

CASE REPORT

KELOIDAL-LIKE LOCAL RECURRENCE AFTER INFILTRATING ADENOSQUAMOUS BREAST CARCINOMA WITH STROMAL-OVERGROWTH MIMICKING A BENIGN SKIN LESION

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We present a very rare case of an adenosquamous infiltrating breast carcinoma with sarcomatous stromal overgrowth of hypocellular collagenised type, which subsequently developed local recurrence, mistaken for a benign skin lesion due to bland keloid-like morphological appearance. All the histological, immunohistochemical, and clinical features must be taken into consideration when distinguishing between a benign skin lesion and a local recurrence of a rare subtype of breast carcinoma.

Key words: adenosquamous carcinoma; recurrence; stromal overgrowth.

Introduction

The adenosquamous carcinoma of the breast is a rare metaplastic type of infiltrating carcinoma, which can be of low grade or high grade, the former being rare and morphologically similar to the syringomatous adenoma arising within the nipple, while the latter, previously called carcinosarcoma, is more frequently encountered, both types originating in the terminal ductal-lobular unit. The precise type of cell origin in both lesions is unknown.

We present herein a unique case of local breast skin recurrence predominantly composed of a keloid-type mesenchymal component after conservative surgical treatment for an adenosquamous carcinoma of the breast with sarcomatous stromal overgrowth (SO). The tumour was associated with a rapid fatal outcome due to development of brain and skull metastases. The local recurrence lacked any squamous

component and only presented a few benign-looking glandular structures, initially misinterpreted as a benign skin lesion.

This very particular case highlights that some of these types of lesions may harbour in both primary tumour and recurrence a massive stromal-overgrowth of keloid-like component, which can be misdiagnosed as benign lesions without a pathological correlation as well as the tumour board approach.

Case report

A 74-year-old patient presented to the Surgery Department in 2017 for rapid onset of a skin lesion. Multiple skin lesions with a total diameter of 45 mm involving the right breast skin were identified on clinical examination. These lesions were of soft consistency and grey colour. A biopsy was taken and sent

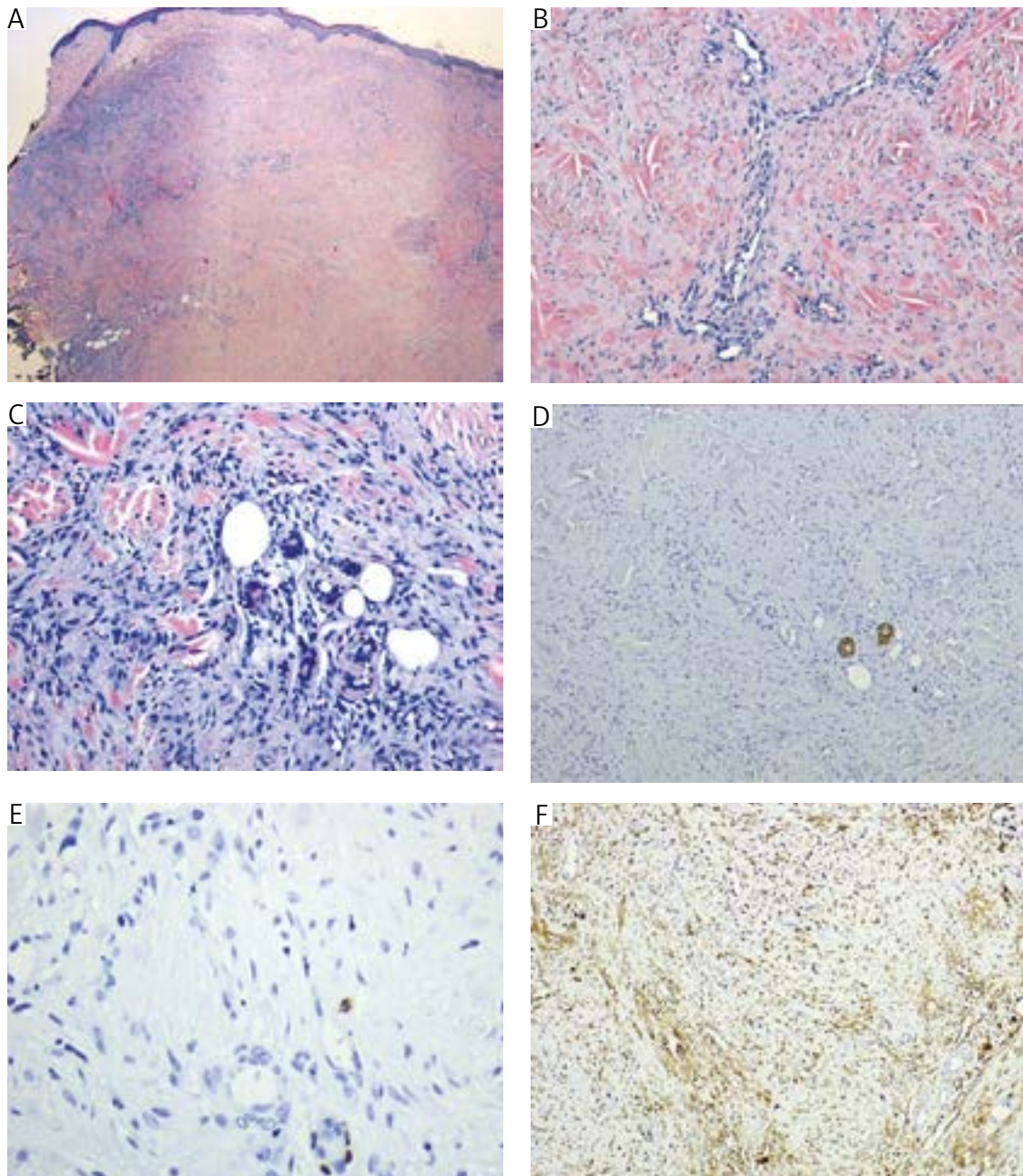


Fig. 1. Biopsy of a skin nodule: at low-power a round, well-delineated nodule involving the dermis (A). Higher-power examination revealed that the tumour consisted of bundles of bland spindle cells arranged in a storiform pattern (B). Small areas of benign-looking tubular structures were identified at the periphery of the nodule (C), with the inner layer positive for Cytokeratin 7 (D) and the outer layer for p63 (E), while the bundles of spindle cells were negative for all these markers and only positive for Vimentin (F)

to the Pathology Department. The clinical history of the patient included a breast carcinoma (of metaplastic type) diagnosed three years before and surgically treated conservatively followed by chemo/radiotherapy. Suspicion of a local recurrence was mentioned by the surgeon. However, a pathologist specialised in dermatopathology initially examined the skin biopsy, without being able to examine also the primary breast tumour.

On microscopic examination, a round, well-delineated nodule involving the dermis was identified,

while the epidermis was of normal appearance. However, no capsule was observed at the periphery of the nodule. Higher-power examination revealed that the tumour consisted of bundles of bland spindle cells arranged in a storiform pattern. The spindle cells did not present atypia or mitotic figures. No malignant tumour cells compatible with a local recurrence of metaplastic breast carcinoma were identified. However, at the periphery, the nodule contained small areas of benign-looking tubular structures with the inner layer positive for Cytokeratin AE1/AE3, Cyto-

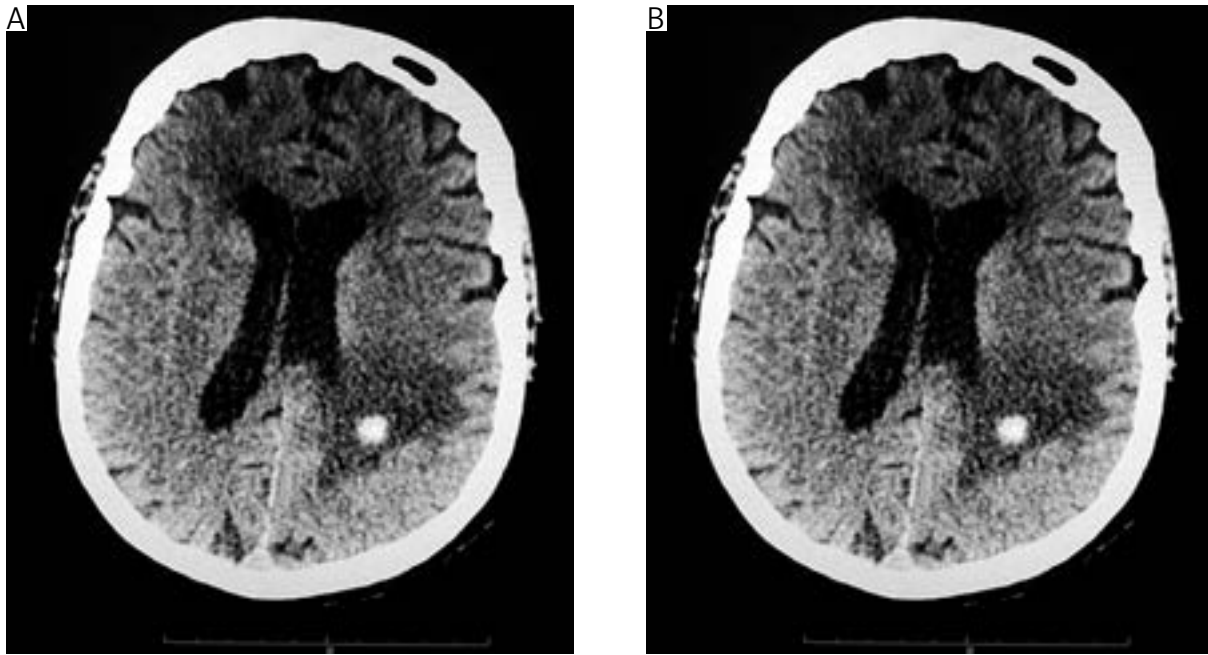


Fig. 2. CT examination: a 10-mm hyperdense space replacing process of the left parietum was noticed with a perilesional digitiform oedema, which induced the displacement of the posterior horn of the left lateral ventricle (A); osteolytic lesion on the left parietum (B)

keratin 7, and focally for Cytokeratin 5/6, and the outer layer for p63, while the bundles of spindle cells were negative for all these markers and only positive for Vimentin (Fig. 1). Final diagnosis was of a benign dermatofibroma and the patient was sent to the tumour board, which recommended further investigations together with a second opinion regarding the primary breast tumour and the skin lesion. On cranial CT examination, a 10-mm hyperdense space replacing process of the left parietum was noticed with a perilesional digitiform oedema, which induced the displacement of the posterior horn of the left lateral ventricle and of the median line to the right. When applying the bone window, an osteolytic lesion on the left parietum was outlined (Fig. 2). These lesions were interpreted as brain and skull metastases possibly originating in the breast carcinoma.

A breast pathologist re-examined both the primary tumour and the skin lesion. The patient was diagnosed in 2014 with microcalcifications associated with a lobulated tumour of 35 mm diameter on ultrasound examination, while mammography revealed the presence of a homogeneous lesion located within the inferior-interior quadrant of the breast (BIRADS 4). On macroscopic examination of the surgical specimen, a 33-mm diameter tumour infiltrating the anterior and posterior surgical margins was found. Microscopically, the primary tumour was a well-demarcated lesion with pushing type margins and presenting massive inflammatory infiltrate at the periphery. A central cystic area lined by squamous stratified bland looking epithelium was detected, and the cyst was surrounded

by extensive areas of less cellular, very hyalinised stroma, which represented more than 75% of the lesion. The remaining volume of the lesion was occupied by areas of more desmoplastic stroma containing bland, elongated glands admixed with nests of squamous cells, some of which presented keratin pearls centrally. Moreover, in some areas, the tumour cells were compressed by the abundant surrounding stroma forming trabeculae and cord-like growths. Both the tubular structures as well as the nests of squamous cells had low-grade atypical nuclei. Areas of calcifications were seen throughout the tumour together with multinucleated cells of osteoclastic type. Tumour emboli were present at the periphery of the tumour. No areas of phyllodes tumour were detected although the tumour had been sampled extensively. The tubular structures as well as the squamous nests and trabecular component were diffusely positive for Cytokeratin AE1/AE3. Cytokeratin 7 was positive in the tubular component, while p63 in the squamous components and trabeculae marked a continuous or discontinuous layer of myoepithelial cell differentiation surrounding the tubular structures. Cytokeratin 5/6, Cytokeratin 34beta E12, and CD 10 were diffusely positive in the tumour cells. In contrast, tumour cells were negative for ER, PR, and HER2, while the Ki67 index was 10% (Fig. 3). The final diagnosis was of an infiltrating adenosquamous breast carcinoma, with a triple-negative and basal-like profile, with myoepithelial differentiation and massive stromal overgrowth of keloid-like component. No metastases were found in the 22 axillary lymph nodes examined. The keloid-like stromal com-

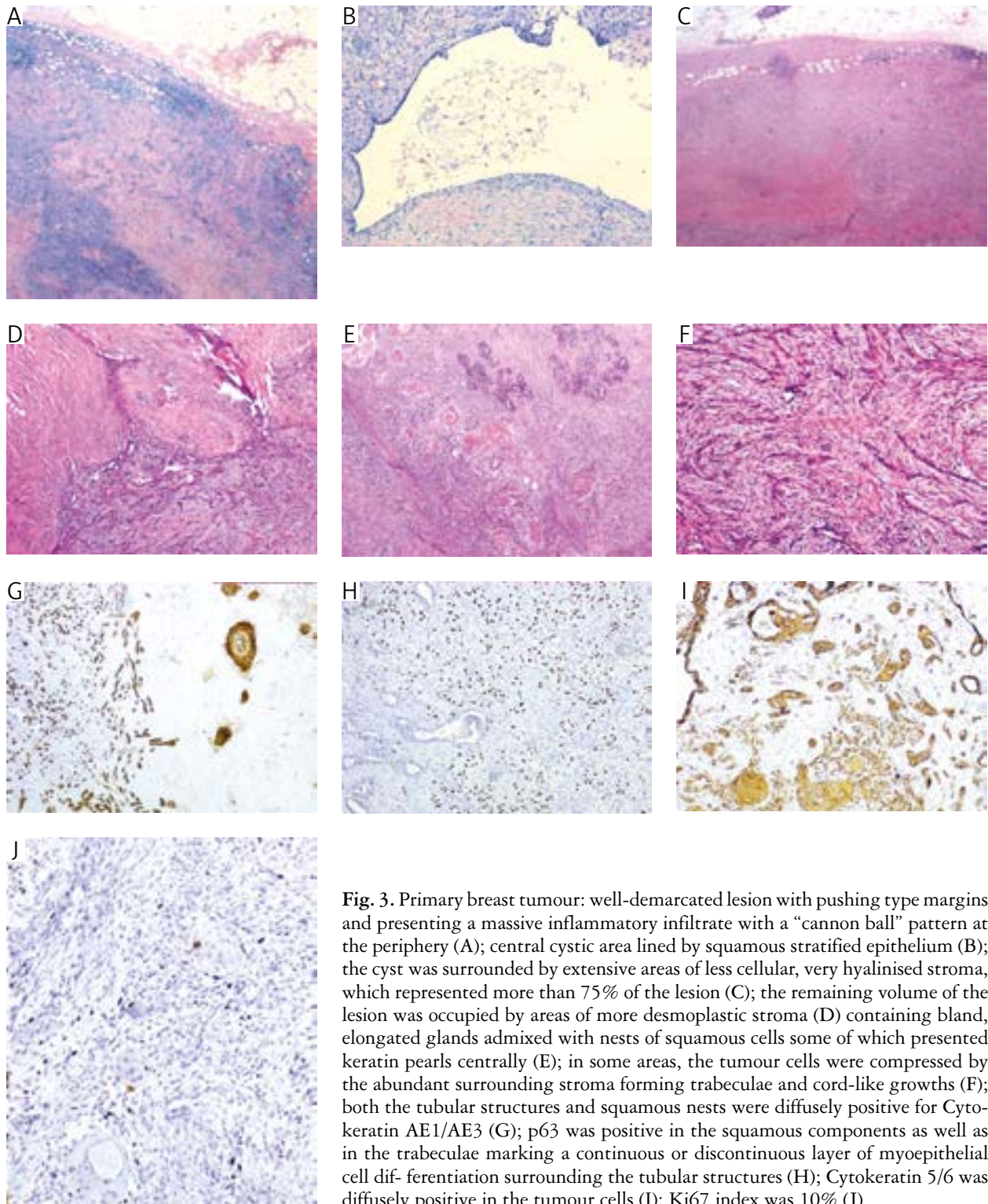


Fig. 3. Primary breast tumour: well-demarcated lesion with pushing type margins and presenting a massive inflammatory infiltrate with a “cannon ball” pattern at the periphery (A); central cystic area lined by squamous stratified epithelium (B); the cyst was surrounded by extensive areas of less cellular, very hyalinised stroma, which represented more than 75% of the lesion (C); the remaining volume of the lesion was occupied by areas of more desmoplastic stroma (D) containing bland, elongated glands admixed with nests of squamous cells some of which presented keratin pearls centrally (E); in some areas, the tumour cells were compressed by the abundant surrounding stroma forming trabeculae and cord-like growths (F); both the tubular structures and squamous nests were diffusely positive for Cytokeratin AE1/AE3 (G); p63 was positive in the squamous components as well as in the trabeculae marking a continuous or discontinuous layer of myoepithelial cell differentiation surrounding the tubular structures (H); Cytokeratin 5/6 was diffusely positive in the tumour cells (I); Ki67 index was 10% (J)

ponent of the breast tumour was identical to the skin lesion diagnosed three years later and misinterpreted as a benign skin lesion. The skin lesion was reinterpreted as skin metastasis from the breast carcinoma.

The general condition of the patient suddenly deteriorated. She denied any surgical or oncological treatment and left the hospital. She died three weeks later.

Discussion

Metaplastic carcinoma is a very heterogeneous group of tumours representing less than 1% of all breast malignant neoplasms [1]. These tumours are generally characterised by either pure epithelial types (like squamous carcinoma, adenocarcinoma, or adenosquamous carcinoma) or a mixture of carcinoma

with areas of spindle, osseous, or chondroid differentiation. The terminology of *metaplastic* is very confusing, especially because it covers a large spectrum of tumours with different microscopic grades and different behaviour and prognosis. Most of the tumours within this spectrum, however, are of triple-negative type and are positive for myoepithelial and basal-like markers, and have a poor prognosis.

Sarcomatous SO has been previously described in tumours of other organs, such as in Mullerian adenosarcoma of the female genital tract. Adenosarcoma is characterised by a synchronous proliferation of sarcoma (usually histologically of low-grade) and benign epithelium. Occasionally, Mullerian adenosarcomas may be overgrown by various types of an aggressive, high-grade SO component, and the presence of the SO is an adverse prognostic finding. However, in the female genital tract, the SO is defined variously by different sources. While the World Health Organisation classification (2014) requires high-grade sarcoma without including a volume criterion, the Gynecologic Cancer InterGroup consensus recommends a diagnosis of SO when > 25% of the tumour is composed of pure high-grade sarcoma [2, 3]. Histologically, low-grade SO has also been reported in the form of sex cord-like elements or bland stroma with prominent hydropic change and smooth muscle metaplasia [4, 5]. Tumours with low-grade SO are associated with a good prognosis. In breast pathology, however, SO has not yet been described in adenosquamous carcinoma.

Low-grade adenosquamous carcinoma of the breast is characterised by either bland spindle cells (fibromatous-like) or more collagenised hypocellular stroma, or, within the same case, it can be more cellular with cytological atypia (raising concern of a high-grade adenosquamous carcinoma). Within this stroma, elongated benign-looking glands admixed with nests of squamous cells, some of which present keratin pearls centrally, are present. By contrast, in the high-grade adenosquamous carcinoma, an epithelial malignant component of either glandular or squamous or both is admixed within a malignant sarcomatous component, the latter being of homologous or heterologous type. Most adenosquamous carcinomas of the breast have a somewhat evenly distributed malignant component and stroma although, in some tumours, the stroma may be more prominent in some areas. The grade of atypia of the stromal/sarcomatous component is prognostically important, while the volume has never been discussed as a diagnostic or prognostic indicator to the best of our knowledge.

Adenosquamous carcinoma has a risk of local recurrence after incomplete excision even in low-grade cases [6]. Very few documented cases develop metastases in the axillary lymph nodes, while especially in the high-grade tumours distant metastases are found

particularly in the brain [1]. Of interest, metastases or local recurrence may demonstrate an epithelial or metaplastic phenotype or both. However, to the best of our knowledge, none of the previously described cases presented a low-grade SO within the primary tumour in association with the local recurrence almost entirely composed of keloid-like component, making the diagnosis very difficult in the absence of data regarding the primary tumour.

In the present case, an adenosquamous carcinoma presented a low-grade SO which represented 75% of the tumour volume and had overgrown the malignant component of the tumour. Most of this, however, was of bland collagenised type. A similar morphological feature was found in the local recurrence. One cannot determine, based on the study of one case, whether the volume or the grade of the SO is more important from a prognostic perspective. However, from a diagnostic perspective, this case illustrates that the SO in adenosquamous carcinoma of the breast is not well-recognised and can be misinterpreted as a benign lesion when the local recurrence is only represented by the mesenchymal component.

The authors declare no conflict of interest.

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