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BRIEF REPORT

Malignant adenomyoepithelioma after breast cancer with multiple local recurrences

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Abstract Malignant adenomyoepithelioma of the breast is a rare and challenging tumor in terms of diagnosis and treatment. It is exceptional to find this condition in a patient who has had breast cancer treated with breast-conserving surgery and radiotherapy. We present the case of a 46-year-old female patient with a history of invasive lobular carcinoma of the breast, who presented one year later with a malignant adenomyoepithelioma in the same breast, which recurred three times, despite undergoing various surgical treatments and even adjuvant chemotherapy regimen. The limited evidence and lack of consensus in the management of this type of tumor highlight the importance of a multidisciplinary approach. Upon reviewing the literature, we observed extensive heterogeneity in treatments and the lack of a gold standard. We believe that surgery is the cornerstone of treatment, and that both chemotherapy and radiotherapy may have a benefit that is still unknown.

PALABRAS CLAVE
Adenomioepitelioma;
Mama;
Radioterapia;
Quimioterapia;
Cáncer de mama

Adenomioepitelioma maligno con recidivas locales múltiples después de un cáncer de mama

Resumen El adenomioepitelioma de mama es un tumor infrecuente y desafiante en su diagnóstico y tratamiento. Es excepcional encontrar esta patología en una paciente que ha tenido cáncer de mama tratado con cirugía conservadora y radioterapia. Presentamos el caso de una paciente de 46 años con antecedente de carcinoma lobulillar invasor que presentó un año más tarde un adenomioepitelioma maligno en la misma mama, y que recidivó en tres oportunidades,

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a pesar de haber realizado varios tratamientos quirúrgicos e incluso quimioterapia adyuvante. La escasa evidencia y la falta de consenso en el manejo de este tipo de tumor destacan la importancia de un enfoque multidisciplinario. Tras una revisión de la literatura observamos amplia heterogeneidad en los tratamientos y la falta de un tratamiento de referencia. Consideramos que la cirugía es el pilar fundamental de tratamiento, y que tanto la quimioterapia como la radioterapia podrían tener un beneficio que aún se desconoce.

Introduction

Adenomyoepithelioma of the breast is an uncommon tumor that typically constitutes a diagnostic challenge. It is a biphasic tumor characterized by two components: epithelial and myoepithelial.[1,2] Although rare, both cellular types can undergo malignant transformation. There are few reports available in the literature of malignant adenomyoepithelioma of the breast, and there is a diversity of treatments performed without an established gold standard. It is even more challenging to find case reports describing this condition in a patient previously treated for breast carcinoma. In most cases, they evolve into aggressive local recurrences and even distant metastases.[3] We present the following case to contribute to the study of this entity, taking into account our experience with a low-incidence condition.

Case report

We present the case of a 46-year-old female patient, with no family history of breast cancer or other relevant medical history, who consulted in September 2019 due to abnormalities found in follow-up studies. A hypoechoic nodule with defined borders and peripheral vascularity, measuring 8 mm × 7 mm (BIRADS 4a), was evidenced on the left breast ultrasound. An ultrasound-guided core needle biopsy was performed, resulting in a diagnosis of *G1* invasive lobular carcinoma with associated lobular carcinoma in situ (LCIS).

In October of the same year, a breast-conserving surgery (lumpectomy + SLNB) was performed. The final pathology study indicated G2 invasive lobular carcinoma, measuring 1.5 cm × 1.2 cm. *Estrogen receptor* (ER) and *progesterone receptor* (PR) were positive, Her2neu was negative, and Ki67 was 10%. There was an absence of vascular emboli and perineural infiltration. The resection margins were free of lesion. The sentinel lymph node biopsy revealed five (5) disease-free lymph nodes. The patient underwent whole breast radiation therapy and a boost (total of 5256 cGy), and then started hormone therapy with tamoxifen in January 2020.

In September 2020, during follow-up studies, a 17 mm × 15 mm nodular image with poorly defined margins and Doppler vascularization (BIRADS4c) was identified adjacent to the scar in the left breast. A core biopsy was performed, and the morphological findings and immunohistochemical profile were reported as consistent with a papillary lesion. Subsequently, a local resection of the left breast was carried out. The pathology study report indicated a biphasic epithelial–myoepithelial neoplasm consistent with adenomyoepithelioma (Fig. 1). The immunohistochemical panel showed positivity for p63, CD10, CK5-6, AML, and S100, with focal and weak expression of ER, negative expression of PR and Her2, and a Ki67 proliferation index of 35%. The resection margins were in contact with the lesion. Considering these results, margin re-excision and reconstruction with a thoraco-epigastric flap were performed, with no evidence of residual lesion.

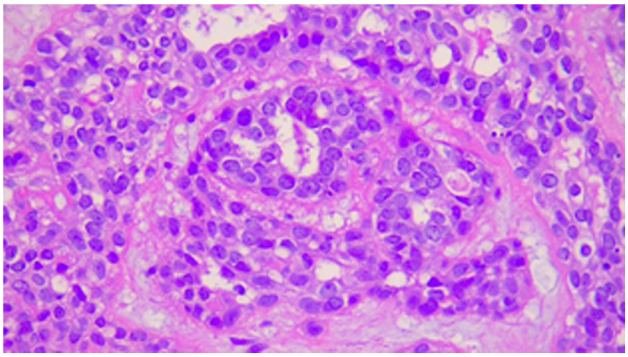

Figure 1 Left breast. HE, 40×. Biphasic proliferation involving both the epithelial and myoepithelial components, with a low mitotic rate and without obvious atypia.

A year later, in September 2021, the patient presented with a fast-growing ulcerated lesion of 2 cm × 2 cm at the scar site. A punch biopsy of this lesion was performed, and it was reported as adenomyoepithelioma.

A left simple mastectomy was performed with a diagnosis of malignant adenomyoepithelioma (tumor size was 4.5 cm × 4 cm × 3 cm). The resection margins were free of lesion. The presence of perineural infiltration and epidermis ulceration was noted (Fig. 2).

After a multidisciplinary evaluation, it was decided to initiate an adjuvant regimen with docetaxel + cyclophosphamide for four cycles (TCx4). Subsequently, the patient responded favorably, with normal follow-up studies.

In October 2023, the patient presented with induration in the axillary area. Upon physical examination, a palpable left

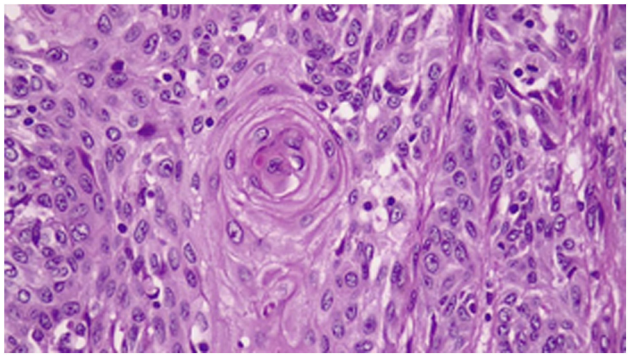

Figure 2 Left breast. HE, 40×. Biphasic proliferation involving both the epithelial and myoepithelial components, exhibiting extensive areas of squamous metaplasia.

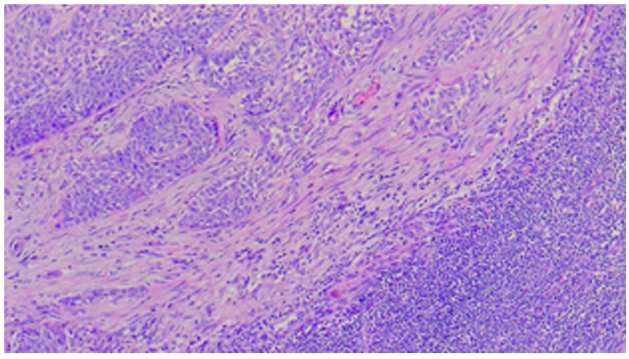

Figure 3 Left lymph node. HE, 10×. Carcinomatous metastasis of malignant adenomyoepithelioma.

axillary lymph node, with suspicious findings on ultrasound, was found. A core biopsy of the lymph node was performed, revealing carcinomatous infiltration with ER (−) PR (−) Her2 (−) and a Ki67 proliferation index of 15%. Staging studies were conducted, showing no evidence of distant metastasis (CT scan and bone scintigraphy).

A left axillary lymph node dissection (ALND) was performed, with pathology results indicating infiltration of adipose tissue by metastatic malignant adenomyoepithelioma and carcinomatous metastasis of malignant adenomyoepithelioma in 5 out of 6 isolated lymph nodes. The tumor showed ER (−) PR (−) Her2 (−) and a Ki67 proliferation index of 30% (Fig. 3).

Following this, after consultation with the multidisciplinary committee, it was decided to proceed with radiation therapy to the mastectomy bed, axilla, and supraclavicular fossa, concurrently with a chemotherapy regimen consisting of paclitaxel (twelve weekly cycles) followed by dose-dense doxorubicin + cyclophosphamide for four cycles (Px12 + ddACx4), aiming to achieve good local control.

However, after less than a month of follow-up (before starting radiation therapy), the patient presented with a dermal lesion in the mastectomy bed. An excisional biopsy was performed and confirmed to be positive for malignant adenomyoepithelioma, margins of resection were clear. It was decided to proceed with the planned radiation therapy (Fig. 4).

Discussion

Malignant adenomyoepithelioma of the breast is an extremely rare tumor. Knowledge of this condition is essential for arriving at an accurate diagnosis, requiring a multidisciplinary team trained in breast diseases, including specialists in diagnostic imaging, breast surgeons, pathologists, and oncologists. Even with an appropriate team, diagnosis can be challenging and may require multiple core needle biopsies, as findings might not be conclusive due to the similarities in imaging or pathology results to those of other conditions. No reports mentioning adenomyoepithelioma after breast cancer were found in the available literature. Cases of mammary adenomyoepitheliomas, both benign and malignant, are described, with both having the potential for local recurrence. In even rarer cases, distant metastases can occur.[3,4]

The time for local recurrence ranges from 0.7 to 5.7 years according to the literature, with a mean of 2.3 years. Notably, initial mastectomy yields better outcomes than excisional biopsy or conservative surgeries (even with disease-free margins), as demonstrated by studies mentioned by Logie et al. In their evaluation of 51 cases (11 mastectomies and 40 conservative surgeries), local recurrences were observed in 8 patients (20%) who underwent conservative surgeries, while none occurred in mastectomized patients. Despite this, there is no information about distant recurrence or overall survival rates associated with these outcomes.[5] Although these studies have a limited sample size, there are currently no larger reviews available. In the present case, it was initially interpreted as a papillary lesion, leading to conservative surgery. Recurrence occurred after 1.25 years, prompting mastectomy at that time.

Although local treatment appears to be the cornerstone of therapy, the probability of hematogenous dissemination of these tumors suggests that adjuvant chemotherapy may be beneficial. In our case, following mastectomy, the patient underwent adjuvant chemotherapy consisting of docetaxel + cyclophosphamide for four cycles.[6,7] She had a favorable outcome, with evidence of axillary recurrence after 1.83 years, but no evidence of distant disease.

There is a lack of information regarding axillary lymph node involvement. Axillary examination is not indicated in these tumors, since dissemination through this pathway is very rare, unless clinically indicated. This is why we did not perform a sentinel lymph node biopsy at the time of the mastectomy, following consultation with the multidisciplinary committee. Later, the recurrence locally involved the entire axillary fossa, raising the possibility that it may not be due to lymphatic spread but rather local progression with invasion of the axillary lymph nodes by contiguity.[8,9]

Following axillary lymph node dissection, concurrent radiation therapy to the axillary fossa was initiated alongside a chemotherapy regimen consisting of paclitaxel followed by doxorubicin + cyclophosphamide. The aim of radiation therapy was to ensure local control. Although evidence is very limited, the use of radiation therapy is reported as performed in patients who, despite mastectomy, experience disease recurrence. There is even a case described where radiation therapy was initiated after a fourth recurrence, resulting in local control for 15 months, although distant disease developed subsequently.[5,10]

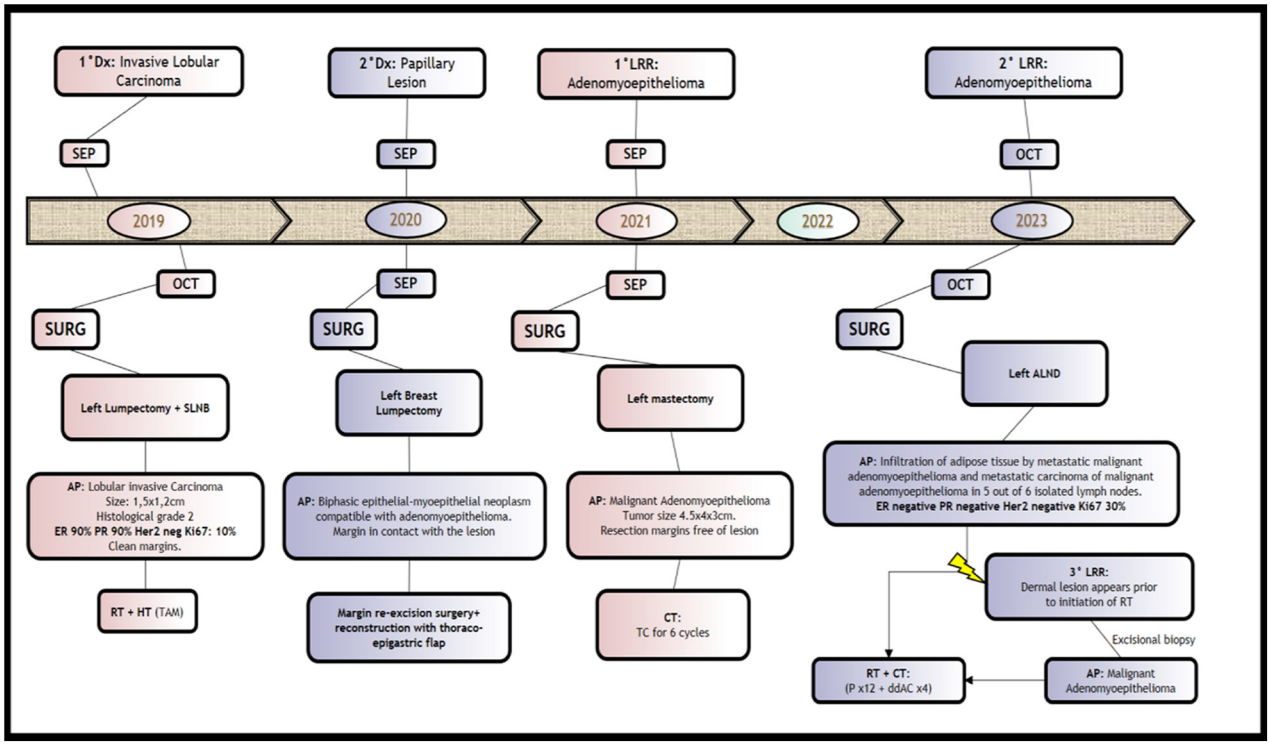

Figure 4 Timeline of the events and treatments provided.

Conclusions

Malignant adenomyoepithelioma of the breast is a rare neoplasm. Our case, like others found in the literature, exhibited a course of multiple local recurrences with short disease-free interval. Mastectomy appears to be the optimal treatment for this entity, offering better long-term outcomes regarding local recurrence; however, there is a lack of information about overall survival or distant recurrence. Limited scientific evidence supports the effectiveness of chemotherapy regimens in reducing recurrence rates. Radiation therapy emerges as a viable option to optimize local disease control, although evidence supporting its use is also insufficient.

We emphasize the importance of having a multidisciplinary team trained in breast diseases to accurately diagnose and treat these patients.

In conclusion, further studies with stronger scientific support are still needed to establish a gold standard treatment.

Ethical considerations

The patient involved in the present study signed an informed consent stating that the information from her medical history may be used. The samples stored in the Pathology Department were collected for diagnostic purposes to promote and safeguard the health of patients and not for experimental procedures on patients.

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Conflicts of interest

We do not have any conflicts of interest to declare.

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