Metaplastic Carcinoma of the Breast: Diagnosis and Multidisciplinary Approach in a Rare Subtype Case

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Carcinoma Metaplásico de Mama: Diagnóstico e Abordagem Multidisciplinar em Caso de Subtipo Raro

Carcinoma Metaplásico de Mama: Diagnóstico y Enfoque Multidisciplinario en un Caso de Subtipo Raro

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ABSTRACT

Introduction: Metaplastic carcinoma of the breast (MCB) is a rare and aggressive subtype of breast cancer characterized by the presence of two distinct cell types, typically epithelial and mesenchymal. Representing less than 1% of invasive breast cancers, it shares similarities with triple-negative breast cancer but exhibits higher resistance to chemotherapy and a worse prognosis. **Case report:** 66-year-old female patient was referred after imaging abnormalities were detected. Mammography revealed a nodular lesion in the left breast, and ultrasound demonstrated cysts with suspicious characteristics. Fine-needle aspiration (FNA) and core biopsy initially indicated "benign fibrocystic conditions." However, following a lumpectomy and histopathological analysis, the diagnosis was confirmed as "adenosquamous metaplastic carcinoma" associated with "intraductal papillary carcinoma and ductal carcinoma *in situ*." The patient underwent an additional surgery (quadrantectomy) to widen the surgical margins, and sentinel lymph node biopsy revealed no evidence of neoplastic involvement. The treatment included adjuvant chemotherapy. **Conclusion:** This case report highlights the rarity of MCB and the complexity of its diagnosis and management. Multidisciplinary collaboration between oncologists, radiologists, pathologists, and surgeons is critical for appropriate treatment. Rigorous follow-up and adjuvant therapy are essential to improve the prognosis for these patients.

Key words: Breast Neoplasms/diagnosis; Chemotherapy, Adjuvant; Carcinoma, Adenosquamous; Mastectomy, Segmental; Immunohistochemistry.

RESUMO

Introdução: O carcinoma metaplásico da mama (CMM) é um subtipo raro e agressivo de câncer de mama, caracterizado pela presença de dois tipos celulares, geralmente, epiteliais e mesenquimais. Com menos de 1% de incidência nos cânceres invasivos de mama, compartilha semelhanças com o câncer de mama triplo-negativo, mas apresenta maior resistência à quimioterapia e pior prognóstico. **Relato do caso:** Paciente do sexo feminino, 66 anos, foi encaminhada após alterações em exames de imagem. A mamografia revelou uma lesão nodular na mama esquerda, e a ultrassonografia demonstrou cistos com características suspeitas. A punção aspirativa por agulha fina (PAAF) e a *core biopsy* indicaram, inicialmente, "condições fibrocísticas benignas". No entanto, após setorectomia e análise histopatológica, o diagnóstico foi de "carcinoma metaplásico adenoescamoso" associado a "carcinoma papilífero intraductal e ductal *in situ*". A paciente foi submetida à nova cirurgia (quadrantectomia) para ampliação das margens cirúrgicas e a biópsia de linfonodos revelou ausência de comprometimento neoplásico. O tratamento incluiu quimioterapia adjuvante. **Conclusão:** Este relato de caso destaca a raridade do CMM, a complexidade do diagnóstico e o manejo dessa condição. A colaboração multidisciplinar entre oncologistas, radiologistas, patologistas e cirurgiões é fundamental para o tratamento adequado. O acompanhamento rigoroso e a terapia adjuvante são essenciais para melhorar o prognóstico desses pacientes.

Palavras-chave: Neoplasias da Mama/diagnóstico; Quimioterapia Adjuvante; Carcinoma Adenoescamoso; Mastectomia Segmentar; Imuno-histoquímica.

RESUMEN

Introducción: El carcinoma metaplásico de mama (CMM) es un subtipo raro y agresivo de cáncer de mama, caracterizado por la presencia de dos tipos celulares distintos, generalmente epiteliales y mesenquimales. Representa menos del 1% de los cánceres de mama invasivos y comparte similitudes con el cáncer de mama triple negativo, pero presenta una mayor resistencia a la quimioterapia y un peor pronóstico. **Informe del caso:** Paciente femenino, 66 años, fue remitida tras detectarse alteraciones en exámenes de imagen. La mamografía reveló una lesión nodular en la mama izquierda, y la ecografía mostró quistes con características sospechosas. La punción aspirativa con aguja fina (PAAF) y la *core biopsy* inicialmente indicaron "condiciones fibroquísticas benignas". Sin embargo, tras una tumorectomía y análisis histopatológico, se confirmó el diagnóstico de "carcinoma metaplásico adenoescamoso" asociado con "carcinoma papilar intraductal y carcinoma ductal *in situ*". La paciente fue sometida a una nueva cirugía (cuadrantectomía) para ampliar los márgenes quirúrgicos, y la biopsia del ganglio linfático centinela no mostró compromiso neoplásico. El tratamiento incluyó quimioterapia adyuvante. **Conclusión:** Este reporte de caso destaca la rareza del CMM , la complejidad de su diagnóstico y su manejo. La colaboración multidisciplinaria entre oncólogos, radiólogos, patólogos y cirujanos es fundamental para un tratamiento adecuado. Un seguimiento riguroso y la terapia adyuvante son esenciales para mejorar el pronóstico de estos pacientes.

Palabras clave: Neoplasias de la Mama/diagnóstico; Quimioterapia Adyuvante; Carcinoma Adenoescamoso; Mastectomía Segmentaria; Inmunohistoquímica.

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INTRODUCTION

Metaplastic carcinoma of the breast (MCB) is a rare and aggressive subtype of breast cancer characterized by the presence of epithelial and mesenchymal cells, which result in a unique biological heterogeneity[1,2]. It represents less than 1% of invasive breast cancers, sharing some characteristics with triple-negative cancer, such as the absence of hormone receptors and HER2, but differing by presenting higher resistance to conventional chemotherapy and worse prognosis[1,3,4]. MCB heterogeneity is evidenced by the diversity of histological subtypes, like squamous and fusiform carcinomas, in addition to chondroid and osteoid components, making it a significant diagnostic challenge[2,4].

The average diagnosis age is 55 years old, and most cases are diagnosed in stage II, reflecting its aggressive biological behavior[3,5]. Although it shares characteristics with other triple-negative subtypes, MCB is associated with significantly lower overall survival rates when compared to triple-negative carcinomas of no special type, as revealed by recent systematic reviews[5,6]. In addition, studies indicate that factors such as tumor size and the presence of tumoral necrosis may negatively influence clinical outcomes, highlighting the importance of early diagnosis[5].

Clinically, MCB usually presents as a rapid-growth mass that can be confused with other forms of breast cancer or even benign conditions. Imaging tools, such as mammograms, ultrasounds, and magnetic resonance, are useful in the initial identification, but the diagnostic confirmation requires biopsy and immunohistochemical analysis, which are essential to differentiate MCB from other breast neoplasms[2,3]. This differentiation is crucial, considering the therapeutic limitations of MCB due to the absence of specific biomarkers that could be targeted by molecular therapies[3,4].

Managing MCB is still challenging, with surgery being the main healing therapeutic approach. However, the high local recurrence and distant metastases rate highlights the need for effective adjuvant strategies[3,5]. Although adjuvant radiotherapy is frequently used, there are controversies regarding its effectiveness in controlling the disease, and chemotherapy has limited effectiveness with low objective response indexes[5]. This difficulty in managing the disease reinforces the importance of a multidisciplinary approach and the key role of research in identifying new prognostic markers and therapies directed at this rare subtype[5,6].

This report describes the case of a 66-year-old woman diagnosed with MCB, highlighting the diagnostic and therapeutic particularities of this rare subtype.

This study has been approved by the Research Ethics Committee of the *Universidade Estadual do Sudoeste da Bahia*, report number 6836099 (CAAE (submission for ethical review): 76960623.3.0000.0055), and the patient signed an Informed Consent Form as recommended in Resolution n.º 466/20127 of the National Health Council.

CASE REPORT

Patient MPC, 66 years, female, black, attended the *Centro Médico de Diagnóstico por Imagem*, in July 2021, referred by the gynecologist after alterations in the tests. Pregnancy (2), delivery (2), abortion (0), breastfed for three years and started climacteric at 52 years old. Denies smoking, use of hormone replacement therapy, nipple discharge, and family history of malign neoplasms of breast and ovary.

The patient showed a mammogram and breast ultrasound, both performed in July 2021. The mammogram showed a nodular image, with partially defined limits, located in the upper medial quadrant of the left breast (Figure 1), measuring about 3.5 cm, BI-RADS 0.

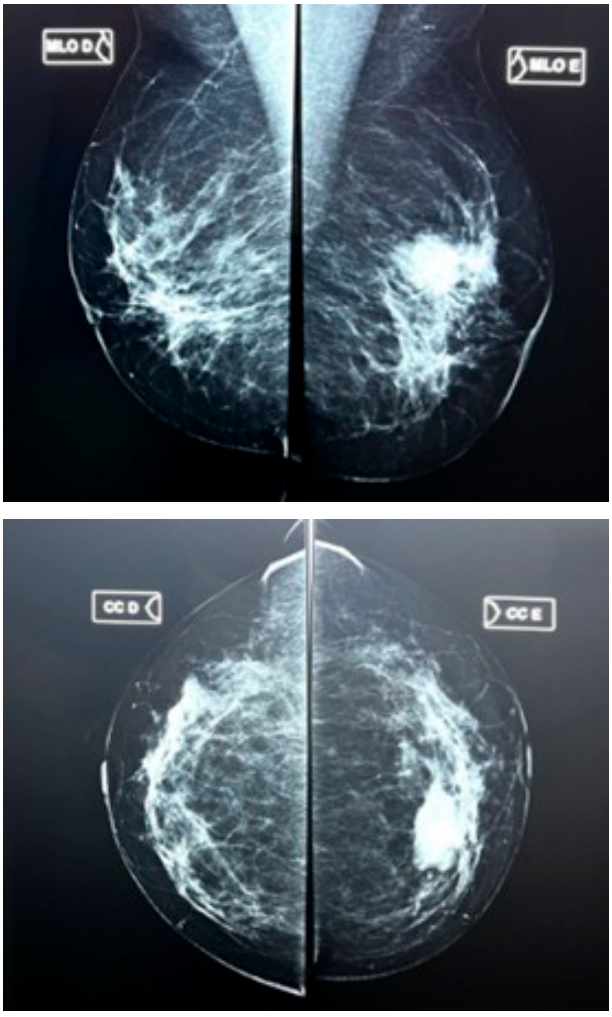

Figure 1. Mammogram: nodular image in the left breast

Presence of lymph nodes in the right armpit, but no pathological characteristics. The breast ultrasound recorded a hypoechoic image in the periareolar region, located at four o'clock, with posterior enhancement, measuring 0.5 x 0.4 cm, suggesting a thick content cyst. At ten o'clock, a cystic/solid area with peripheric and central vascularization at Doppler was observed, measuring 3.8 x 1.7 cm, with free armpits. Those findings were classified as BI-RADS 4A, free armpits.

Fine-needle aspirations (FNA) and core biopsy were conducted in July 2021. In the FNA, the punched material at four o'clock showed groupings of apocrine and ductal cells, both with no atypia, among foamy macrophages, fragments of fibrous tissue, and granular material. The immunohistochemical study of this material indicated steatonecrosis, with no atypia or malignancy.

The cyst samples located at ten o'clock reveal acellular proteinaceous material in one and epithelial cells with apocrine metaplasia in the other. The core biopsy of the same cyst showed distorted ducts among fibrosis and usual ductal hyperplasia. The cytological result was negative for malignancy in both cysts, classified as benign according to the Yokohama system.

The patient was submitted to a lumpectomy in February 2022 for an excision of a solid-cystic lesion at ten o'clock in the left breast. The anatomopathological analysis revealed an "adenosquamous metaplastic carcinoma" associated with an "intraductal papillary carcinoma," with extensive ductal carcinoma "*in situ*" and hypercellular stromal sclerosis. The surgical margins were free from invasive carcinoma, but the upper margin presented a minimum distance of 1.4 mm from the carcinoma, which is considered exiguous.

Given the unusual case, the result was released with the analysis of another specialist. The immunohistochemical study report (Figure 2), released on April 2022, indicated a spindle cell metaplastic carcinoma associated with an intraductal papillary carcinoma (positive RE, negative RP, KI67 25%, HER2 negative and P63 metaplastic biomarkers), complementing the previous anatomopathological result. Thus, the patient was diagnosed with metaplastic carcinoma of the left breast, stage II, T2N0M0, with no neoplastic compromise of sentinel lymph nodes (0/7).

This case report highlights the importance of cooperation and a multidisciplinary approach in managing a cancer patient, especially one with MCB, a rare subtype of breast neoplasm that has a fast and aggressive evolution. Firstly, the gynecologist noticed alterations in the image exams signed by reference radiologists; the pathologists, with professionals from different locations and expertise, were essential to differentiate the case that initially presented characteristics of benign neoplasm, effectively contributing to a correct diagnosis. Moreover, the immunohistochemistry specialist ensured the oncology team a broader panorama regarding the adjuvant therapeutics to be followed. Then came the surgical and oncological team, whose therapeutics ensured the success of finding the case at an initial stage. The collaboration between professionals

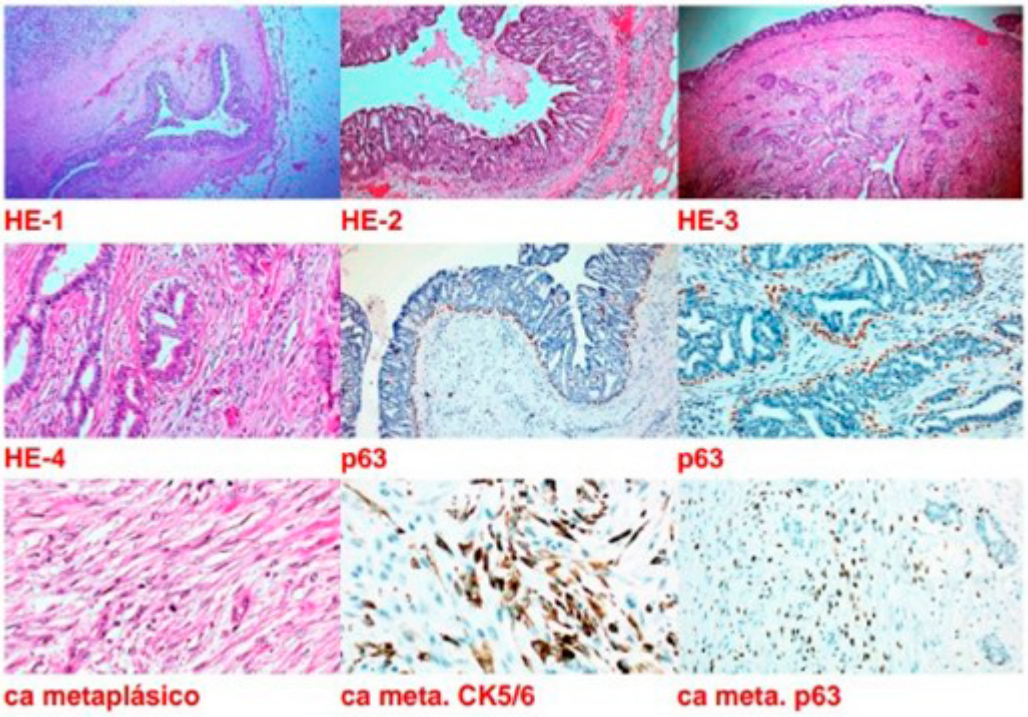

Figure 2. Immunohistochemical analysis of the nodule of the left breast at ten o'clock

of different medical specialties ensured the resolution of the condition, considering the high impact of the interval between early diagnosis and treatment.

Upon return consultation in May 2022, the physical examination showed no signs of local recurrence, and the armpit remained with no palpable lymph nodes. For staging, the tomography and bone scintigraphy showed no metastases, and the armpit ultrasound showed no alterations. The patient was submitted to a new surgery (quadrantectomy) in July 2022, to broaden the margins and for a biopsy of the sentinel lymph node with partial reconstruction through glandular flaps with no intercurrences. The anatomopathological results, released in the same month, showed free margins and lymph nodes with no neoplasm (0/7). In the following consultation in October 2022, there were no signs of phlogosis or wound dehiscence, and the patient followed with adjuvant chemotherapy and radiotherapy.

Since then, consultations have been held every six months, though there were difficulties in scheduling exams via health insurance. In July 2024, the mammogram and ultrasound indicated the absence of pathological alterations, demonstrating the efficacy of the treatment. However, the patient chose not to conclude the recommended radiotherapy arrangement for personal reasons, despite being aware of the therapy's benefits and the risks associated with her decision. This choice was respected by the medical team, preserving the patient's autonomy in caring for her health.

Thus, to summarize the follow-up, the patient did not present local recurrence or metastasis; imaging exams and sentinel lymph node biopsy confirmed the absence of neoplastic compromise.

DISCUSSION

MCBs are rare, representing less than 5% of invasive cancers. These tumors, characterized by epithelial and mesenchymal cells, present significant morphological heterogeneity, and negative prognosis, especially in the triple-negative cases[4]. Among the histological types, squamous cell and spindle cell carcinomas are highlighted[1]. Compared to other breast neoplasms, MCB differentiates by being resistant to conventional chemotherapy and for its aggressive biological behavior, which requires a diagnostic and therapeutic approach, frequently supported by multidisciplinary teams[1].

The MCB classification encompasses varied degrees and subtypes, with low-degree tumors, exemplified by adenosquamous carcinoma and metaplastic similar to fibromatosis, which have less metastatic potential[5]. On the other hand, intermediate subtypes, like metaplastic spindle cell carcinoma, are rare and require greater attention[6]. The morphological characteristics include distinct metaplastic components, like squamous and spindle[8], making the diagnosis challenging even for experienced specialists.

This case illustrates the complexity of the diagnosis and management of MCB. A 66-year-old patient, with no significant family history, was initially diagnosed through inconclusive FNA. The following biopsy revealed an adenosquamous metaplastic carcinoma and an intraductal papillary carcinoma, evidencing diagnostic challenges[9]. The presence of hypercellular stromal sclerosis reinforces the aggressiveness of this neoplasm[10], highlighting the need for detailed tests for a precise diagnostic evaluation[11]. Managing this rare subtype evidences the importance of understanding the peculiarities of neoplasms to make assertive therapeutic decisions and identify specific prognostic markers[12].

Surgery is essential in managing MCB due to its aggressiveness[13]; the quadrantectomy ensures free margins and reduces the risk of recurrence[14]. The immunohistochemical is vital to confirm the diagnosis and plan the treatment[15].

The surgery plays a key role in managing MCB, with quadrantectomy essential to ensure free margins and reduce the risk of recurrence[14]. In this context, immunohistochemistry plays a vital role in confirming the diagnosis and in differentiating other breast neoplasms[15]. MCB is associated with rapid local growth and a worse prognosis, which highlights the need for adequate surgical interventions[16]. Studies show that rigorous follow-up and adjuvant chemotherapy are critical for ensuring better outcomes for these patients[17].

In addition to surgery, the multidisciplinary approach was determinant in this case. The integration between gynecologists, radiologists, pathologists, surgeons, and oncologists allowed effective management. The gynecologist was responsible for the initial identification of changes in the image exams; radiologists helped stratify the risk through the BI-RADS classification, while pathologists have made a decisive contribution in differentiating benign and malign conditions, overcoming diagnostic limitations imposed by initial findings, such as steatonecrosis. The oncology team, in turn, established a therapeutic plan adjusted to the characteristics of the tumor, highlighting the relevance of individualized therapies in fighting MCB.

The clinical outcomes reinforce the importance of a rigorous follow-up, which showed the absence of local recurrence or metastasis, evidencing the efficacy of the performed interventions. The main predictors of survival in MCB include stage, tumor size, and status of the

axillary lymph node[18]. Advanced stages, poor functional condition, and pulmonary and brain metastases are poor prognosis factors, impacting overall survival[19]. Age at diagnosis, TNM stage, radiotherapy, and chemotherapy also influenced survival in patients with MCB[20], highlighting the importance of considering clinical and pathological factors in survival prediction.

This case highlights both similarities and differences regarding previous reports in the literature. As described by other authors, MCB presents diagnostic challenges due to its rarity and histological heterogeneity[1,3]. However, the reported case has its peculiarities, like the confusing initial diagnosis related to the presence of steatonecrosis and the specific histological characteristics, which suggest hypotheses on prognostic and therapeutic factors.

Compared to other breast neoplasms, the multidisciplinary approach takes on an even more prominent role in MCB, given the diagnostic challenge and the need for more individualized therapies[21]. Contrary to ductal and lobular carcinomas, which frequently present more predictable biomarkers for the choice of targeted therapies, MCB is characterized by heterogeneous biomarkers and usually triple-negative phenotype, limiting the therapeutic options[21,22]. Thus, collaboration among different specialties not only facilitates early diagnosis but also optimizes the choice of therapeutic interventions.

New aspects of this case include initial atypical clinical presentation, diagnostic complexity, and detailed immunohistochemical findings, which contribute to understanding this rare subtype and reinforce the need for more investigation in prognostic markers. Despite that, the report contributes significantly to the body of knowledge on the rare subtypes of rare breast carcinoma, with practical implications for multidisciplinary clinical and therapeutic management.

Finally, though the report has limitations, such as the absence of long-term detailed follow-up and the patient's decision not to conclude the radiotherapy, it highlights the importance of individualizing care. The case highlights the impact of a multidisciplinary approach in the diagnosis and treatment of rare and aggressive subtypes of breast cancer, like MCB, contributing to advances in the management of these neoplasms.

CONCLUSION

This rare case of MCB highlights the importance of a broad diagnostic evaluation and individualized treatment approaches. Doctors must remain highly suspicious of atypical and rapid breast lesions, especially in the elderly. The case shows that multidisciplinary collaboration ensures precise diagnosis, adequate treatment planning, and better results for patients. Continuous research is needed to elucidate pathogenesis, prognostic factors, and therapeutic strategies to approach this challenging subtype.

CONTRIBUTIONS

All the authors have substantially contributed to the study design and planning, data acquisition, analysis, interpretation, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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