C A S E R E P O R T

UDC: 618.19-006-07:616-091
DOI:10.2298/VSP1102178J

Multinucleated stromal giant cells in adenoid cystic carcinoma of the breast: a case report and literature review

Multinuklearne džinovske stromalne ćelije u adenoidnocističnom karcinomu dojke: prikaz bolesnice i pregled literature

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Abstract

Background. We presented an unusual case of adenoid cystic carcinoma (ACC) of the breast with multinucleated stromal giant cells (MSGCs). To the best of our knowledge, the occurrence of ACC with MSGCs has not been reported previously. MSGCs should be distinguished from other multinucleated giant cells in breast tumors. The histogenesis of MSGCs still remains obscure. In hope to elucidate the histogenesis of MSGCs, we used a broad range of antibodies. **Case report.** A 40-year-old woman presented with a palpable lump in the subareolar location of her right breast. Excision of the tumor was performed. At gross pathologic examination the tumor was 20 × 15 × 15 mm in size, red-brown and well circumscribed. The surgical margins were positive for carcinoma and skin-sparing mastectomy with axillary dissection was complited. Eighteen lymph nodes examined were uninvolved. Patohistological examination showed ACC with numerous MSGCs scattered within tumor stroma. Immunohistochemical studies indicated that MSGCs are probably derived from stromal fibroblasts. These cells showed strong reactivity only for vimentin. Staining for histiocytic marker (CD68), as well as for epithelial marker (cytokeratin), myoepithelial markers (S-100, α-smooth muscle actin), vascular marker (CD34), hormonal receptors (ER, PR) and HER2 in MSGCs were negative. **Conclusion.** The presence of MSGCs should not alter the prognosis of an otherwise typical breast ACC.

Key words:
breast neoplasms; carcinoma, adenoid cystic; gaint cells; prognosis.

Apstrakt

Uvod. Prikazana je bolesnica sa veoma retkim adenoidnocističnim karcinomom (ACC) dojke sa prisustvom brojnih multinuklearnih džinovskih stromalnih ćelija (MSGC). Prema nama dostupnim podacima iz literature do sada nije opisan nijedan slučaj ACC sa MSGC. Ove ćelije se razlikuju od drugih džinovskih multinuklearnih ćelija koje se mogu naći u tumorima dojke. Da bi otkrili poreklo MSGC primenili smo imunohistohemijsko ispitivanje primenom većeg broja različitih antitela. **Prikaz bolesnice.** Prikazali smo ženu, staru 40 godina, sa palpabilnim tumorom subareolarne regije desne dojke. Urađena je ekscizija tumora. Makroskopski, tumor bio je promera 20 × 15 × 15 mm, crvenobraon boje i jasno ograničen. Zbog pozitivnih resekcionih ivica, urađena je mastektomija sa disekcijom aksile. Osamnaest pregledanih limfnih nodusa nije imalo metastaze. Patohistološki je potvrđen ACC sa brojnim MSGC unutar strome tumora. Imunohistohemijskim ispitivanjem utvrđeno je da MSGC verovatno vode poreklo od fibroblasta strome. Ove ćelije su ispoljile jako pozitivnu reakciju samo na vimentin. Imunohistohemijska bojenja na histiocitne (CD68), epitelne (*cytokeratin*), mioepitelne (S-100, α-*smooth muscle actin*) i vaskularne (CD34) markere, kao i na hormonske receptore (ER, PR) i HER2 bila su negativna u MSGC. **Zaključak.** Prisustvo MSGC ne utiče na prognozu tipičnog ACC.

Ključne reči:
dojka, neoplazme; karcinom, adenoidni cistični; ćelije, gigantske; prognoza.

Introduction

Adenoid cystic carcinoma (ACC) of the breast is a very rare neoplasm accounting less than 0.1% of all invasive breast carcinomas [1]. It is of special interest because of its favorable prognosis and distinctive histological appearance. The clinical features are a well-circumscribed palpable mass centrally located, which is occasionally tender on palpation. Histologically, ACC has a distinctive biphasic pattern that consists of true glandular lumens lined by the epithelial cell component and pseudocystic spaces lined by basaloid myoepithelial cells [1]. To the best of our knowledge, the occur-

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rence of ACC with multinucleated stromal giant cells (MSGCs) has not been reported previously. Multinucleated stromal giant cells in the breast were first described by Rosen [2]. Despite the fact that MSGCs have been well documented in other anatomic locations, only several reports described similar cells in both benign and malignant tumors of the breast [3–7]. They are usually located within the stroma, with no association with the epithelial cells. MSGCs should be distinguished from osteoclast-like giant cells, which most likely represent reactive stromal elements of histiocytic origin [8].

The histogenesis of MSGCs still remains obscure. We present herein the unusual case of ACC with MSGCs. In hopes to elucidate the histogenesis of MSGCs, we utilized a panel of immunohistochemical markers.

Case report

A 40-year-old woman presented with a palpable lump in the subareolar location of her right breast, with no palpable axillary adenopathy. There was no nipple discharge. Family history was negative for breast cancer. On clinical examination a firm nodule was suggestive for fibroadenoma. An ultrasound scan was also compatible with a diagnosis of a fibroadenoma. No further diagnostic attempts were made, and local excision was performed. At gross pathologic examination the tumor was 20 × 15 × 15 mm in size, red-brown and well circumscribed. Despite well-defined borders, the surgical margins were positive for carcinoma. Neither vascular nor lymphatic invasion was seen. The patient underwent a skin-sparing mastectomy. Since the sentinel node procedure was still investigational at that time, the axillary dissection was complited. Eighteen lymph nodes examined were uninvolved. The patient made a good recovery after surgery. She received no adjuvant therapy and was well with no evidence of disease 18 months later.

The obtained tissue was fixed and routinely embedded. Laboratory paraffin sections were stained with hematoxylin-eosin (H&E) and alcian-blue periodic acid-Schiff (AB-PAS) techniques. Immunohistochemical analysis was performed with the alkaline phosphatase anti-alkaline phosphatase (APAAP) technique, using antibodies against: vimentin, CD68, CD34, S-100, α-smooth muscle actin, cytokeratin, estrogen receptor (ER), progesterone receptor (PR) and Herceptest (DAKO, Copenhagen, Denmark).

The histological examination showed a small dark-staining neoplastic cells in islands, containing many pseudocysts filled with eosinophilic material, together with tubular duct-like structures. Both the modified Bloom Richardson grade and the nuclear grade of the lesion were 1. Numerous MSGCs were relatively diffusely scattered within the tumor stroma (Figure 1). The cells appeared to have multiple, aggregated, often hyperchromatic nuclei (5 to 25). The cytoplasm of MSGCs was eosinophilic with a coarsely granular pattern. No mitotic figures were seen in MSGCs. The pseudocysts, which contain amorphous basement membrane material, show positive staining for alcian-blue (Figure 2). The tumor was negative for hormonal receptors. Expression of human epidermal growth factor receptor 2 (HER2) was also negative.

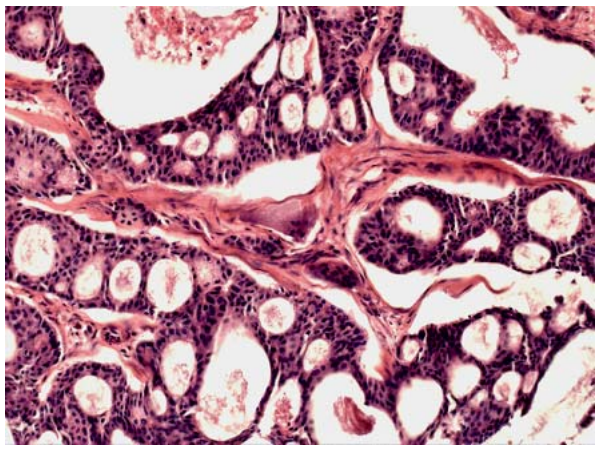

Fig. 1 – Photomicrograph demonstrates multinucleated stromal giant cells scattered within the tumor stroma in adenoid cystic carcinoma of the breast (H&E, 200×)

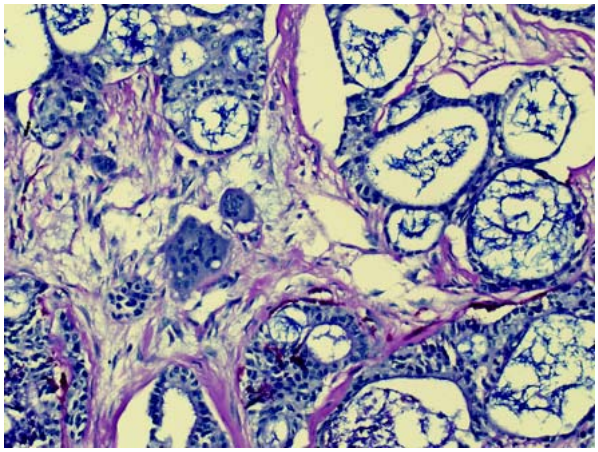

Fig. 2 – Adenoid cystic carcinoma of the breast with multinucleated stromal giant cells (AB-PAS, 200×)

Despite the broad range of antibodies used to elucidate the histogenetic origin of MSGCs, these cells showed strong reactivity only for vimentin (Figure 3). Staining for histiocytic marker (CD68), as well as for epithelial marker (cytokeratin), myoepithelial markers (S-100, α-smooth muscle actin), vascular marker (CD34), hormonal receptors (ER, PR) and HER2 in MSGCs were negative.

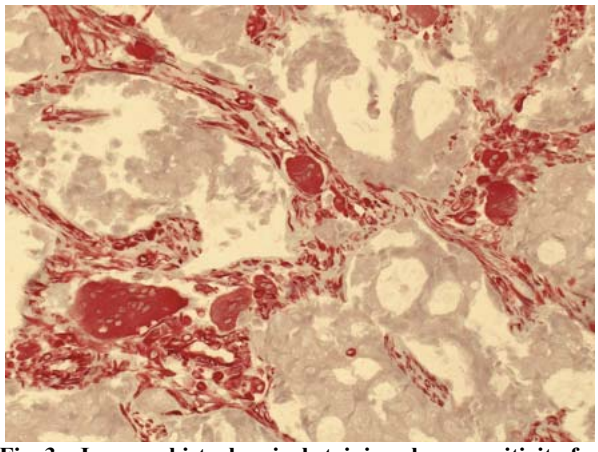

Fig. 3 – Immunohistochemical staining shows positivity for vimentin within the multinucleated stromal giant cells (APAAP, 200×)

Discussion

The presence of MSGCs in breast tumors is a phenomenon of uncertain significance. We reported herein the unusual case of a rare breast neoplasm with numerous MSGCs. To the best of our knowledge, however, no previous reports have described ACC with MSGCs, indicating that this lesion is extremely rare. Originally, Rosen described MSGCs in otherwise normal breast parenchyma [2]. In the series of 200 consecutive mastectomies for carcinoma, he observed MSGCs in nine cases. He interpreted them as a sign of probable reparative process, possibly linked to hormonal changes.

The origin of MSGCs still remains obscure. They could be derived from four different stem cells: fibroblastic, epithelial, myoepithelial and histiocytic. Berean et al. [3] thought the multinucleate giant cells in fibroadenoma were fibroblastic in nature following immunohistochemical and ultrastructural study. Ryska et al. [4] assumed the positivity of p53, in both mononuclear stromal cells and MSGCs, may play a key role in linking together these two cell types. Therefore, MSGCs could presumably originate from mononuclear stromal cells. Powell et al. [5] similarly thought they were fibrohistiocytic in origin based on the finding of a continuum of morphological features ranging from small stromal cells to the fully formed multinucleated cells. They also demonstrated positive CD34 staining of these cells in few cases. In contrast, Nielsen and Ladefoged [6] concluded that the giant cells in their case report were myoepithelial in origin, although the evidence for this was not clearly demonstrated; no immunohistochemistry confirming this hypothesis was performed.

It is difficult to explain the histogenesis of MSGCs. The results of immunohistochemistry in our case of ACC indicate that MSGCs are probably derived from stromal fibroblasts. The MSGCs were positive only for vimentin. No signs of histiocytic (CD68 was negative), epithelial (cytokratin was negative) and myoepithelial (S-100 and α-smooth muscle actin were negative) differentiation were seen in MSGCs. Also, there was no evidence about hormonal (ER and PR), or HER2 positivity in MSGCs.

MSGCs should be distinguished from other multinucleated giant cells in breast tumors, such as osteoclast-like giant cells. The majority of invasive breast carcinomas with osteoclast-like giant cells have been invasive ductal carcinoma; the most common being of the cribriforme type. Less commonly, osteoclast-like giant cells have been described in infiltrating lobular carcinomas, tubular, papillary and rarely in association with ductal carcinoma in situ [7]. Microscopically, osteoclast-like giant cells are indistinguishable from true osteoclasts and it is belived to arise from fusion of stromal cells, thus having a monocyte/macrophage origin. This finding is supported by immunohistochemistry and electron microscopy. They frequently express histiocytic markers, like CD68, α-1-antitrypsin or acid phosphatase [8,9]. The morphology of MSGCs is essentially different from osteoclasts and none of MSGCs in our case showed CD68 positivity. Other lesions that may contain multinucleated giant cells such as tuberculosis, sarcoidosis or granulomatous mastitis must be included in the differential diagnosis. The Langhans-type giant cells, as well as the foreign-body type giant cells should be readily distinguishable from MSGCs. Bizarre malignant giant cells have also been described in breast carcinomas. These giant cells are easily distinguishable from MSGCs by their pleomorphism and immunoprofile, indicating an epithelial (cytokeratin-positive) origin [8].

Conclusion

Immunohistochemical studies indicated that the MSGCs are probably derived from stromal fibroblasts. In contrast to the more aggressive behavior of salivary gland ACC, the prognosis for breast ACC is rather good, with a low incidence of lymph node invasion and of distant metastasis. The presence of MSGCs should not alter the prognosis of an otherwise typical breast ACC. This indicates the probable indolent nature of MSGCs.

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Recived on November 12, 2009.
Revised on February 2, 2010.
Accepted on April 14, 2010.