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International Journal of Surgery 12 (2014) S232–S235

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

The first case of acinic cell carcinoma of the breast within a fibroadenoma: Case report

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ARTICLE INFO

Article history:
Received 23 March 2014
Accepted 3 May 2014
Available online 22 May 2014

Keywords:
Acinic cell carcinoma
Breast cancer
Eosinophilic cytoplasmic granules

ABSTRACT

A case of acinic cell carcinoma of the breast is reported in a 26-year-old woman. She presented a lump in her right breast, that seemed to be a fibroadenoma. The open biopsy revealed a well-bordered fibroadenoma, together with a proliferation of cells characterized by serous acinar differentiation and eosinophilic cytoplasmic granules. Tumor cells stained for amylase, lysozyme, α-1-antichymotripsin, epithelial membrane antigen, S-100 protein, pan-cytokeratin, cytokeratin 7 and E-cadherin. Estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 overexpression, CD10, P63, smooth muscle actin, cytokeratin 5/6 were negative. The sentinel node was negative. 8 months after surgery she is in good clinical conditions without recurrence or metastases.

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1. Introduction

Acinic cell carcinoma (ACC) of the breast is a rare variant of mammarian neoplasm, occurring in less than 2% of cases of breast malignancies. The common embryologic origins of breast and salivary glands as tubuloacinar exocrine glands, led to similarities in pathological processes. ACC is a typical tumor of salivary glands, nevertheless other organs could be interested (stomach, pancreas, retroperitoneum, liver, lung, lacrimal glands). It is characterized by serous acinar differentiation with zymogen-type cytoplasmic granules. Immunoreactivity for amylase, lysozyme, epithelial membrane antigen (EMA) and S-100 protein can help to differentiate ACC from conventional invasive ductal carcinoma of the breast. Ultrastructural examination discloses electron dense granules similar to those seen in parotideal acinar cells. All breast ACCs described in literature since 1996 have affected women, most frequently in their 6th decade of life, and presented as palpable nodules, measuring 2–5 cm, with the right side being more commonly affected. The prognosis of ACC of the breast appears to be good, even if both recurrences and metastases were reported [1–3].

Previous cases of ACC have been associated to microglandular adenosis, invasive or intraductal carcinoma [4–10]. We report the first case of ACC of the breast arising in a fibroadenoma.

2. Case report

A 26-year-old Italian woman who had a lump in her right breast was admitted to our Department for further assessment. She had discovered the mass through self-palpation and felt very anxious. She did not have a familial history of breast or other cancers, and denied any relevant comorbidity. She had had two pregnancies, without breast-feeding. Physical examination revealed a well-demarcated, hard, smooth, mobile, indolent mass at the union of lower quadrants of the breast, approximately 2.5 cm in diameter, with regular margins. The nipple and the skin overlying the mass were normal. No dimpling or palpable axillary and supraclavicular lymph nodes were detected. Results of laboratory tests were all within the reference range. According to the young age she underwent breast ultrasonography, showing a nodular hypoechoic mass, with an ill-defined margin, measuring 2.3 × 2.1 × 1.3 mm, that seemed to be a simple fibroadenoma. We suggested to remove the lump in order to better define its nature. The open biopsy was performed after local anesthesia and the sample was sent to the definitive pathologic examination for diagnosis.

Macroscopically, the specimen was a 3 × 1.6 × 1.5 mammary tissue with a 1.6 × 1.2 × 1 cm, white-pink-colored and hard-elastic

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http://dx.doi.org/10.1016/j.ijsu.2014.05.005
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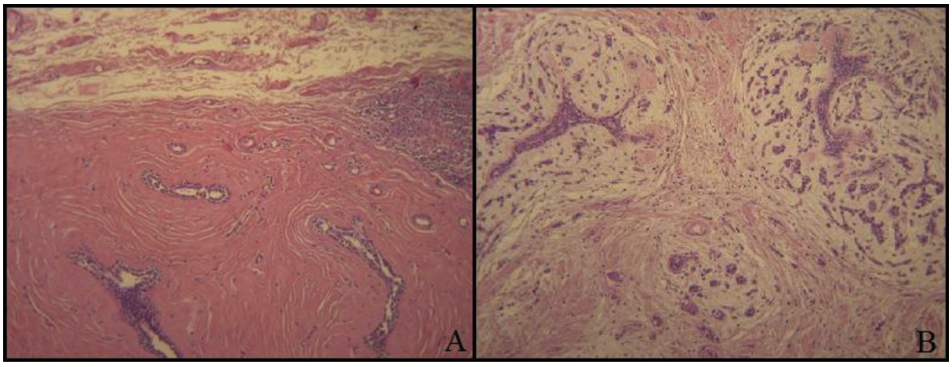

Fig. 1. Panoramic view showing in A. part of a well-bordered a partially capsulated fibroadenoma with fibro-sclerotic stroma and in B. a few acinic neoplastic cells growing within the fibroadenoma.

nodular lesion. Histologically it was a very particular and surprising discovery (Figs. 1 and 2). The most of the lesion was a well-bordered and partially capsulated fibroadenoma with fibro-sclerotic stroma. The near tissue showed several aspects. The first interesting evidence was a proliferation of cells characterized by serous acinar differentiation, polygonal shape, round and often eccentric nuclei with granular chromatin and small nucleoli, large, coarse and bright red cytoplasmic granules resembling zymogen granules of the acinar cells of the salivary gland. These cells were organized in an acinic-glandular or ductal-like pattern, rounded by a fine strip of collagen, or they followed an infiltrating growth pattern with solid and trabecular features in the surrounding stroma and mixoid tissue. Part of the acinic cells showed a more clear and sometimes vacuolar cytoplasm that seemed to form an acinic cell adenocarcinoma, more frequent in salivary glands. The second finding in the smaller part of the tumor was composed by less differentiated cells, organized in cords and aggregates, with atypical and pleomorphic nuclei, focal adeno-squamous metaplasia. These cells showed a wide infiltration of surrounding sclerotic stroma. In addition to these components a lymphoid infiltration of the stroma characterized the tumor, with the spreading of plasmacells. The tumor was present focally on the excision margins. Immunohistochemically, most of the tumor cells stained strongly for amylase, lysozyme, α-1-antichymotripsin (α-1-ACT), epithelial membrane antigen (EMA), S-100 protein, pan-cytokeratin, cytokeratin 7 (CK7) and E-cadherin. Estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 overexpression (HER2/neu) were negative. Myoepithelial markers

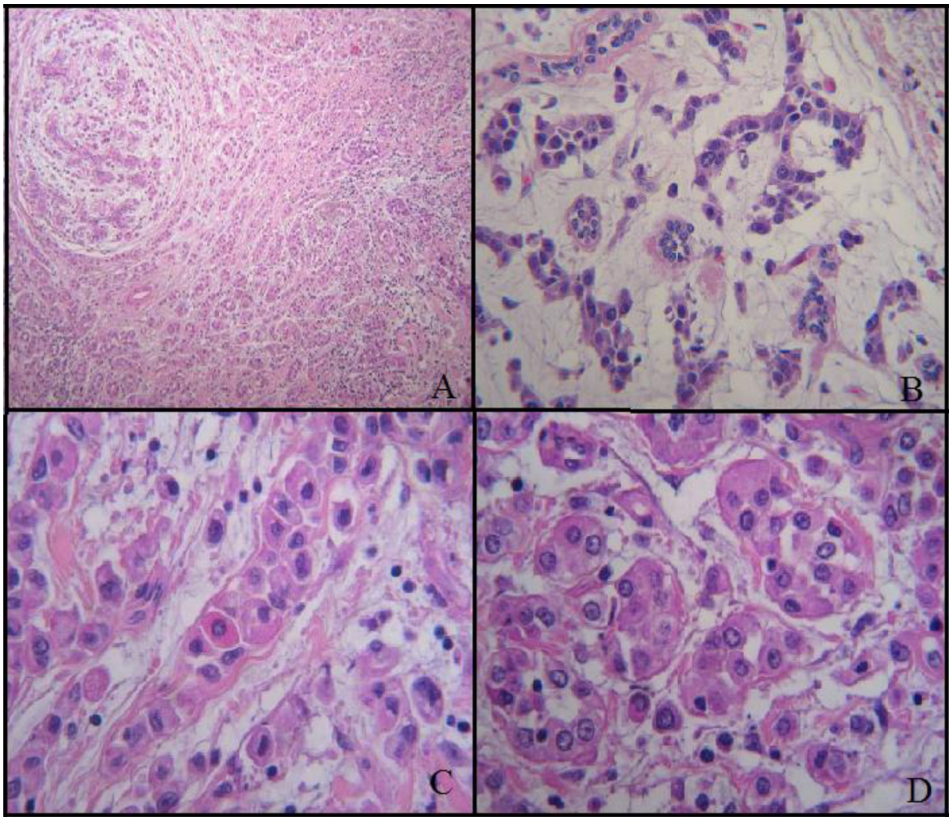

Fig. 2. Hematoxilin and eosin stain showing in A. 200× and B. 400× acinic cells organized in glandular or ductal-like pattern, rounded by a fine strip of collagen, occasionally infiltrating the surrounding stroma; in C-D. 600× ma proliferation of cells characterized by serous acinar differentiation, polygonal shape, round and often eccentric nuclei with granular chromatin, coarse and bright red cytoplasmic granules.

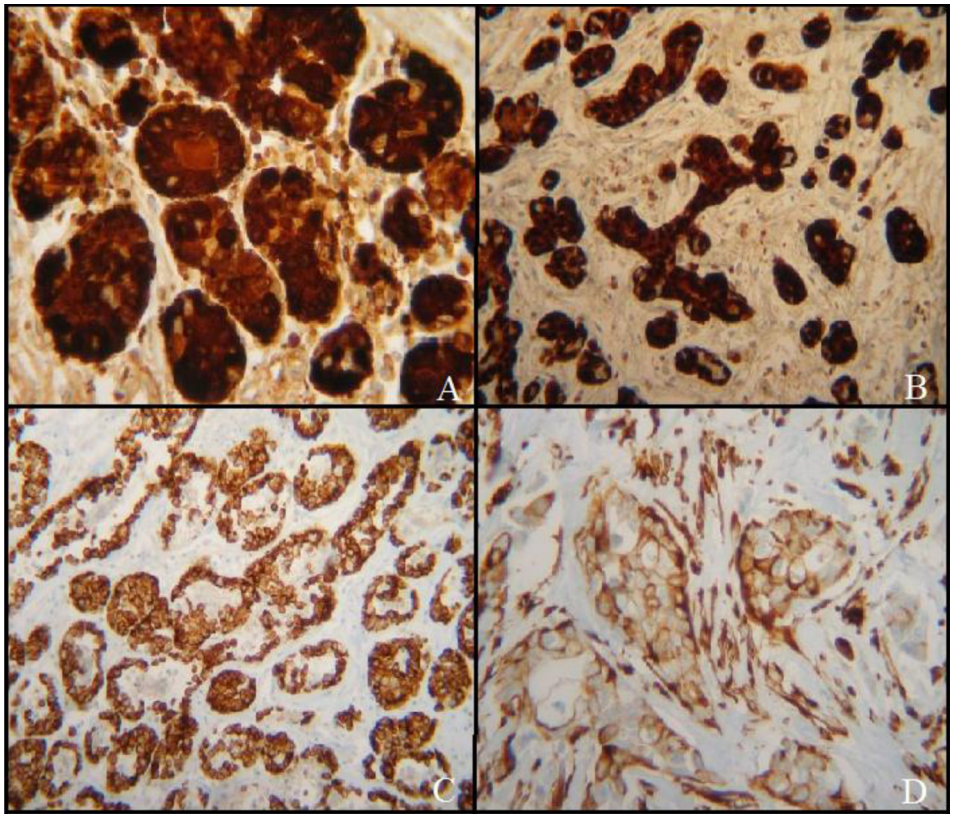

Fig. 3. Immunohistochemical findings showing immunoreactivity to A. lysozyme, B. S-100, C. cytokeratin 7, D. vimentin only in less differentiated cells.

CD10, P63, smooth muscle actin (SMA), cytokeratin 5/6 were negative too. The vimentin was focally positive in less differentiated cell cords (Fig. 3). The endothelial marker CD31 was negative, thus granting no lympho-vascular invasion. The proliferation index ki-67 was difficult to establish univocally, because it varies from an area to another, resulting more intense in the acinar component. The discovery of an acinic cell adenocarcinoma did not allow us to understand if the carcinoma was born within the fibroadenoma or successively infiltrated the fibroadenoma.

This histopathological diagnosis led us to perform further surgery in order to ensure clear margins and to assess the nodal status. Three weeks after the biopsy the patient underwent re-excision on the tumor bed and axillary sentinel node biopsy after preoperative lymphoscintigraphy.

The specimen consisted of 3 × 3.4 × 0.8 mammary tissue overlying skin ellipse with the previous 2 cm surgical scar and two sentinel nodes, measuring 1.2 and 0.5 cm. On cut section the mammary tissue resulted of lobular aspect and with-yellowish color. The two Sentinel nodes were pinkish and round and free from metastasis, showing morphological features of aspecific reactive hyperplasia. Breast parenchyma was site of adenosis, steatonecrosis and chronic inflammatory infiltrate, without any residual neoplasia.

No intra- and/or postoperative complications occurred. The patient was followed until the surgical wounds required medications. Then she consulted oncologists, but no further therapy was suggested. Eight months after diagnosis she is in good clinical conditions, undergoing periodical follow-up. No recurrence or metastases have occurred.

A written consent approved by Ethical Committee was obtained from the patient to the use of her biological samples for research purpose.

3. Discussion

ACC was first described in breast by Roncaroli et al. in 1996 [1], than several case reports have been published [3–24]. It is difficult to diagnose this tumor preoperatively, because serous acinar differentiation is often combined to invasive breast carcinoma or ductal carcinoma in situ. Otherwise ACC often simulates benign lesions with well-defined opacity at mammography or a regular hypoecoic mass at ultrasound [6,8]. In some cases fine needle cytology (FNC) could dictate or suggest the diagnosis showing atypical cells with granular eosinophilic cytoplasm and round nuclei [10,11,20]. In our case we decided to perform an open biopsy in agreement with the patient, who wanted her lump to be removed.

Our case present the third youngest patient described in literature and is the only one showing an association with a fibroadenoma. Even if its true origin in or out from the fibroadenoma remains unclear. Our case showed an extensive infiltration of the sclerotic stroma forming the fibroadenoma. No true fibrous capsule was formed, but only a thin collagen stripe surrounding more differentiated acinic cells was evident. Immunohistochemical features are similar to other reported cases, it showed a common absence of hormonal receptor and myoepithelial differentiation. Nevertheless an uncommon positivity for pan-cytokeratin, cytokeratin 7, E-cadherin and focally for vimentin was observed. Surgical and adjuvant treatment is not standardized in literature. We followed guidelines for invasive breast carcinoma and no further therapy was suggested by oncologists according to tumor biology.

4. Conclusion

ACC of the breast is a very rare entity. Currently, there are no characteristic imaging findings and definitive diagnosis relies on

immunohistochemistry, so only a histological sample could result diriment. Its similarity to salivary counterparts and previous reports suggest a good prognosis. Nevertheless recurrence and metastases have been described. Our case is the first ACC arising in a fibroadenoma. It showed an infiltrating pattern, but the direction towards or far from the benign lesion was unclear. We believe that treating a tumor similar to salivary ACC counterpart as a breast carcinoma only because it arises in breast could not be the most correct solution. In order to elucidate the biological features of the ACC of the breast and define a protocol of treatment, further studies are required.

Funding

All Authors have no source of funding.

Ethical approval

Ethical approval was requested and obtained from the University of Naples Federico II ethical committee.

Conflicts of interest

All Authors have no conflict of interests.

Author contribution

Limite Gennaro: Participated substantially in conception, design, and execution of the study and in the analysis of data, reviewing the manuscript.

Di Micco Rosa: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Esposito Emanuela: Participated substantially in the analysis and interpretation of data, reviewing the manuscript.

Sollazzo Viviana: Participated substantially in the analysis and interpretation of data.

Cervotti Maria: Participated substantially in the analysis and interpretation of data.

Pettinato Guido: Participated substantially in analysis and interpretation of pathologic and immunohistochemical data; he also contributed to edit tables.

Varone Valeria: Participated substantially in analysis and interpretation of pathologic and immunohistochemical data; she also contributed to edit tables.

Benassai Giacomo: Participated substantially in the analysis and interpretation of data.

Monda Angela: Participated substantially in reviewing the manuscript.

Luglio Gaetano: Participated substantially in reviewing the manuscript.

Maisto Vincenzo: Participated substantially in the analysis and interpretation of data.

Izzo Giuliano: Participated substantially in the analysis and interpretation of data.

Forestieri Pietro: Participated substantially in reviewing the manuscript.

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