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Review Article

PRIMARY DUCTAL APOCRINE ADENOCARCINOMA OF AXILLA VS ACCESSORY MAMMARY GLAND CARCINOMA IN AXILLA – A DIAGNOSTIC DILEMMA: CASE REP

[1*]Dr. Deepti Gupta, [2]Dr. Anjali Tewari, [3]Dr. Shefali Agarwal, [4]Dr. Reena Jain and [5]Dr Nupur Trivedi

[1,3,5] Consultant Pathologist, Regency Hospital Ltd, Kanpur, Uttar Pradesh
[2]Consultant Pathologist and Head of the Department of Lab Sciences, Regency Hospital Ltd, Kanpur, Uttar Pradesh
[4]Surgeon, Regency Hospital Ltd, Kanpur, Uttar Pradesh

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ABSTRACT

Primary cutaneous ductal apocrine adenocarcinoma (PCDAA) is a rare malignant cutaneous neoplasm usually arising in areas of high apocrine gland density. To date, there have been 40 cases of apocrine adenocarcinoma reported in the literature. Similarly, male breast cancer arising in ectopic axillary breast tissue is also an extremely rare malignant neoplasm that has a high incidence of misdiagnosis. Due to the atypical location, a correct diagnosis is often reached during the later stages of cancer. The number of previous studies on male axillary ectopic breast cancer is extremely low. In the current study, a case of primary cutaneous apocrine carcinoma arising in male axilla is presented, highlighting the diagnostic dilemma between Primary Ductal Apocrine Adenocarcinoma of Axilla and Accessory Mammary Gland Carcinoma in Axilla. Written informed consent was obtained from the patient.

INTRODUCTION

Cases of primary adenocarcinoma in the axilla are uncommon and can be regarded as sebaceous or sweat gland cancer, mammary carcinoma arising in an accessory mammary gland, or metastatic lymph nodes from breast cancer or another primary cancer.[1] Herein, we describe a rare case of a male patient with a primary axillary malignant tumor which was histopathologically compatible with primary cutaneous apocrine carcinoma of axilla as well as breast cancer arising in an accessory mammary gland.

Case Report

A 66 year old Indian male presented with a right axillary superficial mass that had been present for 2 years. The lesion was slow growing and asymptomatic. A physical examination revealed a seemingly healthy male. No mass was palpable inside either breast. The skin lesion was of an irregular shape and size, with maximum dimensions of 6×4 cm. There was no ulceration, pain or fever. No cervical, supraclavicular or contralateral axillary swollen lymph nodes were observed. Notably, the patient underwent a right axillary lesion excision and the histopathology report revealed a well demarcated tumour in subepithelial tissue (Figure 1).

The tumour was disposed in lobules, cords, tubules and glands (Figure 2). The malignant cells had round to oval nuclei, coarsely granular chromatin, prominent nucleoli and moderate amount of eosinophilic cytoplasm. (Figure 3) These cells were embedded in large extracellular pools of myxoid/mucoid material (Figure 2). Tumour giant cells and atypical mitotic figures were seen too. No normal breast tissue or lymphoid tissue was identified (Figure 1,2,3). On Immunohistochemistry, tumour was positive for estrogen receptors and negative for CK-7, CK 20, CEA and gross cystic

Corresponding author: Dr. Deepti Gupta
Consultant Pathologist, Regency Hospital Ltd, Kanpur, Uttar Pradesh

disease fluid protein 15. USG and MRI revealed no primary lesion in the either of the breasts as well as the breast tails. Similarly, PET scan and CT demonstrated no evidence of any malignant or occult primary lesions apart from the axillary tumor. The differential diagnosis included a Primary Cutaneous Ductal Apocrine Adenocarcinoma, apocrine carcinoma with mucinous carcinoma-like features and primary mammary carcinoma arising in an ectopic axillary breast. Because the mass had no connection to the breast as was confirmed by physical, mammographic, ultrasound and histopathological examination, the lesion was slow growing and present subcutaneously in the axilla, an axillary extension of a mammary carcinoma was not likely. A negative CK 20 helped us to rule out apocrine carcinoma with mucinous carcinoma-like features. Thus, a diagnosis of primary cutaneous ductal apocrine adenocarcinoma was made.

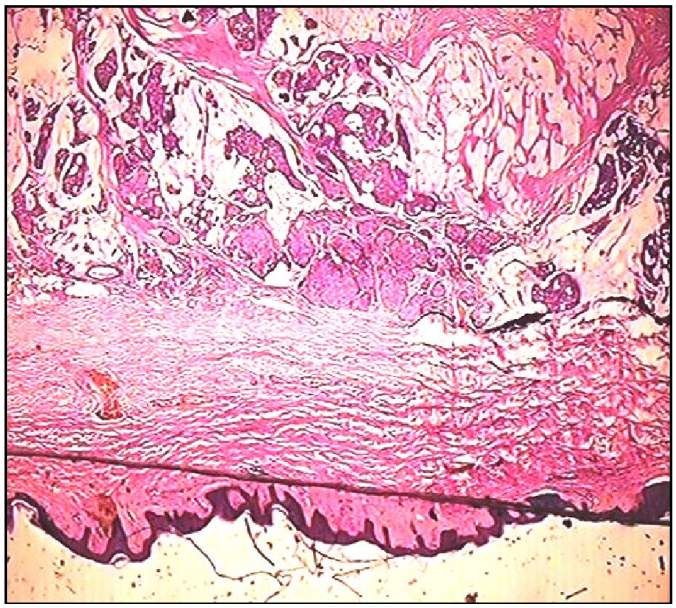

Figure 1. HxE (10x) stained section shows a well demarcated tumour in the subcutaneous tissue

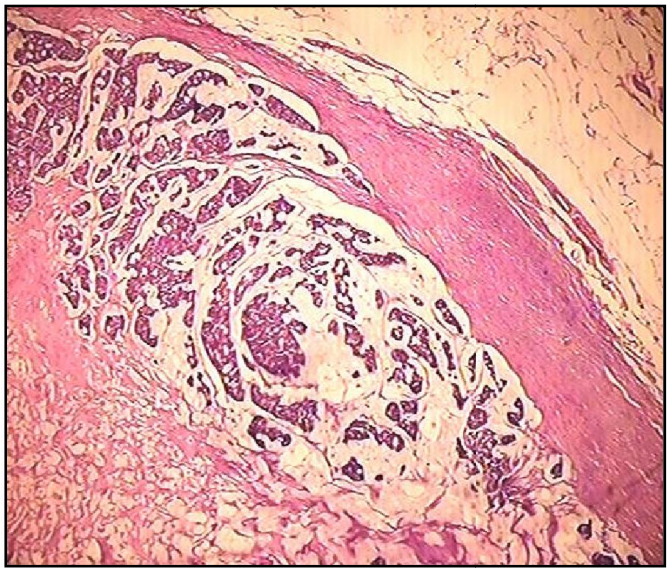

Figure 2. HxE (10x) stained section shows tumour disposed in glandular pattern with pools of mucin

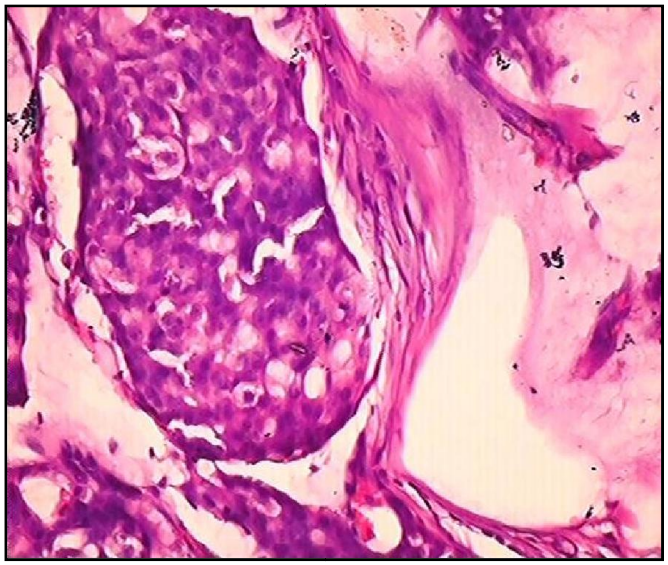

Figure 3. HxE (40x) stained section shows malignant cells having round to oval nuclei, coarsely granular chromatin, prominent nucleoli and moderate amount of eosinophilic cytoplasm

DISCUSSION

PCDAA is an extremely rare malignancy arising in apocrine sweat gland areas (Bitran and Ultmann, 1992). Till date, 40 cases have been reported. The most common site of occurrence is axilla. The highest incidence is between the ages of 40 – 60 years with male predominance. They usually are slow progressing tumours and present as painless, solitary nodules. Upto 50% of the patients present with regional lymph node metastasis at the time of presentation (Pucevich Brian *et al*., 2008). The relatively slow progression of tumour growth in PCDAA and relative lack of symptoms such as pain, swelling or ulceration make the clinical diagnosis of these tumours delayed. The histological examination reveals adenocarcinoma that may be well, moderate or poorly differentiated. The adenocarcinoma shows ductal or glandular structures with apocrine features (Pucevich Brian *et al*., 2008). The differential diagnosis of PCDAA from metastatic mammary adenocarcinoma is not possible only on morphological grounds, and immunohistochemistry, has only been partly helpful in solving this conundrum. It has been suggested in the past that the tumours of apocrine phenotype exhibit estrogen receptors (ER)−, progesterone receptors (PR)− and androgen receptors (AR)+ expression (Robson *et al*., 2008). However, Robson *et al* studied a large series of PCDAA and demonstrated that 62% were ER+, 60% were PR+, and 36% were AR− (Robson *et al*., 2008).

GCDFP-15 is considered as a very specific marker for apocrine differentiation, however, many of the PCDAA reported have shown a weak and focal expression of GCDFP-15, or have failed to show any expression of the marker at all (Watson *et al*., 1999). Once thought as a useful marker to detect neoplasms of mammary origin, in a series, GCDFP-15 failed to mark 4 ductal breast carcinomas, whereas it marked the only PCDAA studied (Ansai *et al*., 1995). CK 5/6 is usually expressed strongly and diffusely by PCDAA (Qureshi *et al*., 2004). On the other hand, only a small percentage of cutaneous metastases of breast tumours express CK 5/6 and they usually do it weakly. However, it is known that breast

carcinomas can express CK 5/6 and its expression usually carries a bad prognosis (Shin *et al*., 2008). Focal CK7 expression is suggestive of a primary adnexal tumour, whereas diffuse immunostaining is mainly seen in metastatic tumours (Qureshi *et al*., 2004). EGFR was once demonstrated as more frequently expressed in sweat gland carcinomas than in breast carcinomas (Busam *et al*., 1999). Nevertheless, some series have demonstrated expression of epidermal growth factor receptor by up to 22% of their cases of primary breast cancers (Busam *et al*., 1999 and Brandt *et al*., 2009). Fernandez used mammaglobin in a small series of PCDAA. In his study, breast carcinomas expressed intense and diffuse staining of mammaglobin, whereas PCDAAs showed only scattered positive cells. However, some of their breast carcinoma cases also showed only scattered positive cells, same as in PCDAAs. He therefore concluded that if mammaglobin marker is positive in the tumours cells with good intensity then a diagnosis of metastatic breast tumour should be made. On the contrary, a negative or weak staining in few scattered cells is non-conclusive (Fernandez-Flores, 2009). The above mentioned long list of immunohistochemical markers shows that none of the markers can be used alone to make a diagnosis of PCDAA. A panel of markers is required in order to reach a correct diagnosis. However, before making a diagnosis of PCDAA, a thorough search for any occult primary is also required.

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