



Miliary pulmonary metastasis secondary to inflammatory breast carcinoma: a case report

Metástase pulmonar miliar secundária a carcinoma inflamatório de mama: um relato de caso

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ABSTRACT

Pulmonary micronodules are classified based on their anatomical distribution pattern: centrilobular, perilymphatic, or random. Accurate classification of these patterns, combined with a detailed history and physical examination, allows for precise and effective narrowing of differential diagnoses. In this article, we report the case of a 66-year-old woman who presented with inflammatory edema of the left breast and randomly distributed pulmonary micronodules, a finding that was crucial for diagnostic clarification.

Keywords: Multiple pulmonary nodules; Neoplasm metastasis; Inflammatory breast neoplasms; Diagnostic imaging, prognosis.

RESUMO

Os micronódulos pulmonares são classificados com base em seu padrão de distribuição anatômica: centrolobular, perilinfático ou randômico. A partir da correta classificação desses padrões, aliada à semiologia detalhada, é possível restringir os diagnósticos diferenciais com precisão e eficácia. Neste artigo, relatamos o caso de uma mulher de 66 anos que se apresentou com edema inflamatório da mama esquerda e micronódulos pulmonares de distribuição randômica, um dado que foi crucial para a elucidação diagnóstica.

Descritores: Nódulos pulmonares múltiplos; Metástase neoplásica; Neoplasia inflamatória da mama; Diagnóstico por imagem, prognóstico.

INTRODUCTION

Pulmonary micronodules are focal, small (<3mm in diameter), solid parenchymal opacities, with a rounded shape that may demonstrate soft tissue, fat, or calcium density. Conceptually, they are characterized according to the following anatomical patterns: centrilobular, perilymphatic, and random^[1].

Perilymphatic nodules are distributed along the pulmonary lymphatic system, which includes interlobular septa, visceral pleura, and the peribronchovascular interstitium. They are almost always visible in a subpleural location, particularly along the fissures. In contrast, centrilobular nodules are limited to the central regions of the secondary pulmonary lobules,

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sparing the pleural surfaces. Random nodules, however, are distributed randomly throughout the pulmonary parenchyma and may involve pleural surfaces and fissures, though without subpleural predominance, due to the associated hematogenous spread^[1].

The correct identification and classification of the tomographic distribution pattern of micronodules, combined with a thorough medical interview and physical examination, allow for a more accurate and effective narrowing of the differential diagnoses (Table 1).

Therefore, the aim of this study is to report the case of a 66-year-old woman diagnosed with inflammatory breast cancer, with emphasis on the identification, through chest computed tomography with Maximum Intensity Projection (MIP) reconstruction, of a miliary distribution pattern of metastatic micronodular lesions — an imaging finding not previously reported in the scientific literature for this rare breast cancer subtype.

CASE REPORT

A 66-year-old Black woman, married, and a homemaker, with metabolic syndrome (class II obesity,

stage 3 according to the Edmonton classification; grade 3, stage 3 systemic hypertension according to the European Society of Cardiology classification; and dyslipidemia), heart failure with preserved ejection fraction (HFpEF), a former smoker (16 pack-years), and chronic respiratory symptoms. In July 2024, she presented with progressive inflammatory edema of the left breast, which subsequently extended distally along the left upper limb (LUL) to the ipsilateral forearm.

After multiple visits to healthcare services, with an unsuccessful course of empiric antibiotic therapy for presumed bacterial cellulitis, she was admitted in September 2024 to the University Hospital of the Federal University of Juiz de Fora (HU/UFJF - MG).

On inspection, moderate to severe edema was noted in the LUL, with localized warmth, induration, and a 12 cm asymmetry relative to the mid-arm circumference of the right arm. There was also a noticeable asymmetry of the breasts, with increased volume on the left side and mild erythema, desquamation, and a peau d'orange appearance. There was ipsilateral axillary lymphadenopathy but with a reactive appearance (Figure 1).

Table 1. Differential diagnoses according to tomographic distribution pattern

Distribution pattern	Main differential diagnoses
Perilymphatic	Sarcoidosis, silicosis, lymphangitic carcinomatosis
Centrilobular	Lepidic adenocarcinoma, hypersensitivity pneumonitis, bronchiolitis, bronchopneumonia, aspiration
Random	Metastasis, miliary tuberculosis, miliary fungal infection

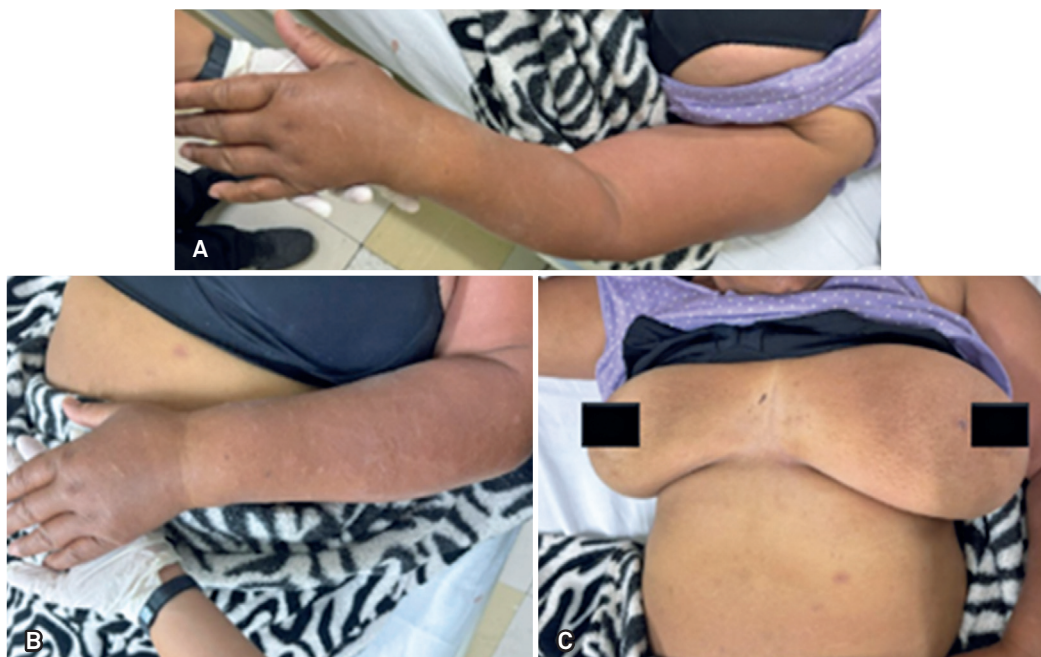


Figure 1. A and B – Inflammatory edema of the left upper limb; C – Breast asymmetry.

The main diagnostic hypotheses were inflammatory breast cancer and deep vein thrombosis in the LUL, with bacterial cellulitis due to a resistant pathogen also being considered. Therefore, coverage aimed at *Staphylococcus aureus* was initiated, including amoxicillin-clavulanate, clindamycin, and vancomycin, but there was no change in the clinical course.

The venous Doppler ultrasound of the LUL was unremarkable, and the result of a punch biopsy from the inferomedial quadrant of the left breast, performed in August 2024 by the attending breast surgeon, was negative for malignancy. Additionally, mammography and breast ultrasound were reviewed and classified as BI-RADS 3.

The analysis of the chest X-ray, performed during the hospitalization, revealed a relevant finding that

contributed to refining the clinical reasoning: the presence of reticulonodular hypotransparency in both pleuropulmonary fields, with a bibasal predominance. The complementary chest CT, processed in Maximum Intensity Projection, aimed, among other aspects, to highlight the architecture of the micronodules, showing a random distribution pattern, characteristically miliary (Figure 2).

Pulmonary micronodules with a random distribution pattern present a myriad of differential diagnoses, including miliary tuberculosis, fungal infections, and hematogenous metastases^[1]. Given the low suspicion of disseminated systemic infectious disease, the working diagnosis considered was metastatic malignancy. Among the most common metastatic cancers in this context, thyroid carcinoma, renal cell carcinoma, me-

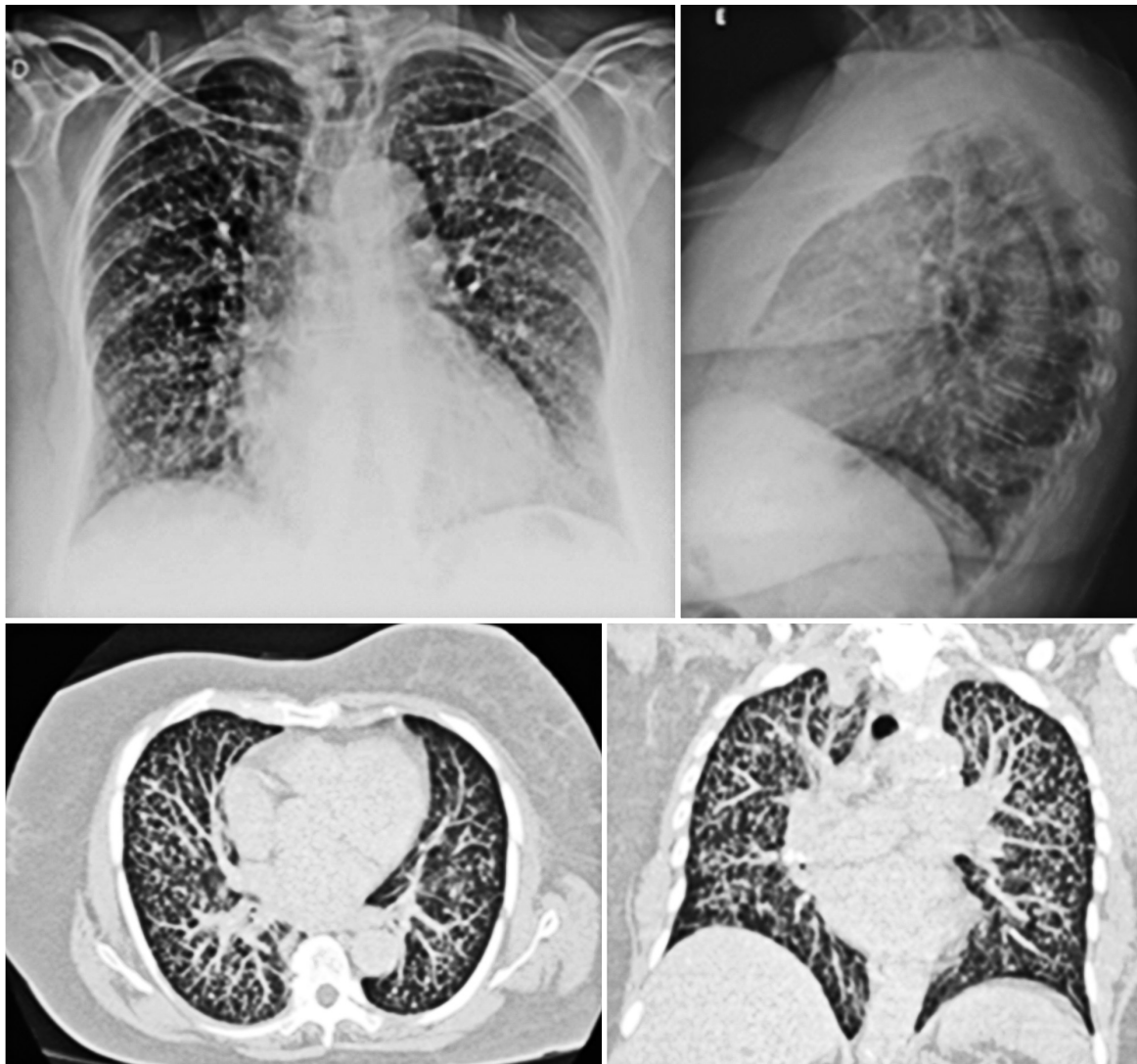


Figure 2. Chest radiography in posteroanterior and lateral views and chest tomography in maximum intensity projection (MIP) processing, showing the random distribution of pulmonary micronodules in axial and coronal sections.

lanoma, osteosarcoma, colorectal carcinoma, and testicular tumors stand out, with the latter naturally being excluded.

Given this finding, after discussion with the pulmonology and thoracic surgery teams, it was decided to perform a wedge pulmonary biopsy via thoracotomy. The histopathological analysis revealed multifocal invasive adenocarcinoma in the pulmonary parenchyma, with a higher clinical likelihood of being secondary lesions rather than lepidic adenocarcinoma. Immunohistochemistry showed positivity for TRPS1, GATA3, and estrogen receptor antibodies, confirming inflammatory breast cancer as the primary site of malignancy, despite the absence of significant axillary lymph node involvement (Figure 3).

The diagnosis was communicated following established and empathetic communication strategies, and the patient, who had a good performance status, was referred to the city's oncology referral center to initiate targeted therapies in accordance with palliative care principles.

DISCUSSION

Inflammatory breast cancer (IBC), first described in 1924, is a rare subtype of breast cancer (BC), accounting for less than 4% of all cases. It has an aggressive behavior

and a high metastatic potential, with a median overall survival of less than 4 years, despite multimodal therapeutic options^[2].

It predominantly affects black women, aged between 40 and 50 years, from developing countries, with lower educational levels and socioeconomic status^[3,4]. Other risk factors include exposure to radiation in the thoracic region, and obesity. The literature indicates that a high body mass index ($\geq 30\text{kg/m}^2$) can increase the risk of inflammatory breast cancer independently of menopausal status or estrogen receptor expression, worsening the prognosis by enhancing the risk of metastases^[4].

From a clinical perspective, skin changes are sudden and can manifest up to 6 months before the diagnosis of invasive disease. Common findings include edema, erythema, skin thickening with a texture characteristically resembling, orange peel" (*peau d'orange*), breast asymmetry, morphological changes in the nipple-areolar complex, increased temperature, and localized pain, often without identification of a palpable underlying mass or significant changes in inflammatory biomarkers in laboratory tests. Because of this, other benign conditions can mimic the clinical presentation of IBC, such as bacterial mastitis and other skin and soft tissue infections, contributing to delays in diagnosis and treatment^[2,3].

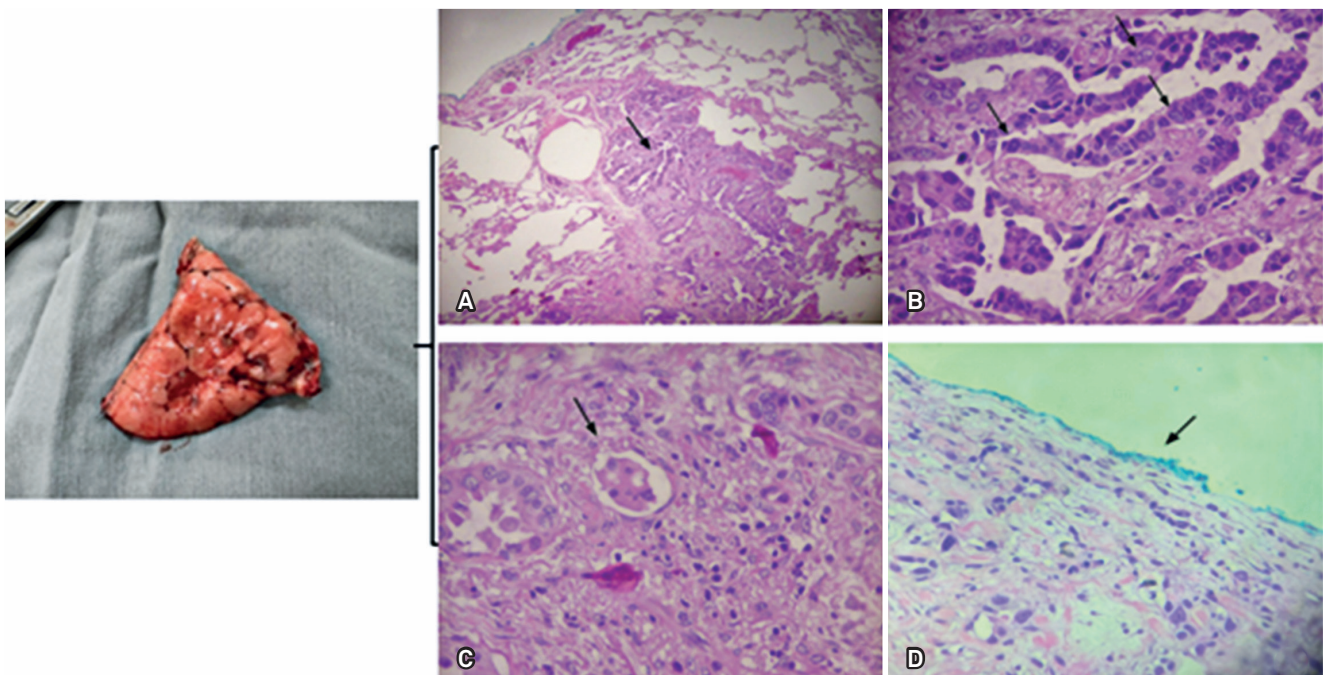


Figure 3. Surgical specimen with wedge resection by open thoracotomy marked on the left, with the respective histopathological slides, being (A) - neoplasia (arrow) infiltrating the lung parenchyma. Magnification: 4x; (B) - glandular neoplastic cells with nuclear pleomorphism. Magnification: 40x; (C) - tumor angiolympathic invasion. Magnification: 40x; (D) - visceral pleura marked with India ink, with infiltration of neoplastic cells. Magnification: 40x. Histological sections of lung, stained with Hematoxylin-Eosin.

Imaging modalities such as mammography, magnetic resonance imaging (MRI), and breast ultrasound play a fundamental role in the diagnostic process by demonstrating skin thickening, increased tissue density, and malignant-pattern microcalcifications. Additionally, they allow for the assessment of axillary lymph nodes and muscle invasion sites, aiding in the identification of potential biopsy targets^[5]. Positron emission tomography combined with computed tomography (PET/CT), in turn, has proven to be a valuable tool for determining disease extent, enabling appropriate staging and playing a crucial role in the development of individualized therapeutic plans^[6].

Regarding the evaluation of disease extent, it is important to note that the incidence of pulmonary metastases originating from extrathoracic primary neoplasms ranges from 20% to 54%^[7]. Specifically in patients with IBC, studies have shown a higher likelihood of metastasis being detected at the time of diagnosis compared to non-inflammatory breast cancer^[4].

Additionally, there are notable differences in the pattern and chronology of metastatic dissemination between these two breast cancer subtypes. In patients with inflammatory breast cancer, bone metastases commonly emerge at more advanced stages of the disease, usually following involvement of the liver, lungs, or chest wall. This pattern contrasts with that observed in non-inflammatory breast cancer, where bone metastases tend to occur earlier, sometimes preceding visceral metastases^[8].

Concerning pulmonary metastases, those associated with non-inflammatory breast cancer are well documented in the radiological literature, typically presenting as multiple well-defined nodules, predominantly located in the peripheral and lower regions of the lungs. Other patterns include lymphangitic spread, consolidations, and, less frequently, solitary metastases^[9]. In contrast, specific patterns of pulmonary dissemination in inflammatory breast cancer remain poorly described in the scientific literature, lacking the consistent characterizations observed in non-inflammatory breast cancer^[10].

In this context, chest computed tomography (CT) with maximum intensity projection (MIP) processing plays a particularly important role in assessing patterns of micronodular distribution. This technique enhances sensitivity in detecting and characterizing lesions that may be difficult to visualize on conventional axial slices^[5,6,10]. In the present case report, chest CT with MIP reconstruction was one of the main tools utilized during the diagnostic investigation, significantly contributing

to clinical decision-making by revealing a miliary distribution pattern of micronodular metastatic lesions - an imaging finding not previously described in the scientific literature for inflammatory breast cancer.

In conclusion, persistent inflammatory changes in the breast, despite treatment for mastitis or presumed infectious cellulitis, should raise suspicion for inflammatory breast cancer. Histopathological diagnosis is often challenging due to the absence of nodules or masses, which may result in negative biopsies for malignancy due to sampling limitations. The definitive diagnosis in the present case was established following the identification of a miliary pattern in the distribution of pulmonary micronodules, which were subsequently confirmed as hematogenous metastases through wedge lung biopsy obtained via thoracotomy. This observation underscores the exceptional nature of the case, as, to the best of our knowledge, there are no prior reports in the literature describing a metastatic imaging pattern of this nature in locally advanced inflammatory breast cancer - a clinical entity that requires early detection and timely initiation of therapeutic intervention.

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