fine needle aspiration cytology. *Radiology* 1989; 173: 57-9.
6. Marluce Bibbo, editor. *Comprehensive Cytopathology*. 2nd ed. WB Saunders 1997; 533.
7. De May RM, Kay S. Granular cell tumor of the breast. *Pathol Annu* 1984; 19: 121-48.
8. Adachi Y, Shiraishi N, Kitano S. Modern treatment of early gastric cancer: review of the Japanese experience. *Dig Surg* 2002; 19: 333-9.

Journal Scan

Craig M Capeci, Nirmal C Tejawani, Bilateral low energy simultaneous or sequential femoral fractures in patients on long term alendronate therapy. *Journal of Bone and Joint surgery* 2009; 91:2556-61.

Osteoporotic fractures remain a major cause of morbidity and mortality amongst the elderly. Since the 1990s, bisphosphonate (synthetic pyrophosphate) therapy has shown significant fall in the risk of osteoporotic fractures [1]. Alendronate remains the most commonly used bisphosphonate though new drugs with less frequent doses have been launched e.g. Risedronate, Zoledronate, Ibandronate etc. However, the optimum duration of Alendronate other bisphosphonate therapy remains unknown. Physicians/orthopaedic surgeons continue to use bisphosphonates on long term basis. Recently, there have been a number of reports which have associated low energy subtrochanteric and diaphyseal fractures of femur with long term alendronate therapy [2].

In this retrospective case series, authors have identified patients who were on long term alendronate therapy and sustained bilateral low-energy subtrochanteric/diaphyseal fractures of femur. All the patients were on alendronate therapy for more than 5 years with an average of 8.6 years (range 5 to 13 years). A medial fractures spike and cortical thickening was identified in all cases. There were two patients with sequential subtrochanteric fractures, one patient with bilateral simultaneous femoral diaphyseal fractures and four patients with unilateral femoral fractures, with impending subtrochanteric fracture on the contralateral side. The patients with unilateral fracture were identified to have impending fracture on contralateral side as they had prodromal pain and their radiographs revealed cortical thickening before fracture occurred.

Bisphosphonates remain the drug of first choice for treatment and prevention of osteoporotic fractures. Bisphosphonates inhibit bone resorption by suppression of osteoclast function and inducing osteoclast apoptosis leading to decreased bone turnover leading to relative increase in degree of mineralization. However, decreased bone turnover and remodeling also leads to accumulation of microdamage as well as a hypermineralized bone which is likely to

be more brittle [3].

No causative association has been confirmed till date about long term bisphosphonate therapy leading to low energy subtrochanteric and femoral diaphyseal fractures. However, increasing number of reports of these atypical fractures in patients on long term bisphosphonate therapy do raise questions about safety and optimal duration of long term bisphosphonate therapy. Close monitoring of patients on long term bisphosphonate therapy is required with due diligence required for any new onset hip or thigh pain [2,4]. Also, case series like this publication do indicate a requirement for prospective randomized trials to determine the safety of long term bisphosphonates as well as to establish any need for radiological screening for femoral stress fractures in patients on long term bisphosphonates.

References

1. Ensrud KE, Barrett-conner EL, Schwartz A, Santora AC, Bauer DC, Suryawanshi S. Fracture Intervention Trial Long Term Extension Research Group. Randomized trial of effect of alendronate continuation versus discontinuation in women with low BMD: results from the fracture Intervention Trial long term extension. *J Bone Miner Res* 2004; 19: 1259-69.
2. Kwek EB, Goh SK, Koh JS, Png MA, Howe TS. An emerging pattern of subtrochanteric stress fractures: a long term complication of alendronate therapy? *Injury* 2008; 39: 224-31.
3. Li J, Mashiba T, Burr DB. Bisphosphonate treatment suppresses not only stochastic remodeling but also the targeted repair of microdamage. *Caleif Tissue Int* 2001; 69: 281-6.
4. Visekruna M, Wilson D, MCKiernan FE. Severly suppressed bone turnover and atypical skeletal fragility. *J Clin Endocrinol metab* 2008; 93: 2948-52.

Contributed by

Lt Col N Kumar*

*Classified Specialist (Orthopaedics), Joint Replacement Centre, Army Hosp (R & R), New Delhi-10.