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clinical practice

Axillary lymph node metastases in adenoid cystic carcinoma of the breast. A rare finding

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SUMMARY: **Axillary lymph node metastases in adenoid cystic carcinoma of the breast. A rare finding.**

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Adenoid cystic carcinoma (ACC) of the breast is a rare malignant salivary-type neoplasm that has a good prognosis and represents less than 1% of all breast cancers. It is a triple negative carcinoma that presents as a painful mass. The mean age at the time of diagnosis is 50-60 years old. The solid variant of this type of tumour with basaloid features and presence of nodal metastases is very rare and considered to have a more aggressive clinical course. We present a case with presence of axillary lymph node metastases that was successfully treated with no evidence of recurrence one year after the diagnosis and review the literature.

KEY WORDS: Adenoid cystic carcinoma - Solid variant - Basaloid - Breast - Mammary - Immunohistochemistry - Lymph node metastases.

Introduction

Adenoid cystic carcinoma (ACC) was first described by Billroth in 1856 and was characterised as cylindroma (1). Geschickter and Copeland refer to adenocystic basal cell cancer of the breast in 1945, acknowledging its eccrine gland origin and slow growth (2). It is a malignant tumor with very low incidence (0.1% of all breast carcinomas) (3) and it is histologically indistinguishable from ACC arising from other sites. Being a basaloid tumor, it is hormone (estrogen and progesterone) receptor negative, it does not express human epidermal growth factor receptor 2 (Her2) and expresses one or more basal/myoepithelial cell markers (CKs 5, 5/6, 14 and 17) (4). The mammary ACC has got an excellent prognosis, unlike other triple-negative breast cancers, due to the fact that it has a biological course that is slower than the extramammary ACC and does not present commonly with lymph node or distant metastases (5, 6). The solid variant of ACC though, is a rare high grade variant that occasionally gives rise to metastatic disease and has a more aggressive clinical course both in the salivary glands (7-9) and the breast (10-12). Having a favorable prognosis and distinct clinicopathologic characteristics, it is important to mention the significance of an accurate differential diagnosis of mammary ACC. The possibility of metastases can influence the radicality of surgery and the approach to adjuvant treatment. We present a rare case of a solid variant of adenoid cystic carcinoma of the breast with presence of axillary lymph node metastases.

Case report

A 52-year-old woman presented with a subarachnoid haemorrhage that was treated with clip surgery. During her assessment, a large palpable mass was identified in her right breast. Appearances were those of a large locally advanced breast cancer. On subsequent imaging (mammography) a 55mm dense mass with associated skin thickening was identified behind the right nipple. No nodes were palpated in the ipsilateral axilla. The left breast was normal. Computed tomography (CT) scan of thorax, abdomen and pelvis as well as bone scan, were unremarkable. Core needle biopsy confirmed the presence of invasive adenocarcinoma, with features raising the possibility of a salivary gland type tumour. The tumour was negative for oestrogen, progesterone and HER-2 antibodies (triple negative).

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A right modified radical mastectomy with accompanying level 3 axillary clearance was performed after discussion in the multidisciplinary oncology meeting.

The specimen sent to the histology lab measured 240 x 180 x 90mm with axilla extending 170 x 120mm and attached nipple bearing ellipse of skin measuring 230 x 150mm. On sectioning, there was a central tumour measuring 60 x 60 x 40mm that was ulcerating through the nipple. The rest of the breast parenchyma was largely unremarkable. Apical tissue was received separately.

On microscopy, the tumour was composed of a nested proliferation of basaloid cells with granular chromatin pattern and visible eosinophilic nucleoli (Figure 1). Occasional pseudoglandular spaces were also present that appeared to contain Alcian Blue reactive material and were lined by larger epithelioid cells with eosinophilic cytoplasm. Occasional mitotic figures were noted. On immunohistochemistry, tumour cells were strongly positive for CK7 and CD117 and negative for CK20, CD56, chromogranin, synaptophysin and p63. There was focal immunoreactivity for SMA immunostain, being indicative of myoepithelial differentiation. The tumour was involving the overlying epidermis (pT4) (Figure 2). There was no definite in-situ component or lymphovascular invasion, but a single focus of perineural invasion was present. Two out of a total of eighteen axillary lymph nodes were involved by metastatic tumour with focal extracapsular extension (Figure 3).

Overall morphological and immunohistochemical appearances were those of a solid variant of adenoid cystic carcinoma of the breast. Negativity for neuroendocrine markers excluded the possibility of a neuroendocrine carcinoma.

Adjuvant chemotherapy and radiotherapy was administered to the patient. There was no clinical or radiological evidence of recurrence 12 months after treatment.

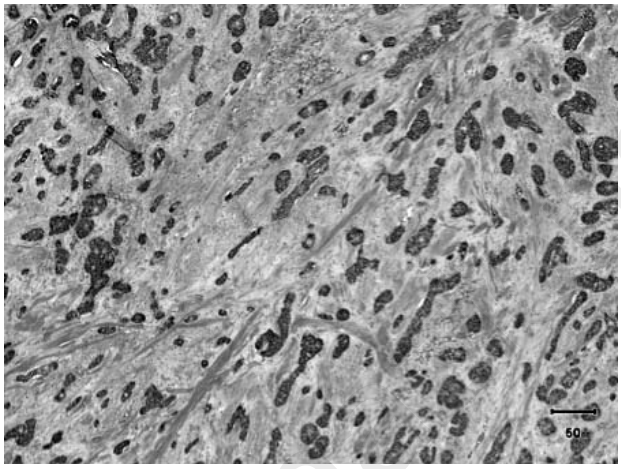

Fig. 1 - H&E x40. Tumour composed of nested proliferation of basaloid cells, embedded within desmoplastic stroma.

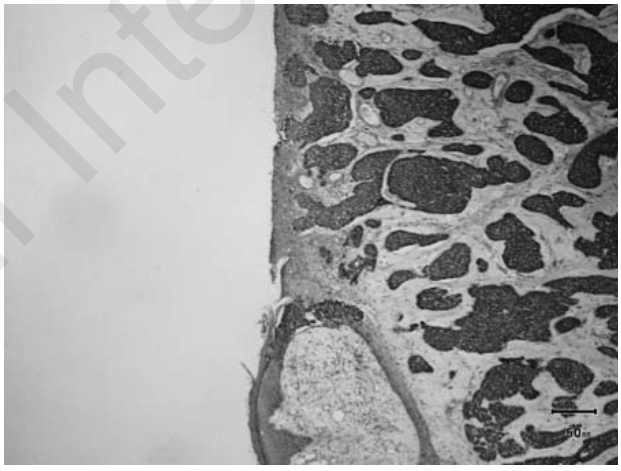

Fig. 2 - H&E x40. Tumour infiltrating and ulcerating overlying epidermis (pT4).

Discussion

Adenoid cystic carcinoma of the breast is a rare subtype representing less than 0.1% of the cases of breast carcinoma (13). It occurs mainly in women during their 6th decade (Table 1), but has been described between the ages of 30 and 90 years. It does not show any predilection for a particular side and is rarely bilateral (14). Mammary ACC rarely involves the axillary lymph nodes (frequency of 0-2% according to most authors but even up to 15% in small case series) (15) and can spread to distant sites without first involving local axillary lymph nodes (6, 16). Distant metastases most commonly involve the lungs (6, 16). Perineural invasion is also rare, unlike salivary ACC, reported in up to 8% of cases (5). Sumpio et al. (17) reviewed 120 cases from the literature and

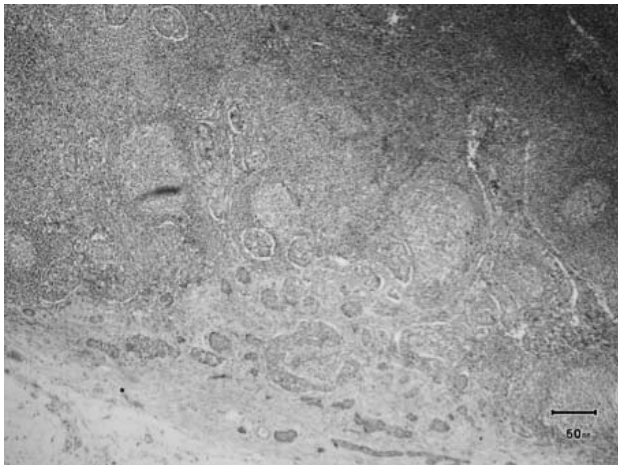

Fig. 3 - H&E x40. Lymph node involved by metastatic tumour.

TABLE 1 - PUBLISHED CASE SERIES OF ADENOID CYSTIC CARCINOMA OF THE BREAST.

Case series	Patients (no)	Mean age (years)	Tumour stage (T3 – T4)	Lymph node involvement	Distant metastases	5-year survival
Sumpio et al. 1987 (17)	14	64	No	No	No	64.2%
Arpino et al. 2002 (18)	28	66	3.6%	Axillary 4%	3.5%	85%
Coates et al. 2010 (35)	376	62	5.6%	4.3%	1%	90%
Ghabach et al. 2010 (36)	338	63	5%	Unknown	Unknown	98.1%
Defaud-Hénon et al. 2010 (37)	30	60.7	Unknown	10 axillary 2 Sentinel All negative	3 local recurrences 3 metastatic events	100%
Thompson et al. 2011 (38)	244	61.9	2.9%	Not present in tumors <1.4 cm	2.9%	95.6%
Khanfir et al. 2012 (39)	61	59	No	No	No	94%
Vranic et al. 2013 (40)	20	61	10%	No	20%	90%
Franzese et al. 2013 (15)	13	51	No	15%	7.7%	100%

showed lymph node metastases in only four cases, and distant metastases in only eight cases, the majority of which occurred in the lung. Arpino et al. (18) noted that in four out of 182 cases, lymph node metastases were present, and only 14 cases developed distant metastases ten years after surgical treatment. The 5-year survival rate for ACCs of the breast is reported in various case series to be 85-90% (Table 1), with a 100% disease-free survival rate (19).

Histologic growth patterns originally described in the salivary gland (20) have also been used to subtype these tumors in the breast. These are: cribriform, solid, glandular (tubular), reticular (trabecular), and basaloid growth patterns (21). ACC has been divided into three groups according to the proportion of solid growth (I: no solid elements; II: <30% solid; III: >30% solid) (11). Solid variants tend to be larger in size and present with recurrences more frequently. The histologic growth pattern is associated with prognosis in breast ACC and solid variants are more aggressive clinically, according to various reports (10, 11). The presence of basaloid features is also associated with a less favorable outcome (22). As a result, mammary ACC that has got solid or basaloid characteristics can be considered a "high-grade" tumor.

Despite been a "high grade tumor", the majority of women diagnosed with solid type mammary ACC, do not develop recurrences on follow-up (23-25). Kleer and Oberman (23) reported that five patients with the solid variant of mammary ACC were free of disease 2-13 years after diagnosis. In our case, the patient was free of disease 12 months after treatment. Rare examples with a predominantly basaloid growth pattern have also done well (26).

Differential diagnosis of ACC arising in the breast is a very sensitive issue since it can influence planning of both surgical and adjuvant treatment. It depends on the predominant tumor growth pattern. Well-differentiated ACC of the breast must be differentiated from cribriform and mucinous carcinoma and collagenous spherulosis. Mucinous carcinoma can be considered in some cases because some mammary ACCs have particularly abundant, myxoid stroma. Collagenous spherulosis is a structural alteration seen in benign lesions and rarely is associated with in situ carcinoma.

Mammary ACC with a predominantly solid architecture must be distinguished with the use of immunohistochemistry from small cell carcinoma, metaplastic carcinoma, solid papillary carcinoma and lymphoma. Glandular structures that resemble intercalated ducts are more apparent in low-grade mammary ACC than in solid or basaloid variants. These are a frequent component of various types of tumors that arise in the salivary glands including mixed tumor and ACC.

In our case, the tumor was not reactive to estrogen and progesterone (ER, PR) receptors, as it happens with conventional mammary ACC (27). It did not show 3+ cell membrane staining intensity for HER2/neu in >10% of tumor cells.

In terms of imaging, mammary ACC could be distinguished due to its different characteristics. Some studies (28-31) have found that these tumors appeared as ill- to well-defined masses. Tsuboi et al. (31) reported that mammary ACC could be distinguished from conventional types of breast carcinoma by dynamic MRI. Santamaria et al. (30) discovered that the majority of carcinomas were located in the upper quadrant of the breast or in the area of the areola. ACC may present as a cir-

cumscribed lobulated nodule in mammography. When the limits of the nodular shadow were not clear, microscopic invasion was usually present (30). Our case did not present these characteristics though.

Presence of metastases in the lungs has been reported, especially after local recurrence has been identified (6, 16). Local recurrence may present in the breast after lumpectomy, especially when the excised specimen's margins are infiltrated with tumor. As is the case with conventional ACC, our case showed perineural invasion.

The optimal treatment of ACC of the breast has not yet been determined due to its low incidence. In the literature several surgical treatment modalities have been proposed, ranging from a simple lumpectomy without radiotherapy to a radical mastectomy. The higher the radicality of the procedure the higher is the risk of physical and psychological consequences to the patient. McClenathan et al. (32) suggested that even limited lymph node dissection was unwarranted. Instead, simple mastectomy has been widely used and is the preferred method of approach by many surgeons. On the other hand, simple lumpectomy is associated with unacceptably high rates of local recurrence. Wang S. et al. (33) are suggesting a combination of lumpectomy with adjuvant systemic chemotherapy or local radiotherapy. They recommend simple lumpectomy for grade I tumors, simple mastectomy for grade II tumors and mastectomy with axillary clearance for grade III tumors.

The utility of adjuvant radiotherapy after excisional biopsy has not been well documented for mammary ACC. However, reports have stated that ACC of other sites (34) have been controlled locally with radiotherapy.

Conclusion

In conclusion, the solid variant of ACC is a rare form of breast carcinoma reported to have a more aggressive clinical course than conventional mammary ACC. We have described a case of solid variant mammary ACC, which has a striking basaloid appearance and presented with axillary lymph node metastases. Our patient did not have local or systemic recurrence. It is of fundamental importance to accurately differentiate this type of mammary ACC in order to plan treatment. The diagnosis can be made with the use of the specific histological, immunohistochemical and imaging characteristics that this type of tumor seems to possess. Clinicians should consider including axillary lymph node staging in their primary approach of these cases.

Conflict of interest

The Authors declare that there is no conflict of interests regarding the publication of this article.

References

1. Billroth T. Untersuchungenüber die Entwicklung der Blutgefäßenebst Beobachtungenaus der Königlichenchirurgischen Universitäts-Klinikzu Berlin (Google eBook). Reimer;1856.
2. Geschickter CF, Copeland MM. Diseases of the breast: diagnosis, pathology, treatment. J.B. Lippincott; 1945.
3. Law YM, Quek ST, Tan PH, Wong SL. Adenoid cystic carcinoma of the breast. Singapore Med J. 2009;50(1):e8-e11.
4. Rakha EA, Elsheikh SE, Aleskandarany MA, Habashi HO, Green AR, Powe DG, El-Sayed ME, Benhasouna A, Brunet JS, Akslen LA, Evans AJ, Blamey R, Reis-Filho JS, Foulkes WD, Ellis IO. Triple-negative breast cancer: distinguishing between basal and nonbasal subtypes. Clin Cancer Res. 2009;15(7):2302-10.
5. Cavanzo FJ, Taylor HB. Adenoid cystic carcinoma of the breast: an analysis of 21 cases. Cancer. 1969;24(4):740-5.
6. Peters GN, Wolff M. Adenoid cystic carcinoma of the breast. Report of 11 new cases: Review of the literature and discussion of biological behavior. Cancer. 1983;52(4):680-6.
7. Cleveland D, Abrams AM, Melrose RJ, Handlers JP. Solid adenoid cystic carcinoma of the maxilla. Oral Surg Oral Med Oral Pathol. 1990;69(4):470-8.
8. Nascimento AG, Amaral AL, Prado LA, Kligerman J, Silveira TR. Adenoid cystic carcinoma of salivary glands: a study of 61 cases with clinicopathologic correlation. Cancer. 1986;57(2):312-9.
9. Perzin KH, Gullane P, Clairmont AC. Adenoid cystic carcinomas arising in salivary glands: a correlation of histologic features and clinical course. Cancer. 1978;42(1):265-82.
10. Pastolero G, Hanna W, Zbieranowski I, Kahn HJ. Proliferative activity and p53 expression in adenoid cystic carcinoma of the breast. Mod Pathol. 1996;9(3):215-9.
11. Ro JY, Silva EG, Gallager HS. Adenoid cystic carcinoma of the breast. Hum Pathol. 1987;18(12):1276-81.
12. Shin SJ, Rosen PP. Solid variant of mammary adenoid cystic carcinoma with basaloidfeatures: a study of nine cases. Am J Surg Pathol. 2002;26(4):413-20.
13. Boujelbene N, Khabir A, Jeanneret Sozzi W, Mirimanoff RO, Khanfir K. Clinical review-breast adenoid cystic carcinoma. Breast. 2012;21(2):124-7.
14. Rosen PP. Adenoid cystic carcinoma of the breast. A morphologically heterogeneous neoplasm. Pathol Annu. 1989;24pt 2:237-54.
15. Franzese C, Zei G, Masoni T, Cecchini S, Monteleone E, Livi L, Biti G. Adenoid cystic carcinoma of the breast. The double face of an exocrine gland carcinoma. Strahlenther Onkol. 2013;189(12):1049-50.
16. Herzberg AJ, Bossen EH, Walther PJ. Adenoid cystic carcinoma of the breast metastatic to the kidney. A clinically symptomatic lesion requiring surgical management. Cancer. 1991;68(5):1015-20.

17. Sumpio BE, Jennings TA, Merino MJ, Sullivan PD. Adenoid cystic carcinoma of the breast. Data from the Connecticut Tumor Registry and a review of the literature. Ann Surg. 1987;205(3):295-301.
18. Arpino G, Clark GM, Mohsin S, Bardou VJ, Elledge RM. Adenoid cystic carcinoma of the breast: molecular markers, treatment and clinical outcome. Cancer. 2002;94(8):2119-27.
19. Veeratterapillay R, Veeratterapillay S, Ward E, Khout H, Fasih T. Adenoid cystic carcinoma of the breast: case report and review of literature. Ann R Coll Surg Engl. 2012;94(4):e137-8.
20. Azumi N, Battifora H. The cellular composition of adenoid cystic carcinoma: an immunohistochemical study. Cancer. 1987;60(7):1589-98.
21. Rosen PP. Adenoid cystic carcinoma. In: Rosen's Breast Pathology. Philadelphia: Lippincott Williams & Wilkins, 1997:465.
22. Fukuoka K, Hirokawa M, Shimizu M, Sadahira Y, Manabe T, Kurebayashi J, Sonoo H. Basaloid type adenoid cystic carcinoma of the breast. APMIS. 1999;107(8):762-6.
23. Kleer CG, Oberman HA. Adenoid cystic carcinoma of the breast: value of histologic grading and proliferative activity. Am J Surg-Pathol. 1998;22(5):569-75.
24. Qizilbash AH, Patterson MC, Oliveira KF. Adenoid cystic carcinoma of the breast: light and electron microscopy and a brief review of the literature. Arch Pathol Lab Med. 1977;101(6):302-6.
25. Rosen PP. Adenoid cystic carcinoma. In: Rosen's Breast Pathology. Philadelphia: Lippincott Williams & Wilkins, 2001:541, 543.
26. Lamovec J, Us-Krašovec M, Zidar A, Klijun A. Adenoid cystic carcinoma of the breast: a histologic, cytologic, andimmunohistochemical study. Semin Diagn Pathol. 1989;6(2):153-64.
27. Prioleau PG, Santa Cruz DJ, Buettner JB, Bauer WC. Sweat gland differentiation in mammary adenoid cystic carcinoma. Cancer. 1979;43(5):1752-60.
28. Bourke AG, Metcalf C, Wylie EJ. Mammographic features of adenoid cystic carcinoma. Australas Radiol. 1994;38(4):324-5.
29. Dinkel H-P, Clees M, Gassel AM. Role of sonography in detecting recurrence in adenoid cystic carcinoma of the breast. AJR Am J Roentgenol. 1999;173(2):497-8.
30. Santamaría G, Velasco M, Zanón G, Farrús B, Molina R, Sole M, Fernandez PL. Adenoid cystic carcinoma of the breast: mammographic appearance and pathologic correlation. Am J Roentgenol. 1998;171(6):1679-83.
31. Tsuboi N, Ogawa Y, Inomata T, Nishioka A, Yoshida D, Yoshida S, Moriki T. Dynamic MR appearance of adenoid cystic carcinoma of the breast in a 67-year-old female. Radiat Med. 1998;16(3):225-8.
32. McClenathan JH, de la Roza G. Adenoid cystic breast cancer. Am J Surg. 2002;183(6):646-9.
33. Wang S, Ji X, Wei Y, Yu Z, Li N. Adenoid cystic carcinoma of the breast: Review of the literature and report of two cases. Oncol Lett. 2012;4(4):701-704.
34. Kato N, Yasukawa K, Onozuka T. Primary cutaneous adenoid cystic carcinoma with lymph node metastasis. Am J Dermatopathol. 1998;20(6):571-7.
35. Coates JM, Martinez SR, Bold RJ, Chen SL. Adjuvant radiation therapy is associated with improved survival for adenoid cystic carcinoma of the breast. J Surg Oncol. 2010;102(4):342-7.
36. Ghabach B, Anderson WF, Curtis RE, Huycke MM, Lavigne JA, Dores GM. Adenoidcystic carcinoma of the breast in the United States (1977 to 2006): a population-based cohort study. Breast Cancer Res. 2010;12(4):R54.
37. Defaud-Hénon F, Tunon-de-Lara C, Fournier M, Marty M, Velasco V, de Mascarel I, MacGrogan G. Adenoid cystic carcinoma of the breast: clinical, histological and immunohistochemical characterization. Ann Pathol. 2010;30(1):7-16.
38. Thompson K, Grabowski J, Saltzstein SL, Sadler GR, Blair SL. Adenoid cystic breast carcinoma: is axillary staging necessary in all cases? Results from the California Cancer Registry. Breast J. 2011;17(5):485-9.
39. Khanfir K, Kallel A, Villette S, Belkacémi Y, Vautravers C, Nguyen T, Miller R, Li YX, Taghian AG, Boersma L, Poortmans P, Goldberg H, Vees H, Senkus E, Igdem S, Ozsahin M, Jeanneret Sozzi W. Management of adenoid cystic carcinoma of the breast: a Rare Cancer Network study. Int J Radiat Oncol Biol Phys. 2012;82(5):2118-24.
40. Vranic S, Bender R, Palazzo J, Gatalica Z. A review of adenoid cystic carcinoma of the breast with emphasis on its molecular and genetic characteristics. Hum Pathol. 2013;44(3):301-9.