



## Male breast cancer: a case report

Câncer de mama masculino: um relato de caso

Cáncer de mama masculino: reporte de un caso

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### ABSTRACT

**Objective:** This article aims to report a case of breast cancer in a male patient, who also had tumor lysis syndrome and suspected metastasis to the cranial vault. **Case details:** The present study reports the case of a male patient, 77 years old, with no family history of cancer, who presented with gynecomastia and an irregular mass in the infra-axillary region, with central cystic degeneration, classified as BIRADS IV-A. The patient evolved with tumor lysis syndrome and also had multiple lytic bone lesions scattered throughout the skull, with the possibility of secondary neoplastic involvement. **Final considerations:** Breast cancer in men is usually diagnosed in more advanced stages and is usually managed according to the procedures recommended for female breast cancer. It is important to understand the disease and its clinical manifestations, as well as to raise awareness about this type of cancer in men. In addition, further studies on specific therapeutic options for male breast cancer are needed to establish an evidence-based standard of care for this population.

**Keywords:** Male Breast Neoplasms, Case Reports, Gynecomastia, Men's Health, Pathology.

### RESUMO

**Objetivo:** Este artigo tem como objetivo relatar um caso de câncer de mama em um paciente do sexo masculino, que também apresentava síndrome de lise tumoral e suspeita de metástase para calota craniana. **Detalhamento do caso:** O presente estudo relata o caso de um paciente do sexo masculino, 77 anos, sem histórico familiar de câncer, que apresentava ginecomastia e massa irregular na região infra-axilar, com degeneração cística central, classificada como BIRADS IV-A. O paciente evoluiu com síndrome de lise tumoral e com múltiplas lesões ósseas líticas espalhadas pelo crânio, com possibilidade de acometimento neoplásico secundário. **Considerações finais:** O câncer de mama em homens geralmente é diagnosticado em estágios mais avançados e geralmente é tratado de acordo com os procedimentos recomendados para o câncer de mama feminino. É importante compreender a doença e as suas manifestações clínicas, bem como do aumento da conscientização sobre esse tipo de câncer no homem. Ademais, mais estudos sobre opções terapêuticas específicas para o câncer de mama masculino são necessários, a fim de estabelecer um padrão de atendimento baseado em evidências para essa população.

**Palavras-chave:** Neoplasias da Mama Masculina, Relatos de Casos, Ginecomastia, Saúde do Homem, Patologia.

### RESUMEN

**Objetivo:** Este artículo tiene como objetivo reportar un caso de cáncer de mama en un paciente masculino, quien además presentaba síndrome de lisis tumoral y sospecha de metástasis en cráneo. **Detalles del caso:** El presente estudio reporta el caso de un paciente masculino, de 77 años, sin antecedentes familiares de cáncer, que presentó ginecomastia y masa irregular en región infraaxilar, con degeneración quística central,

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clasificada como BIRADS IV-A. El paciente evolucionó con síndrome de lisis tumoral y múltiples lesiones líticas óseas diseminadas por el cráneo, con posibilidad de afectación neoplásica secundaria. **Consideraciones finales:** El cáncer de mama en los hombres generalmente se diagnostica en etapas posteriores y generalmente se trata de acuerdo con los procedimientos recomendados para el cáncer de mama femenino. Es importante comprender la enfermedad y sus manifestaciones clínicas, así como generar conciencia sobre este tipo de cáncer en los hombres. Además, se necesitan más estudios sobre opciones terapéuticas específicas para el cáncer de mama masculino con el fin de establecer un estándar de atención basado en la evidencia para esta población.

**Palabras clave:** Neoplasias de la Mama Masculina, Informes de Casos, Ginecomastia, Salud del Hombre, Patología.

## INTRODUCTION

Breast cancer in men is a rare event, representing about 1% of all breast cancers and less than 1% of all types of cancer that affect men (ELBACHIRI M, et al., 2017; GUCALP A, et al., 2019). Female breast cancer is the most frequent in all Brazilian regions except for non-melanoma skin tumors. The estimated number of new cases of breast cancer in Brazil, for the three years from 2023 to 2025 is 73,610 cases (INSTITUTO NACIONAL DE CÂNCER, 2022). Estimates for breast cancer in men in the United States for 2023 are about 2,800 new cases and nearly 530 deaths (AMERICAN CANCER SOCIETY, 2023). Brazil lacks concrete epidemiological data on the prevalence and incidence of male breast cancer.

Family history is relevant for the occurrence of cancer in both sexes. In male breast cancer, genetic mutations, particularly in the BRCA2 gene, play an important role. (ZEHR KR, 2019). Other risk factors include exposure to radiation and volatile organic compounds and conditions that co-occur with an abnormal relationship between estrogens and androgens, such as obesity, exogenous estrogen use, and Klinefelter syndrome (ABDELWAHAB YOUSEF AJ, 2017; RUDDY KJ e WINER EP, 2013). The most common presentation of male breast cancer is the presence of a breast mass, usually retroareolar, which may be present in isolation or accompanied by other less common symptoms such as nipple discharge, skin retraction, ulcerations, and lymphadenopathy in more advanced cases (BRINTON LA, et al., 2008; KHAN NA e TIRONA M, 2021). The diagnosis of breast cancer in men is most often made through a triple evaluation: clinical, radiological (mammography and ultrasound), and histopathological (tissue biopsy), similar to what is done in cases of female breast cancer (NOFAL MN e YOUSEF AJ, 2019).

Diagnosis of breast cancer in males often occurs in more advanced stages and the survival rate tends to be lower compared to female breast cancer (ELBACHIRI M, et al., 2017; GUCALP A, et al., 2019). Among men, findings of larger tumors, compromised lymph nodes, and distant metastases at the moment of diagnosis are also frequent (GUCALP A, et al., 2019). The low index of suspicion may contribute to the late identification of this neoplasm in male patients, leading to a worse prognosis and higher morbidity and mortality (METHAMEM M, et al., 2020). Furthermore, the smaller amount of breast tissue and the closer proximity of the tumor to the skin and muscles could facilitate the invasion of adjacent structures and earlier dissemination of tumor cells (FARIA RA, et al., 2020).

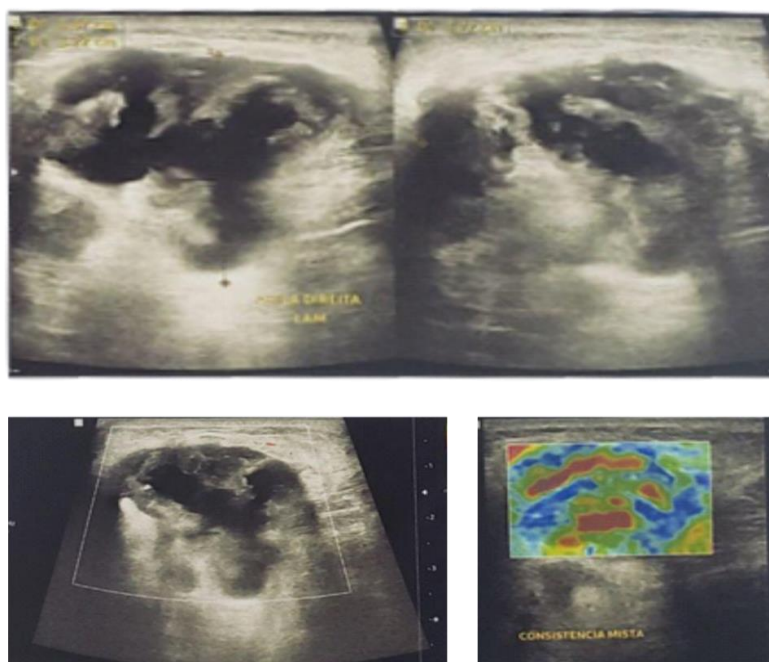
Nipple retraction and palpation of a retroareolar mass are common findings on physical examination and may be the first clinical manifestations of male breast cancer (ELBACHIRI M, et al., 2017; GUCALP A, et al., 2019). Due to the low incidence of breast cancer in men, the literature still lacks evidence related to therapeutic options and individualized care protocols in these cases. This means that this disease is normally managed according to the procedures recommended for female breast cancer (ELBACHIRI M, et al., 2017; FARIA RA, et al., 2020). This article aims to report a case of breast cancer in a male patient, as well as the conduct adopted in the case.

## CASE DETAILS

The present study was approved by the Research Ethics Committee of the Federal University of Piauí under opinion number 5.999.809 and CAAE number 67892123.6.0000.0192. A male patient, 77 years old, hypertensive, diabetic, and with no family history of cancer, developed a mass in the left breast 16 years ago,

which was performed with surgical excision without histopathological investigation. At the time, there were no complaints of pain, local skin changes, or papillary effusion. In May 2021, with the help of his children, the patient sought care from an oncologist to investigate a painful nodule in the right infra-axillary region. This was followed by an ultrasound investigation showing a hypoechogenic, irregular, and heterogeneous nodule, located in the right mid-axillary line, measuring 4.1 x 2.5 x 2.7 cm, associated with an adjacent atypical lymph node (**Figure 1**).

**Figure 1** – Ultrasonography of a nodule in the right infra-axillary region.



Source: Silva IR, et al., 2023.

A new ultrasound in the right breast showed gynecomastia and an irregular, heterogeneous mass, with central cystic degeneration to be clarified, with the BIRADS IV-A classification (**Figure 2**).

**Figure 2** - Ultrasonography of a nodule associated with an altered lymph node in the right mid-axillary line.

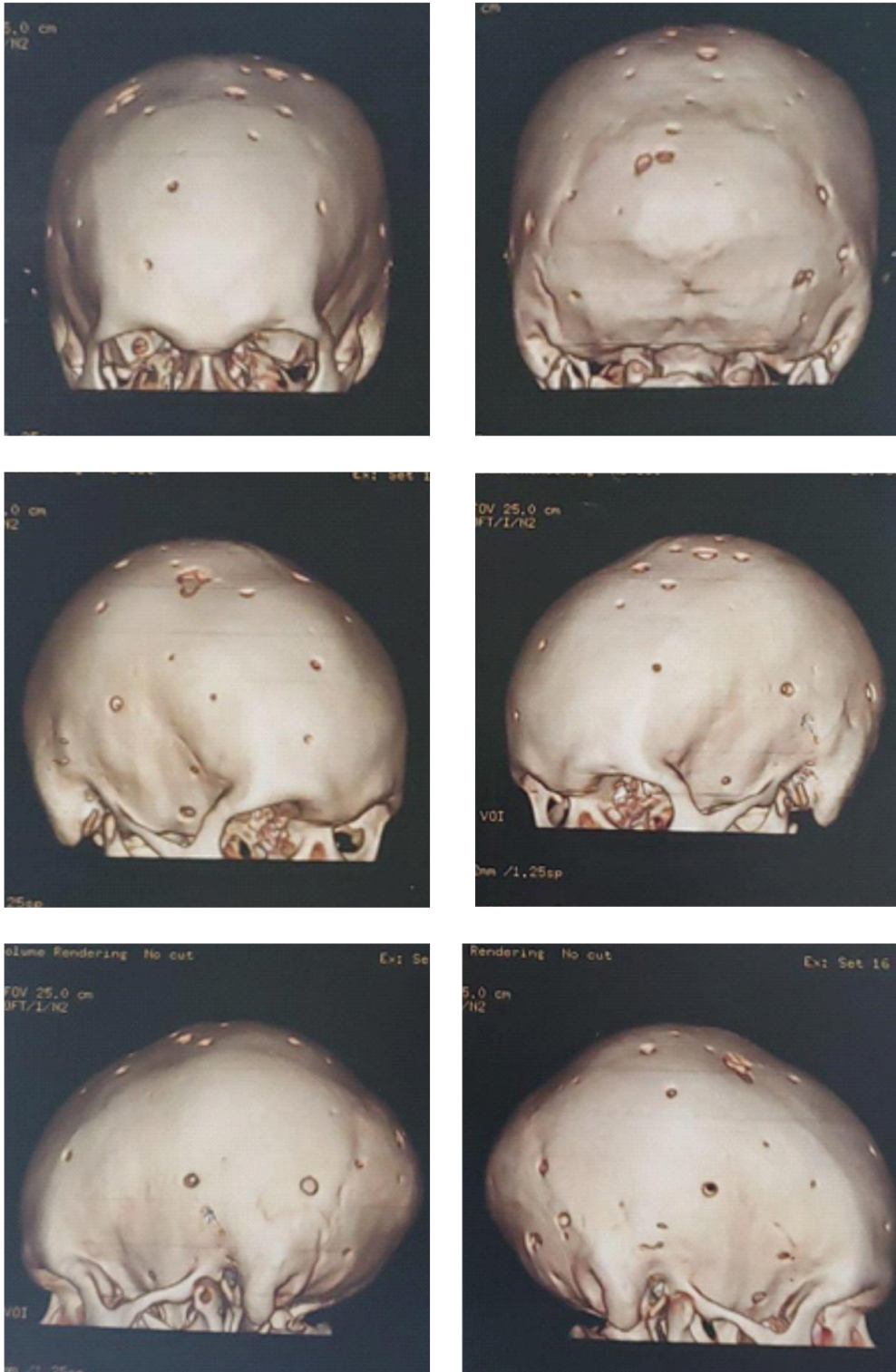


Source: Silva IR, et al., 2023.

Follow-up and new tests were hampered by the COVID-19 pandemic. Thus, in September 2021, the patient had an episode of falling from a standing height followed by a confusional state, aphasia, ataxia, and right hemiparesis. When seeking care at a local emergency room, the main diagnostic hypothesis was a stroke,

which was followed by computed tomography. With the result of the tomography, the hypothesis of intracranial hemorrhage was excluded and it evidenced the presence of multiple lytic bone lesions scattered throughout the cranial vault, some with soft tissue components, with the possibility of secondary neoplastic involvement (**Figure 3**). After hospitalization for stabilization, the patient was referred to the local oncological assistance service.

**Figure 3** - Three-dimensional reconstruction of the skull using computed tomography.



Source: Silva IR, et al., 2023.

In October 2021, the patient was admitted to the emergency service with disorientation and psychomotor agitation, referred by the oncology care service after diagnosis of tumor lysis syndrome and acute kidney injury (serum creatinine 3.9 mg/dL), with stabilization objective for biopsy. After the initial investigation, he was referred to the medical clinic sector.

On physical examination, the patient had a regular general condition, tachycardia, a score of 14 on the Glasgow coma scale, with no alterations on pulmonary and cardiac auscultation, and no abdominal alterations. Chest examination showed a floating mass in the right infra-axillary region, hard and mobile, measuring approximately 5 cm in diameter and painful on palpation. We proceeded with a treatment protocol for delirium and administration of volumes to recover hydro electrolyte balance. On November 20, 2021, the patient died of cardiac arrest, without recovery, even after administering an adequate care protocol. The death prevented a further histopathological investigation.

## DISCUSSION

This report describes a case that has not yet been reported in the literature. The extensive bibliographical research did not show any study with a description of manifestations such as the one presented in the present report. Breast cancer in male patients is a rare event, with a much lower incidence than that seen in women (ABDELWAHAB YOUSEF AJ, 2017; SERDY KM, et al., 2017), corresponding to approximately 1% of cases of breast cancer and 1% of malignant neoplasms in men. Despite this, there has been an increase in the number of diagnoses of new cases in the last two decades, making it necessary to produce more evidence about this health problem (KONDURI S, et al., 2020). The lifetime risk of breast cancer is approximately 1:1000 for men, while it is approximately 1:8 for women (HASSETT MJ, et al., 2020).

The genesis of breast cancer in men remains poorly understood (ABDELWAHAB YOUSEF AJ, 2017), but the current literature already recognizes the main risk factors associated with its development. Major risk factors include a family history of breast cancer, mutations in the BRCA1 and BRCA2 genes, elevated estrogen levels, obesity, radiation exposure, gynecomastia, Klinefelter syndrome, and advanced age (KHAN NA e TIRONA M, 2021). Breast cancer incidence rates increase with age for both men and women, however, in men, the average age at diagnosis is about five years older (67 years) when compared to women (62 years) (HASSETT MJ, et al., 2020). In males, as well as in females, family history is a very important risk factor, being more prominent when observed in first-degree relatives (ZEHR KR, 2019). In a prospective cohort study, it was shown that the risk almost doubled in men with a history of breast cancer in first-degree relatives, with the risk being particularly greater for those who had both an affected mother and sister (BRINTON LA, et al., 2008).

Genetic risk also plays a particularly important role in the development of breast cancer in men. International studies demonstrate that mutations in the BRCA2 gene, a tumor suppressor gene, are present in a considerable number of male breast tumors, with a much higher distribution than mutations in the BRCA1 gene (DING YC, et al., 2011). Although the association with genetic alterations is already well described, the relationship with environmental risk factors is still not fully understood. Reports of increased risk for male breast cancer among atomic bomb survivors and among individuals who have had occupational exposure or who have received therapeutic irradiation support the role of ionizing radiation as an important risk factor (ABDELWAHAB YOUSEF AJ, 2017; BRINTON LA, et al., 2008). Hormonal factors have also been implicated in several studies, mainly related to physical inactivity, obesity, alcohol consumption, and exogenous use of estrogens and androgens (BRINTON LA, et al., 2008; METHAMEM M, et al., 2020).

The diagnosis of male breast cancer involves clinical, radiological, and histopathological evaluation, similar to what is done in cases of female breast cancer. A high index of suspicion and careful clinical evaluation of breast complaints in male patients, especially those with known risk factors, are essential steps to avoid diagnostic delays (NOFAL MN e YOUSEF AJ, 2019). The most common clinical picture is the presence of a painless retroareolar mass, which is suspicious on mammography and ultrasound (NOFAL MN e YOUSEF AJ, 2019). The American College of Radiology (ACR) currently recommends that ultrasonography should be the initial method used to evaluate palpable changes in the male breast in patients younger than 25 years. For

patients over 25 years of age, mammography should be chosen as the initial evaluation method, to be complemented with ultrasonography if the findings are inconclusive or suspicious. Also according to the ACR, magnetic resonance imaging has restricted use in the initial evaluation, and should be used in individualized cases, mainly in the staging of confirmed cases (EXPERT PANEL ON BREAST IMAGING, et al., 2018; MAKDISSI FBA, et al., 2022).

The main differential diagnosis of breast tumors in men is gynecomastia, which can be differentiated from carcinomas by imaging methods. As the presence of fibroadenomas and cysts is very rare in males, any solid mass identified on imaging tests should be considered suspicious for malignancy. For diagnostic confirmation, an ultrasound-guided percutaneous biopsy followed by histological examination is required (EXPERT PANEL ON BREAST IMAGING, et al., 2018; MAKDISSI FBA, et al., 2022). The most commonly encountered histological type is stage II or III invasive ductal carcinoma. As for histological subtypes, invasive carcinoma without a special type stands out (more than 90% of cases), followed by papillary carcinoma and invasive micropapillary carcinomas (NOFAL MN e YOUSEF AJ, 2019).

The low incidence of male breast cancer does not allow the indication of periodic screening tests, however, the possibility of screening in men at high risk of developing breast cancer, such as those with mutations in the BRCA genes, is already being discussed (MAKDISSI FBA, et al., 2022). National Comprehensive Cancer Network (NCC) guidelines recommend that men with mutations in the BRCA genes receive training in breast self-examination and annual clinical examination starting at age 35. In addition, annual mammography can be considered in men with gynecomastia from the age of 50 or in men with a positive family history of breast cancer (DALY MB, et al., 2021).

The current literature describes that cases of breast cancer in men generally have a worse prognosis when compared to that observed in female patients (GILBERT SF, et al., 2011). The case described refers to a patient with a diagnosis made after years of complaints and with clinical and radiological evidence of a long course of the disease, such as the presence of a compromised lymph node, bilateral nodules, and tomographic signs of metastases in the skull and brain. The literature corroborates the case described concerning lymph node involvement, showing a high frequency already at the time of diagnosis of breast cancer in men (EL OMARI-ALAOUI H, et al., 2002).

According to the literature, axillary lymph node involvement at presentation is more common in men than in women. Furthermore, due to the smaller size of the breast tissue in men, nipple involvement is common and can occur early, with the presence of ulceration in 6% of cases, papillary discharge in 6%, and retraction in 9% of patients. (NOFAL MN e YOUSEF AJ, 2019).

The most exuberant clinical manifestation of the case described and that possibly justifies the development of neurological symptoms clinically identified in the patient is the presence of lytic lesions in the skull due to secondary neoplastic involvement. This pattern demonstrates differences about the present in the literature. In a study using bone scintigraphy in a group of patients diagnosed with malignant neoplasms, it was observed that the most frequent sites of metastases for breast cancer were vertebrae, ribs, and sternum, demonstrating that the involvement of the cranial vault is a rare event (KAKHKI VRD, et al., 2013).

Bones are the third most common target for cancer metastases, after the lungs and liver. Metastases to skull bones represent about 14% of all metastases to the skeletal system. Furthermore, breast, lung, and prostate cancer together account for about 80% of bone metastases (ZAJĄCZKOWSKA R, et al., 2019).

Cranial metastases are usually multiple and have an expansive and osteolytic character, which is consistent with the presentation of the case described. According to the literature, most of these lesions are asymptomatic and tend to be clinically less important than intraparenchymal lesions, however, they can cause severe discomfort and neurological symptoms due to compression of cranial nerves and dural venous sinuses when they grow significantly. There may be symptoms related to increased intracranial pressure, especially due to obstruction of cerebral venous outflow (PEREIRA CU e MELO MS, 2009; STARK AM, et al., 2003). The patient in the case presented a focal neurological condition and an acute confusional state that was mistaken for a cerebrovascular accident at first. According to the literature, in some cases, focal neurological deficits may be

caused by progressive ingrowth of a metastatic cranial lesion. Other symptoms such as seizures and hemiparesis may also be present (PEREIRA CU e MELO MS, 2009; STARK AM, et al., 2003). Metastatic lesions of the cranial vault do not present pathognomonic signs that differentiate them from other lesions (PEREIRA CU e MELO MS, 2009). The differential diagnosis includes benign tumors and primary tumors. A study that retrospectively evaluated 38 patients who underwent surgery for cranial lesions identified that patients with metastases were older and had a shorter duration of symptoms compared to patients with primary and benign tumors (STARK AM, et al., 2003).

In the case described, the patient also presented a clinical picture compatible with the diagnosis of tumor lysis syndrome. This syndrome is a rare phenomenon that occurs more commonly in patients with aggressive hematologic tumors or tumors that are highly sensitive to chemotherapy. The association of tumor lysis syndrome with highly responsive tumors, such as lymphomas and leukemias, is already well described in the literature, but its occurrence in solid tumors is uncommon (HANDY et al., 2021; SKLARIN; MARKHAM, 1995).

Tumor lysis syndrome is a set of metabolic changes associated with the rapid lysis of neoplastic cells and characterized by hyperuricemia, hyperphosphatemia, hyperkalemia, and hypocalcemia. It can cause acute kidney injury and severe hydroelectrolytic disorders, which in turn predispose to the occurrence of arrhythmias, seizures, and sudden death (HANDY C, et al., 2021). In the acute setting, the initial approach should include intravenous hydration, correction of hydroelectrolytic disturbances, drugs directed at hyperuricemia and, in severe cases, hemodialysis may be necessary (BARBAR T e JAFFER SATHICK I, 2021).

A low index of suspicion due to the rarity of the disease and the lack of awareness of doctors and patients about the presence of breast cancer in men are implicated in important diagnostic delays, with an average delay of 6 to 10 months after the onset of symptoms. More than 40% of men with breast cancer have stage III or IV, and in North Africa, this percentage reaches 50 to 60% (NOFAL MN e YOUSEF AJ, 2019; SERDY KM, et al., 2017). Therefore, raising awareness about the presence of this type of cancer in men is necessary to promote the search for care in cases of breast changes in this group of patients (NOFAL MN e YOUSEF AJ, 2019).

Treatment for male breast cancer generally follows the pattern used for tumors in women (RUDDY KJ e WINER EP, 2013). The low incidence of these tumors makes it difficult to study specific therapies and analyze patients' responses to different approaches. The patient in question did not have the opportunity to undergo therapeutic interventions, especially due to the situation resulting from the COVID-19 pandemic, which culminated in the delay of therapeutic measures in oncology worldwide (ARAUJO SEA, et al., 2020; BOZOVICH GE, et al., 2020; CARVALHO HDEA, et al., 2020; FELETTI E, et al., 2020).

Breast cancer in men is a rare event and, for this reason, studies and research about it are still scarce. This neoplasm is often diagnosed in more advanced stages, with a high rate of lymph node involvement and distant metastases, probably as a reflection of late diagnosis in male patients.

Therefore, it is important to understand the disease and its clinical manifestations, as well as to raise awareness about this type of cancer in men, considering the importance of early diagnosis for a better prognosis. In addition, further studies on specific therapeutic options for male breast cancer are needed to establish an evidence-based standard of care for this population.

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