Case Report

Low-grade adenosquamous carcinoma of the breast: A case report and review of literature

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ABSTRACT

Low-grade adenosquamous carcinoma (LGAS) is an uncommon form of invasive mammary carcinoma. Though, it is categorized as a variant of metaplastic carcinomas, which are highly aggressive tumors, this tumor is relatively indolent with a good prognosis. Even though, it shows infiltrative growth LGAS carcinoma exhibits bland cytological features and can be mistaken for benign and other low-grade lesions. Hence, it poses a diagnostic challenge on cytology, core needle biopsy and frozen sections. It has a risk of local recurrence after incomplete excision and has a low metastatic potential. Hence, distinction from the benign mimics is essential in order to plan a proper treatment of either wide excision or mastectomy. We report a case of LGAS carcinoma of breast in a 57-year-old female along with the review of literature and differential diagnosis to highlight the diagnostic challenge it poses.

Key words: Breast, core biopsy, immunohistochemistry, low-grade adenosquamous carcinoma, metaplastic carcinoma

INTRODUCTION

Metaplastic carcinomas accounts for 0.3% of invasive breast carcinomas.[1] Low-grade adenosquamous (LGAS) carcinoma also known as "syringomatous squamous tumor" is rare low-grade variant of metaplastic carcinoma with 51 cases reported in the literature until 2012.[2] It has characteristic morphological features with triple negative phenotype and variable positivity for myoepithelial and cytokeratin markers. It can also arise in association with benign complex sclerosing lesions.[3] It should be considered in the differential diagnosis of small glandular proliferations such as sclerosing adenosis, microglandular adenosis, and tubular carcinoma. All these lesions have different management and prognosis.[4] We report a case of LGAS carcinoma of breast highlighting its distinct morphological features.

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CASE REPORT

A 57-year-old postmenopausal woman presented with 2 months history of the left breast lump. There was no family history of breast cancer. Palpation revealed a nontender, mobile, hard lump in the lower outer quadrant of the left breast. There was no axillary lymphadenopathy. Mammography revealed a high density mass with ill-defined spiculated margins, characterized as BIRADS category 4C. Core biopsy showed an infiltrative proliferation of small ducts, which showed a double layered epithelium against a collagenous stroma. Focally, there were small nests of cells with squamoid appearance. Abluminal cells expressed p63, smooth muscle actin (SMA) and calponin due to which a differential of benign lesion was favored and excision was advised. On frozen section diagnosis was difficult due to the bland cytology of the cells; however, due to the infiltrative margins of the tumor diagnosis of low-grade malignancy was given. Patient underwent a modified radical mastectomy. Grossly, an ill-circumscribed tumor was seen measuring 2 cm × 1.5 cm. It was hard in consistency with a tan yellow cut surface and infiltrative margins. On microscopy, tumor was composed of infiltrative round to irregular glandular structures, some appearing compressed and some having a syringoid comma shaped contour [Figure 1]. Most of the

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tubules were lined by double layered epithelium. Some glands showed the presence of squamoid differentiation with cells showing glassy cytoplasm and intercellular bridges [Figure 2]. Lumen of some tubules showed eosinophilic material. Stroma was collagenous with the presence of spindle cells. Collection of lymphocytes was seen throughout the tumor, at places with follicle formation. There was no cytological atypia, mitosis or necrosis and the tumor was categorized as Grade I. All 13 axillary lymph nodes dissected were negative for metastasis. On immunohistochemistry (IHC), the tumor was negative for estrogen receptor (ER), progesterone receptor (PR) and HER2-neu. SMA and calponin were positive and highlighted the myoepithelial cells, but p63 was focally positive [Figures 3 and 4]. Stromal cells around tubules showed lamellar staining pattern with calponin. Based on the distinct histological features and IHC profile a diagnosis of LGAS carcinoma was made.

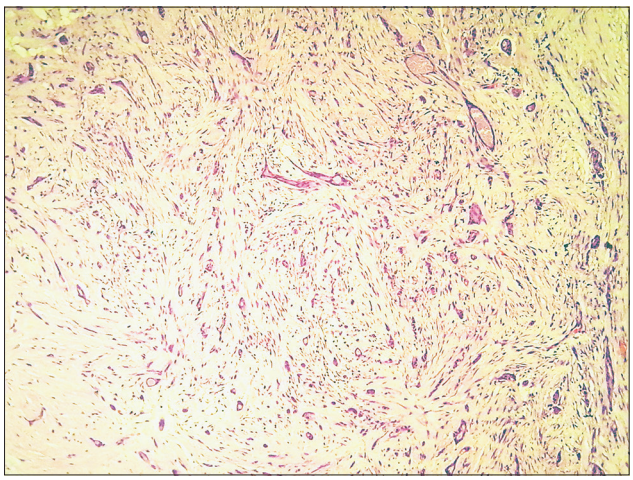

Figure 1: Photomicrograph showing syringoid and compressed tubules against a spindle and collagenous stroma (H and E; original magnification, ×100)

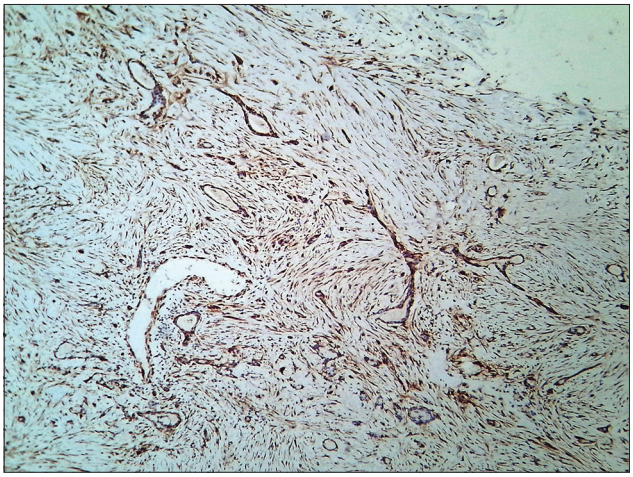

Figure 3: Immunohistochemical staining with calponin showing characteristic lamellar staining of the stromal cells (immunohistochemistry stain; original magnification, ×100)

DISCUSSION

Low-grade adenosquamous carcinoma of the breast is an uncommon variant of metaplastic carcinoma of the breast. It presents as a palpable mass and has been found in women whose age ranges from 31 to 87 years.[5] It was first described by Rosen and Ernsberger in 1987. They reported 11 cases of this tumor describing its characteristic histologic features.[6] Van Hoeven *et al*. have reported 21 cases of this lesion.[7] Both studies described the histological growth pattern of infiltrative small round to irregular glands, often comma shaped, embedded in collagenous and spindle cell stroma. Varied amount of squamoid differentiation was noted. Presence of lymphocytes was a consistent feature. Our case showed all these histological features reported in earlier studies. Despite the infiltrative nature, these tumor exhibit low-grade cytologic atypia few or absent mitosis and no necrosis. Lymph nodes are usually negative for metastasis. Kawaguchi and Shin have described the IHC profile of this tumor. The fact that LGAS carcinoma is consistently negative for ER, PR, and HER2-neu expression, may be a useful diagnostic tool. Myoepithelial and cytokeratin stains are positive, but the extent of staining is highly

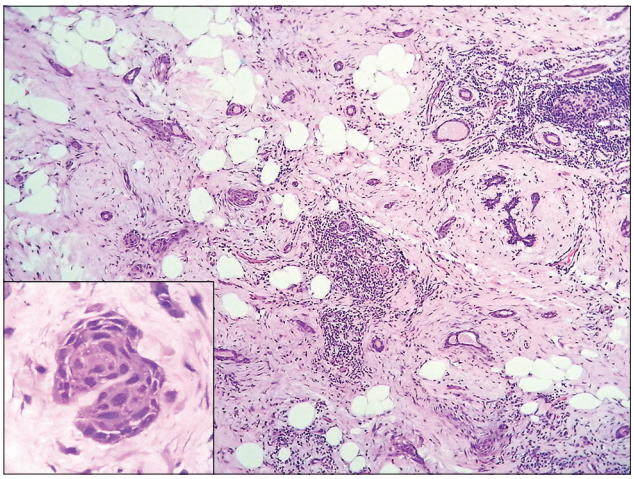

Figure 2: Photomicrograph showing infiltrating tumor with squamoid differentiation (inset) and lymphoid aggregates (H and E; original magnification, ×400)

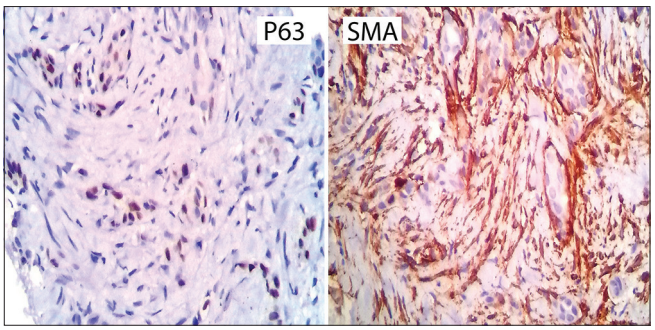

Figure 4: Immunohistochemical staining with p63 and smooth muscle actin highlighting myoepithelial cells (immunohistochemistry stain; original magnification, ×100)

variable. SMA, p63, calponin, and CD10 showed variable degree of positivity.[2,8] This case was positive for SMA and calponin with characteristic lamellar staining around tubules as described in this study. Diagnosis on fine-needle aspiration cytology is difficult. The usual criterion for malignancy are not applicable for this lesion, as reported by Krigman *et al*.[9] Even on core biopsy, diagnosis is challenging as all histological features of LGAS carcinoma may not be available on the biopsy material, especially the infiltrative borders.[4] LGAS carcinoma shows a range of differential diagnosis with benign sclerosing lesion at one end to tubular carcinoma at other end. Sclerosing adenosis is a benign epithelial proliferation that mimics LGAS carcinoma, especially on core biopsy, when lobular architecture of sclerosing adenosis may not be seen. Moreover, presence of myoepithelial cells compounds the diagnostic difficulty. Syringoid tubular configuration, focal squamoid differentiation, and aggregates of lymphocytes favor a diagnosis of LGAS carcinoma. Tubular carcinoma is characterized by small angulated glands lined by mildly atypical cells with prominent apocrine snouts surrounded by fibrotic stroma. Unlike LGAS carcinoma, it lacks squamous differentiation and is devoid of myoepithelial cell lining. LGAS carcinoma is triple negative for ER, PR HER2-neu, which is not the case in tubular carcinoma. Histological and IHC characters of LGAS carcinoma are identical to syringomatous adenoma of the nipple, but its superficial subareolar location distinguishes the two lesions.[10] Microglandular adenosis shows the presence of small round irregularly distributed acinar structures, but lacks the stellate configuration and stromal reaction of tubular carcinoma. Unlike LGAS carcinoma, it lacks myoepithelial layer. Hence, a combination of clinical, histological and IHC features can aid in its correct diagnosis, while a definite preoperative diagnosis may at times be difficult.

Small glandular proliferations, which are seen in the breast, consist of the spectrum of benign and malignant conditions with similar growth pattern often lacking cytological atypia. The common ones are benign sclerosing adenosis and the malignant are tubular carcinoma. Included in this group are the uncommon benign microglandular adenosis and malignant LGAS carcinoma. Despite the histological overlap in most cases, the morphology and IHC help in the diagnosis, when complete specimens are available. In core biopsy with limited material, diagnosis is challenging. Distinction is necessary because these small glandular proliferations have different prognosis and require different management. Hence, it is important to identify LGAS carcinoma of the breast.

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