CASE REPORT

Adenoid cystic carcinoma: triple negative breast cancer with good prognosis

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SUMMARY

Adenoid cystic carcinoma of the breast (ACCb) is a rare type of breast cancer. The treatment is not consensual. The authors report two cases of ACCb. *Case 1*: A 59-year-old woman with T1bN0M0, who went for lumpectomy and adjuvant radiation therapy (RT) (60 Gy in 30 fractions); *Case 2*: A 43-year-old woman, who went for modified radical mastectomy with T3N1M0, and underwent adjuvant chemotherapy, and a sequential regimen with antracyclin and taxane, prior to adjuvant RT (50 Gy/25 fractions).

BACKGROUND

Breast cancer is the leading cause of cancer-related deaths in women of the so-called Western world.¹ Adenoid cystic carcinoma of the breast (ACCb) is a rare type of breast cancer, representing 0.1% of all breast tumours.² Is more frequent in postmenopausal women with a typically triple negative phenotype (negative for oestrogen and progesterone receptors, and negative human epidermal growth factor receptor (HER2)),³ and has a histologically unique identity with biphasic pattern, consisting of laminate and pseudocystic spaces lined by myoepithelial cells, and glands lined by epithelial cells.⁴ This tumour has an indolent course and a good prognosis, with 5 years and 10 years overall survival of 94% and 86%, respectively,^{5,6} contrary to triple negative, 'basal-like' breast cancer. This can eventually be explained by the down regulation of some regulator genes involved in immune response, cell proliferation and cell migration.⁷ Systemic and lymph node metastatisation is not common, and when it occurs, the systemic metastatisation is prior to lymph node involvement.²

ACCb treatment is not consensual, and growth pattern-based histological classifications have been made: glandular, tubular and solid. The grade is related to the solid component, resulting in higher grade, when the proportion of solid component increases (grade 3—tumours with more than 30% of solid component).⁸ Some authors propose different surgical treatment strategies based on the tumour grade: lumpectomy for grade I, simple mastectomy for grade II and mastectomy plus axillary dissection for grade III. This classification was not validated. As the surgical treatment, with axillary dissection and sentinel node search, the role of radiation therapy (RT) and chemotherapy has not been established.⁹

The authors present and discuss the treatment approach to two ACCb cases.

CASE PRESENTATION

Clinical case 1

A 59-year-old woman with no relevant familial and no personal clinical history presented, in 2009, with a routine mammogram showing a 6.3 mm irregular nodule in the central quadrant of the right breast. She was submitted to 'tru-cut' biopsy, with Histology (H) compatible with of ACCb (10×7 mm), negative sentinel lymph node, negative for hormonal receptors (oestrogen and progesterone receptors (PR)) and negative HER2.

Clinical case 2

A 43-year-old premenopausal woman with no relevant clinical and no familial history presented, in 2010, with a 12×9 mm palpable left breast nodule, confirmed by mammography. Histology by 'tru-cut' biopsy was compatible with ACCb (figures 1 and 2), 6 cm in diameter, with ER, PR and HER2 negative (figure 3), and low proliferation index (figure 4A) and positive sentinel lymph node with gross extranodal disease (figure 4B), staged in T3N1M0.

DIFFERENTIAL DIAGNOSIS

ACCb commonly presents as a periareolar mass and may be associated with breast tenderness and pain.¹⁰ Differential diagnosis comprises both benign and malignant aetiologies such as fibroadenomas, collagenous spherulosis (CS), mucinous carcinomas, cribriform carcinomas and invasive ductal carcinomas of no specific type. Although imaging techniques are non-specific, some common findings can be found. Mammography findings are compatible with an irregular or lobular mass, with no distinct margins. Rarely, some calcifications may be described. On ultrasound, some non-specific and

Figure 1 Cystic adenoid carcinoma. H&E stain ×200. Inset: Alcian blue/PAS stain ×100. PAS, periodic acid-Schiff.

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Figure 2 (A) Positive cytoplasmic staining for: Actin, Bcl2, CK14, CD117. (B) Positive nuclear staining for p63.

variable features are revealed, with authors describing both, poorly circumscribed and well-circumscribed masses showing peripheral vascularity and heterogeneous echotexture.¹¹ Histologically, there are two findings that are compatible with ACCb: true glandular space, with positive material staining for periodical acid-Schiff (PAS) and pseudolumina which results from stroma invagination, surrounded by basal-myoeplithelial cells (figures 1 and 2). Cribriform carcinoma (CribC) shares some characteristics with ACCb, such as a low nuclear grade and the cribriform pattern. CribC is positive for hormonal receptors and negative for PAS/Alcian blue stain. Desmoplastic stromal reaction can be found in CribC but not in ACCb.¹² CS can also have a cribriform architecture, with central eosinophilic material (acellular spherules) such as an adenoid cystic pattern. In CS cases, the lumens are irregular, compared to those in ACCb.¹⁰

TREATMENT

Clinical case 1

The patient underwent lumpectomy and was staged in T1bN0M0. Adjuvant RT was proposed, at 60 Gy and in 30 fractions.

Clinical case 2

The patient underwent modified radical mastectomy and submitted to adjuvant chemotherapy FEC $\times 3$ (5-fluorouracil,

epirubicin and cyclophosphamide) plus docetaxel $\times 3$, prior to adjuvant RT, at 50 Gy and in 25 fractions.

OUTCOME AND FOLLOW-UP

Clinical case 1

Six years postsurgery and RT, in August 2015, the patient was evaluated; she had no symptoms and no evidence of disease. She continues under annual follow-up.

Clinical case 2

Five years have passed since the diagnosis. The patient was evaluated in October 2015 and presented moderated left arm lymphoedema, but no evidence of disease. She will continue on annual follow-up.

DISCUSSION

ACCb is a rare type of invasive breast cancer and represents less than 0.1% of all cases.^{13 14} The treatment for this kind of breast tumour has not been well established, nor is it consensual, and the role of mastectomy, chemotherapy and RT remains unknown.² Ghabach *et al*,¹⁵ in a population-based cohort study, describe ACCb as being more frequent in women aged above 50 years. We presented a younger, premenopausal patient, less frequent in the literature.

These tumours can be divided into three categories, the solid component being the most important factor. Grade 1 tumour has no solid component, grade 2 has less than 30% of solid component and grade 3 tumour has more than 30% of solid component.^{8 16} Based on this classification system, we can recommend local excision for grade 1, simple mastectomy for grade 2 and modified mastectomy for grade 3.^{8 16} This classification is not accepted by the WHO. In the first case presented, the patient underwent lumpectomy, followed by adjuvant RT; while in the second case, the patient underwent mastectomy with axillary dissection, followed by adjuvant chemotherapy and adjuvant RT, not only because of the dimension of the tumour, but also because of the sentinel lymph node positiveness, with gross extranodal disease. There are some series showing a benefit in mastectomy rather than in conservative surgery, for local control.¹⁷ The presence of positive axillary lymph nodes is rare and occurs in less than 2% of cases.⁷ In most series, the sentinel lymph node, when available, was negative in almost all cases,^{6 7 18} suggesting the omission of routine axillary dissection. As mentioned above and as described in the literature, the

Figure 3 Triple negative tumour.

Figure 4 (A) Low proliferation index; (B) Sentinel node with extranodal gross disease. H&E stain.

role of axillary dissection is unknown. Some authors recommend sentinel lymph node sampling when the tumour is >3 cm, of high grade, or when other invasive types of breast cancer are present.⁷ In the second case, the patient underwent axillary lymph node dissection because of the positiveness of the sentinel node with extranodal gross disease and because of tumour dimension (6 cm).

The role of RT after lumpectomy or mastectomy is not clear, but some series showing possible benefit from RT have been published, with slight advantages in disease-free survival⁹ and one study showing RT as a strong prognostic factor for overall and cause-specific survival.¹⁹ On the contrary, some authors suggest RT only when surgical margins are positive.⁶ Some series have shown that the local recurrence rate after conservative surgery was 6% compared to 1.5% after mastectomy.⁹ Other authors suggest conservative surgery leaving mastectomy for salvage if a local recurrence occurs.^{8 18 20}

In the first case, lumpectomy was the surgical choice, considering the small tumour size. RT was performed based on some studies.^{9 19} In the second case, the choice of mastectomy was made considering the tumour size. The patient underwent RT because of extranodal gross disease, for preventing local recurrence.

Considering these types of tumours have a good prognosis, with a low propensity to distant metastatisation, the role of systemic chemotherapy is less understood, with the literature suggesting no benefit on patient survival rates.^{9 19} The decision to submit the second patient to adjuvant chemotherapy therapy was extrapolated from evidence that adjuvant systemic treatment for other types of breast cancer brings benefits and based on the young age, tumour size and positive lymph node with gross extranodal disease.

Learning points

- ▶ Adenoid cystic carcinoma of the breast of the breast is an extremely rare type of breast cancer, and is triple negative with a good prognosis.
- ▶ There is no consensus regarding optimal treatment.
- ▶ Conservative breast surgery or mastectomy and radiotherapy are recommended for local control, given the low probability of distance metastatisation, with local recurrence being the most worrying aspect.

Competing interests None declared.

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