



Invasive carcinoma of breast with adnexal differentiation of trichoblastic type

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ABSTRACT

We present a rare distinctive variant of invasive carcinoma of breast characterized by adnexal differentiation of tumor of trichoblastic type. The neoplasm was identified in a mastectomy specimen from an 83-year-old Chinese woman. Morphologically, the trichoblastic differentiation was characterized by the formation of solid sheets and nests of basaloid cells. The tumor cells were positive for cytokeratin 5/6, BER-EP4, *bcl-2*, and β -catenin. Stromal cells were positive for CD10. The tumor cells exhibited a "triple negative" profile; the nuclei did not react with antibodies to estrogen and progesterone receptors but failed to show overexpression of the HER2/neu protein. The MIB-1 labeling index averaged 20%. It is hoped that this case increases awareness for this unique morphological variant of invasive ductal carcinoma.

KEY WORDS: Adnexal differentiation, breast carcinoma, trichoblastic

INTRODUCTION

Adnexal carcinoma of the breast is a rare malignant tumor that resembles tumor of the skin appendages such as sweat or sebaceous glands and hair follicles. Herein, we report an exceedingly rare case of invasive mammary carcinoma with adnexal differentiation of trichoblastic type.

CASE REPORT

An 83-year-old Chinese woman presented with a left breast mass for 4 years, which was slowly increasing in size. There was a recent sudden increase in size and the lump became painful. Apart from diabetes mellitus, she has no major medical problems. Clinically, there was a large lump occupying almost the whole of the left breast with bluish discoloration of the skin [Figure 1]. Mammogram was not possible and an ultrasound showed a large solid irregular lesion with a cystic component. Chest X-ray was normal, and there was no evidence of distant metastases. No biopsy was done and she proceeded to a left mastectomy and axillary dissection. Surgery was

uneventful and she recovered well. Postoperatively, the wound healed well. No adjuvant therapy was given.

On gross examination, the breast measured 11 cm × 9 cm × 8.5 cm and was covered by a piece of ellipsoidal skin bearing a distorted and vaguely visible nipple. The skin appeared inflamed. There was a markedly hemorrhagic and necrotic tumor with solid and cystic areas and measuring 8 cm in greatest dimension involving all the four quadrants. The tumor was extensively sampled.

Histologically, the tumor showed solid sheets and nests of basaloid looking cells, which in areas formed pseudo cystic spaces [Figures 2 and 3]. The tumor cells exhibited moderately pleomorphic nuclei. Small nucleoli and nuclear grooves were observed in the neoplastic cells. The tumor infiltrated the dermis with no involvement of the overlying epidermis. The nipple was free of Paget's disease. The tumor cells were reactive for cytokeratin 5/6 (CK5/6), BER-EP4, *bcl-2*, and β -catenin [Figure 4a-d]. The stromal cells were positive for CD10 [Figure 5]. Estrogen and progesterone receptors were



Figure 1: Lump occupying almost the whole of left breast with bluish discoloration of skin

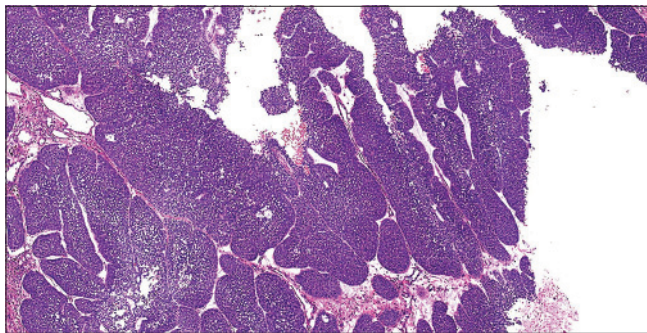


Figure 2: Solid sheets and nests of basaloid looking cells (H and E, $\times 100$)

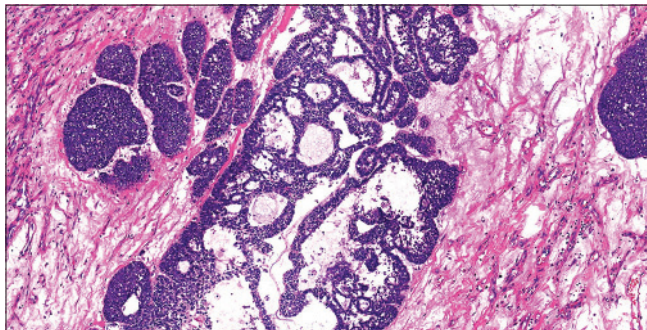


Figure 3: Pseudo cystic spaces within the tumor (H and E, $\times 200$)

negative and HER-2/neu was not overexpressed. The MIB-1 proliferative index was 20%. Based on the morphological features and immunohistochemical profile, the final diagnosis of invasive carcinoma with adnexal differentiation of trichoblastic type was made.

DISCUSSION

Adnexal differentiation of skin type is a rare phenomenon encountered in invasive carcinomas of the breast. There are case reports of sebaceous differentiation in mammary carcinoma [1-3]. The first case of microcystic adnexal carcinoma

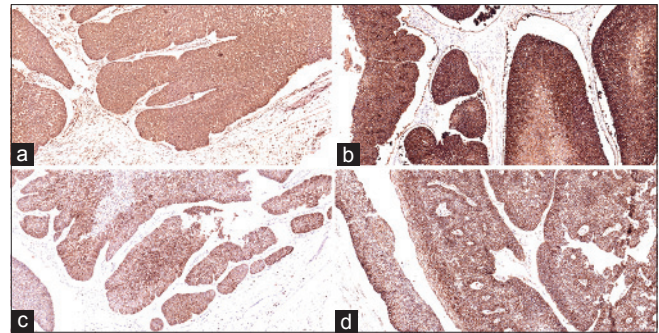


Figure 4: (a) Tumor cells expressing cytokeratin 5/6 (immunohistochemistry, $\times 100$). (b) Tumor cells expressing BER-EP4 (immunohistochemistry, $\times 200$). (c) Tumor cells expressing *bcl-2* (Immunohistochemistry, $\times 100$). (d) Tumor cells expressing β -catenin (immunohistochemistry, $\times 200$)

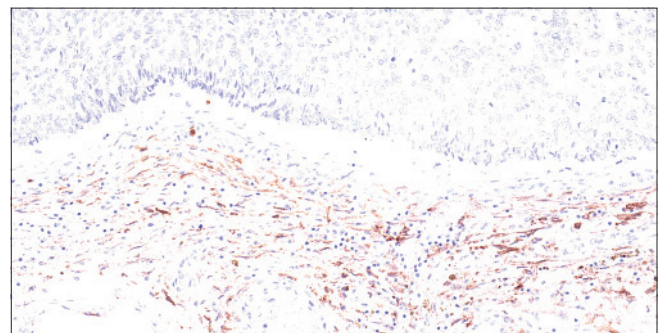


Figure 5: Positive immunostaining of stromal cells for CD10 (immunohistochemistry, $\times 100$)

of the breast was published in 2002 by Yavuzer *et al.* [4]. To the best of our knowledge, only one case of breast cancer showing trichoblastic germinative differentiation has been reported so far in the breast [5].

A review of the embryogenesis of dermal appendages may cast some light on the underlying basis for this aberrant differentiation in mammary cancers. Since dermal appendages are of ectodermal origin, most epithelial cells of skin appendages are derived from multipotent stem cells localized in the basal epidermal layer of the developing fetal hair follicles. These multipotent stem cells may represent the ultimate epidermal stem cell. A single cell thick layer of ectoderm and underlying mesoderm begins to proliferate during the 4th week of development and also differentiates toward skin appendages such as the pilosebaceous units, the eccrine sweat glands, and the apocrine glands.

In the areolar skin surrounding the nipple, sebaceous glands occur as Montgomery tubercles. These glands drain via the lactiferous duct lumina or may terminate directly in the epidermis.

Due to the complex structure of the non-neoplastic hair follicle and the proliferation of pluripotent stem cells from which the sebaceous and apocrine glands emerge, it is not surprising that differentiation patterns corresponding to these diverse adnexal

types may occur, as these tumor cells recapitulate ontogenic pathways. Tumors of the pilosebaceous units most often occur as single lineage tumors; however, on occasions, complex tumors with multidirectional differentiation including the germinative component of the hair bulb, the inner or outer root sheath epithelium, sebaceous glands and also the sweat glands can emerge [6-8]. Despite the morphological and developmental connections between mammary gland and skin appendages, adnexal differentiation is rarely encountered in tumors of the breast. A similar hypothesis related to cutaneous adnexal neoplasms could be proposed for the skin type of adnexal differentiation in breast tumors.

Trichoblastic adnexal tumors of skin are rare and arise from the follicular germinative epithelium and occur in the deep dermis and subcutaneous tissue, most common in the elderly individuals, with a predilection for head and neck region, trunk, and extremities. The major differential diagnosis for trichoblastoma is basal cell carcinoma [9,10]. Some authors argue that basal cell carcinoma is trichoblastic carcinoma [11]. The neoplastic cells of basal cell carcinoma and trichoblastoma appear similar to the germinative cells in an embryo that give rise to the entire folliculosebaceous-apocrine unit. Expression of BER-EP4, CK5/6, and CK 14 is seen in trichoblastomas as well as basal cell carcinomas [12,13]. The tumor cells are positive for *bcl-2* in both the tumors. Peritumoral stromal cells in trichoblastoma and the epithelial cells in basal cell carcinoma are immunoreactive for CD10 [14]. Calretinin positivity may be observed in these tumors [15]. The use of immunohistochemical staining has only limited value in the diagnosis of follicular neoplasms [12,16]. An immunohistochemical profile described in trichoblastic tumors was similarly present in our case.

A differential diagnosis of basal-like and triple negative carcinoma of the breast may arise on encountering these types of neoplasms. The majority of basal-like breast cancers is of invasive breast carcinoma of no special type with high histological grade, and characterized by a very high mitotic rate, central necrosis or fibrosis, pushing borders, prominent lymphocytic infiltrate, and typical or atypical medullary features. Basal-like phenotype is also observed in the majority of medullary and atypical medullary, metaplastic, secretory, myoepithelial, and adenoid cystic carcinomas of the breast [17]. However, in our case report, histological findings of basaloid morphology of the cells forming solid sheets and nests with pseudo cystic spaces and a proliferative index of 20% were observed.

Neoplasms showing cutaneous adnexal type of differentiation can occur outside the skin. Glandular adnexal lesions of the skin show morphologically striking similarities to salivary gland tumors and comprise well-established entities [18]. Extracutaneous occurrence of skin type adnexal neoplasms in the majority of cases is rarely encountered and often diagnostically an extremely challenging entity.

In our case, the histomorphological and immunohistochemical features favor a trichoblastic differentiation of tumor cells. The circumscription and clear surgical margins which enabled complete excision, favor an overall good prognosis, despite the

triple negative immunohistochemical profile. However, more case reports are needed for a detailed understanding of these types of complex neoplasms.

CONCLUSION

This case serves to highlight the rare type of breast cancer exhibiting trichoblastic differentiation. The paucity of published reports underscores the importance of recognizing and documenting these lesions so that we may better understand the molecular pathogenesis and biological behavior of this unique subtype of mammary cancer.

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