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Case report

Primary acinic cell carcinoma of the breast associated with an intraductal acinic cell component

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RESUMEN

Por primera vez se comunica un caso de carcinoma de células acinares infiltrante primario en una paciente anciana asociado con un componente intraductal, el cual también estaba constituido de células tumorales de tipo acinar. La positividad de ambos componentes para lisozimas excluyó otras lesiones mamarias primarias o metastásicas que simulan carcinoma de células acinares. Su asociación con una lesión precursora de bajo grado de malignidad puede explicar el buen pronóstico de esta lesión.
Palabras clave: mama, carcinoma, carcinoma de células acinares, lisozima.

ABSTRACT

We present for the first time a case of primary infiltrating acinic cell carcinoma in an elderly patient associated with an intraductal component, which was also composed of tumor cells of acinic type. The positivity of both components for lysozyme excluded other either primary or metastatic breast lesions mimicking acinic cell carcinoma. Its association with a precursor lesion of a low grade of malignancy may explain the good prognosis of this lesion.
Key words: breast, carcinoma, acinic cell carcinoma, lysozyme.

Acinic cell carcinoma (ACC) represents a rare variant of mammary neoplasm, similar to a comparable tumor occurring in the salivary glands.[1] It was first described in the breast in 1996 by Roncaroli and named acinic cell-like breast carcinoma.[2] Since then, only eleven cases of this entity have been published, all of them corresponding to the infiltrative type but nevertheless associated with a favourable prognosis.[3-9] We present here, a case of primary ACC in an elderly patient that, for the first time, was associated with an intraductal component of acinic type. The association with a precursor lesion of a low grade of malignancy may explain the usual good prognosis of this lesion.

CASE REPORT

A 79-year-old patient was admitted for a painless tumor in the left breast that was identified through self-palpation and was situated in the supero-external quadrant. Previous ultrasound and mammographic examinations supported the diagnosis of a malignant lesion which was confirmed in the frozen section. As a result, a total left mastectomy with axillary lymphadenectomy was carried out.

Macroscopic examination revealed a 2.5 x 2cm a yellow-grey solid tumor, with an irregular outline and infiltrative margins. Its consistency was uniformly hard. The surrounding breast tissue was unremarkable. Fifteen lymph nodes were identified in the axillary fat.

Microscopically, the tumor was invasive of both stroma and lymphatic vessels and had a variable histol-

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En homenaje al Dr. Mario A Luna, quien tanto contribuyó al conocimiento de este tumor en las glándulas salivales.

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ogy, revealing solid, microcystic, microglandular and trabecular areas. Its cells, however, were monotonous, had distinct borders and presented abundant cytoplasm with fine eosinophilic granulations. In areas, a multivacuolated cytoplasmic change resembled lipoblasts. Nuclei were oval or round and had minimal pleomorphism and prominent nucleoli. The mitotic activity was variable, with 3-5 mitoses/10 HPF.

There were also intraductal areas of cribriform, micropapillary and solid type, also composed of cells with eosinophilic intracytoplasmatic granulations and minimal atypicality. This intraductal component lacked areas of necrosis. Ten out of the fifteen axillary lymph nodes examined presented with metastases.

Immunohistochemistry was performed using the following antibodies: ER (estrogen receptor), PR (progesterone receptor), AR (androgen receptor), GCDFP-15 (gross cystic disease fluid protein- 15), cytokeratin 8, 18, 5/6, beta-catenin, lysozyme, HER2/neu (human epidermal growth factor receptor 2), E-cadherin (all prediluted, Master Diagnostica, Granada, Spain) and bcl-2 (Dako, 1/50 dilution). Their intracytoplasmatic granulations were PAS positive. Cells displayed positivity for PR and AR but were negative for ER. They were also positive for CK 8, CK 18, GCDFP-15, e-cadherin (membranous), β-catenin (membranous) whilst they were negative CK 5/6, bcl 2 and HER2. Lysozyme was positive in both intraductal and infiltrative components (Table 1). This immunophenotype was consistent with an infiltrating primary acinic cell carcinoma of the breast metastatic to 10/15 axillary lymph nodes and associated with an acinic cell intraductal component.

The patient did not undergo any further treatment and 9 months after surgery, she is alive and well without local recurrence or distant metastases.

Table 1. Immunophenotype of both intraductal and invasive areas

Antibodies	*Intraductal component*	*Infiltrative component*
ER	-	-
PR	+	+
AR	+	+
GCDFP-15	+	+
CK 8	+	+
CK 18	+	+
CK 5/6	-	-
Beta-catenin	+	+
Lysozyme	+	+
HER2/neu	-	-
E cadherin	+	+
Bcl-2	-	-

DISCUSSION

The mammary and salivary glands share many histological similarities and consequently, some types of tumor may originate indistinctively in either tissue. Breast tumors of salivary gland type can be with and without myoepitelial differentiation. The latter ones have only been described recently and are included in the WHO 2003 classification as distinct entities such as acinic cell carcinoma, oncocytic carcinoma and mucoepidermoid carcinoma.[10]

Acinic cell carcinoma of the breast is a rare tumor, characterized by serous acinic differentiation, represented by the presence of tumor cells with zymogen-type granules in the cytoplasm. Initially, it was described by Roncaroli in 1996 in a 42-year-old patient, where its cells were positive for lysozyme and salivary-type amylase and contained electron-dense cytoplasmatic globules, similar to those found in carcinoma of the parotid gland.[2] This patient had a single metastasis in the axillary lymph nodes and after a year, she presented a favorable evolution. Subsequently, 10 other cases of acinic cell carcinoma (ACC) of the breast have been reported; all of them associated with an infiltrative component but in the majority, they had a favorable prognosis.

Acinic cell carcinomas of the breast occur in the 6th decade of life and their size varies from 2 to 5cm in diameter, having usually well-outlined margins, although sometimes they can be infiltrative. Microscopically, the tumor is arranged in either solid, trabecular or microcystic patterns which can be similar to classical infiltrative ductal carcinoma but with a different cellular component. Similar microglandular areas can be found in adenosis which can also contain a luminal colloid-like eosinophilic material. They are surrounded by a layer of epithelial cells without atypia that have a recognizable basement membrane. In contrast, in ACC atypia is present and a basement membrane is absent. Both microglandular adenosis and the ACC are positive for S-100 protein; the latter is however, negative for lysozyme.

Acinic cell carcinoma cells characteristically contain an abundant cytoplasm with positive PAS granulations corresponding to zymogen granules and round, uniform

nuclei that are centrally situated and have clear eosinophilic nucleoli. Rarely, the tumor may present bizarre cells with pleomorphic nuclei and numerous mitotic figures. This aspect involves differential diagnoses with other breast carcinomas displaying cells with granular cytoplasm such as apocrine carcinoma, in which the tumor cells have eosinophilic granular cytoplasm and marked nuclear pleomorphism and are usually positive for GCDFP15 and AR but negative for ER, PR and lysozyme. Oncocytic carcinoma contains cytoplasmic granules negative for lysozyme corresponding to mitochondria. Sometimes, however, acinic cell carcinoma (ACC) can have cells with a clear vacuolated cytoplasm, which can lead to confusion with lipid-rich cell (Sudan-positive) or glycogen-rich (PAS-positive) carcinomas; however, in both instances, again, lysozyme is negative.

Finally, breast carcinomas treated with preoperative chemotherapy may present important modifications that include the presence of the cytoplasmatic vacuoles.[7,11]

In all cases, ACC is immunohistochemically positive for alpha-1-antitrypsin, alpha-1-antichymotrypsin, anti-lysozyme and anti-amylase. This immunophenotype is crucial in differentiating this tumor from its other mimics.

Cytogenetically, ETV 6 rearrangement is absent from the ACC of the breast whereas they are present in the secretory carcinoma, this one displaying t(12;15) ETV6-NTRK3 translocation, proving that indeed, the two lesions represent different entities.[12]

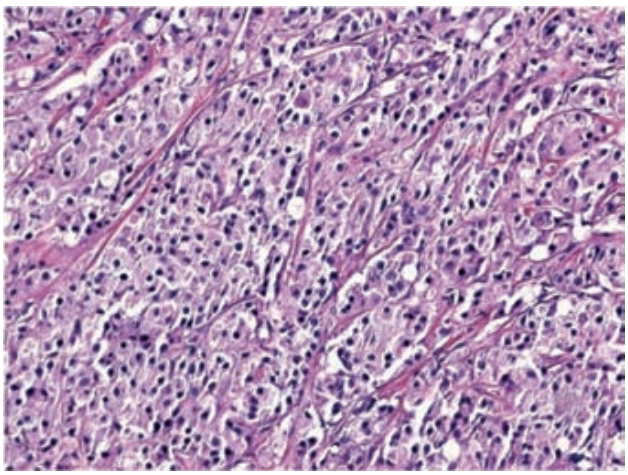

Figure 1. Solid type of intraductal component composed by granular eosinophylic cytoplasm cells; same cells are observed in the infiltrating component. Color figures of this article appear in the appendix 6 of this issue.

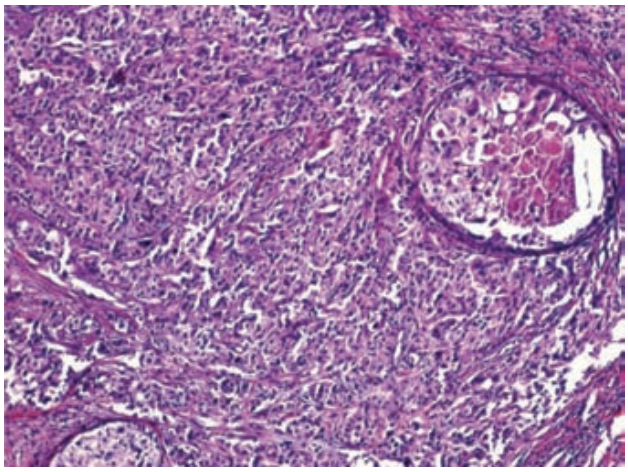

Figure 2. Tumor cells in the infiltrating component with distinct borders and abundant cytoplasm with fine eosinophilic granulations.

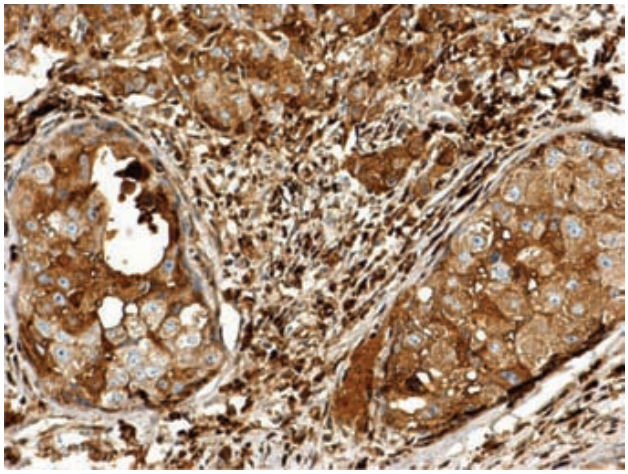

Figure 3. The tumor cells from both intraductal and infiltrating component are positive for lysozyme.

Metastatic origin of the tumor has to be excluded (salivary gland, kidney, pancreas) however, in this case its association with an intraductal component with granular cytoplasm was of great help. The differential diagnoses mentioned above are summarized in Table 2.

Whilst ACC has a good prognosis in the salivary glands, in the breast it has a debatable one, especially due to the small number of cases published to date.[13] Roncaroli et al, Schmitt et al, as well as Damiani reported a good survival associated with the tumor.[2,5,8] On the other hand, Coyne reported in 2002 a case of ACC of the breast in a 49-year-old patient who died after three years with multiple hepatic metastases.[7] In this case, unfavorable prognosis

Table 2. Differential diagnoses of ACC with other lesions

Type of lesion	*Morphologic and genetic features*	*Immunohistochemical pattern*
Classic infiltrative ductal carcinoma	Similar architecture, different cellular component	Lysozyme negative
Microglandular adenosis	Microglandular areas, epithelial layer present without atypia, basement membrane present	Lysozyme negative
Apocrine carcinoma	Eosinophilic granular cytoplasm, pleomorphic nuclei	GCDFP-15 positive, AR positive, ER and PR negative, lysozyme negative
Oncocytic carcinoma	Intracytoplasmatic granules (mitochondria)	Antimitochondrial Ab positive, lysozyme negative
Lipid-rich cell carcinoma	Clear vacuolated cytoplasm, Sudan positive	Lysozyme negative
Glycogen-rich cell carcinoma	Clear vacuolated cytoplasm, PAS positive	Lysozyme negative
Secretory carcinoma	Similar architecture with granular eosinophilic cytoplasm, ETV 6 rearrangement	Lysozyme positive
Chemotherapy treated-carcinoma	Cytoplasmic vacuoles	Lysozyme negative
Metastasis	Granular cytoplasm, absence of intraductal component	Lysozyme positive

was related to high cellular grade and both a high mitotic rate and tumoral vascular emboli.

In the present case, the hitherto unreported existence of an intraductal low-grade component with cells of acinic type, with morphological and immunohistochemical features similar to those of the infiltrative type, may suggest that this tumor develops from a precursor lesion of intraductal type and this may be related with a good prognosis. However, the high frequency of axillary metastases is worrying and should determine a guarded prognosis.

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REFERENCES

1. Batsakis JG, Luna MA, el-Naggar AK. Histopathologic grading of salivary gland neoplasms: II. Acinic cell carcinomas. Ann Otol Rhinol Laryngol 1990;99:929-933.
2. Roncaroli F, Lamovec J, Zidar A, Eusebi V. Acinic cell-like carcinoma of the breast. Virchows Arch 1996;429:69-74.
3. Tanahashi C, Yabuki S, Akamine N, Yatabe Y, Ichihara S. Pure acinic cell carcinoma of the breast in an 80- year-old Japanese woman. Pathol Int 2007;57:43-46.
4. Elster EA, Markusic J, Ball R, Soballe P, et al. Primary acinic cell carcinoma of the breast. Am Surg 2002;68:993-995.
5. Damiani S, Pasquinelli G, Lamovec J, Peterse JL, Eusebi V. Acinic cell carcinoma of the breast: an immunohistochemical and ultrastructural study. Virchows Arch 2000;43:74-81.
6. Hirokawa M, Sugihara K, Sai T, Monobe Y, et al. Secretory carcinoma of the breast: a tumor analogous to salivary gland acinic cell carcinoma? Histopathology 2002;40:223-229.
7. Coyne JD, Dervan PA. Primary acinic cell carcinoma of the breast. J Clin Pathol 2002;55:545-547.
8. Schmitt FC, Ribeiro CA, Alvarenga S, et al. Primary acinic cell-like carcinoma of the breast-ma variant with good prognosis? Histopathology 2000;36:286-289.
9. Peintinger F, Leibl S, Reitsamer R, Moinfar F. Primary acinic cell carcinoma of the breast: a case report with long-term follow-up and review of the literature. Histopathology 2004;45:645-648.
10. Tavassoli FA, DeVilee P. Pathology and genetics of tumors of the breast and female genital organs. IARC Press Lyon, 2003.
11. Kennedy S, Merino MJ, Swain SM, et al. The effects of hormonal and chemotherapy on tumoral and non neoplastic breast tissue. Hum Pathol 1990;21:192-198.
12. Reis-Filho JS, Natrajan R, Vatcheva R, Lambros MB, et al. Is acinic cell carcinoma a variant of secretory carcinoma? A FISH study using ETV6 split apart probes. Histopathology 2008;52:840-846.
13. Seifert G, Broucheriou C, Cardesa A, Everson JW. WHO international histological classification of tumors. Tentative histological classification of salivary gland tumors. Pathol Res Pract 1990;186:555-581.