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Silent Layers: An Uncommon Case of Breast Amyloidosis

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Abstract **Case Report**

Amyloidosis is a rare condition characterized by the abnormal accumulation of amyloid fibrils in various organs and tissues, leading to organ dysfunction. Breast amyloidosis is a rare and poorly understood condition characterized by localized deposition of amyloid fibrils in breast tissue. This report describes an 86-year-old female diagnosed with localized bilateral breast amyloidosis. The patient's history of gynecological malignancy treated with chemotherapy and radiotherapy may have contributed to the localized amyloid deposition. Histopathological examination confirmed the diagnosis through Congo red staining, which demonstrated characteristic green birefringence under polarized light. This case emphasizes the diagnostic challenges associated with breast amyloidosis and underscores the need for heightened awareness among clinicians to distinguish it from other breast pathologies. It also highlights the potential role of cancer treatments and chronic inflammation in the development of amyloidosis. Management strategies are discussed, emphasizing individualized care and the role of conservative versus surgical approaches.

Keywords: Breast amyloidosis, amyloidosis, Congo red staining, chronic inflammation, cancer therapy.

INTRODUCTION

Amyloidosis is a rare disease caused by the extracellular deposition of insoluble amyloid fibrils - misfolded proteins that infiltrate various tissues and organs, which can compromise organ function. Although systemic amyloidosis has been extensively studied, localized amyloidosis, particularly in the breast, remains exceedingly rare.

Breast amyloidosis can be primary or secondary. Primary amyloidosis is linked to hematological diseases such as multiple myeloma, while secondary amyloidosis often arises in the context of chronic inflammation, infections, or malignancy. Localized breast amyloidosis is even rarer, frequently discovered incidentally and often confused with malignancies due to imaging similarities. Chemotherapy and radiotherapy are known to induce chronic inflammatory responses, which could serve as triggers for amyloid deposition in breast tissue [1, 2].

This case report describes an elderly patient with bilateral breast amyloidosis, exploring its pathophysiology, diagnostic pathway, and management, thus broadening the understanding of this rare condition. It also discusses the role of chronic inflammation and cancer treatments as potential contributors to amyloid deposition in breast tissue [3, 4].

CASE REPORT

An 86-year-old female presented for evaluation of bilateral breast masses detected during a routine examination. The patient had a significant medical history, including small cell carcinoma of the cervix treated 8 years earlier with hysterectomy, bilateral adnexectomy, chemotherapy, and radiotherapy. She also had comorbidities including hypertension, dyslipidemia, ischemic heart disease, and prior stroke.

On physical examination, the breasts were firm and non-tender, resembling calcified masses, prompting further investigation. Imaging studies, including mammography and CT (Figure 3), revealed dense calcifications suggestive of amyloid infiltration without evidence of malignancy (Figure 1 and Figure 2).

Core needle biopsies were performed on both breasts, and histopathological analysis, including Congo red staining, confirmed the presence of amyloid deposits in the tissue, which exhibited green birefringence under polarized light [5]. The findings indicated localized amyloidosis confined to the breast, likely secondary to the patient's prolonged inflammatory state, induced by

both her cancer treatments and ongoing systemic conditions, without evidence of systemic involvement.

Given the patient's advanced age, comorbidities, and lack of significant symptoms related to the breast masses, conservative management was chosen. She was monitored closely for systemic amyloidosis signs and complications from her other medical conditions.

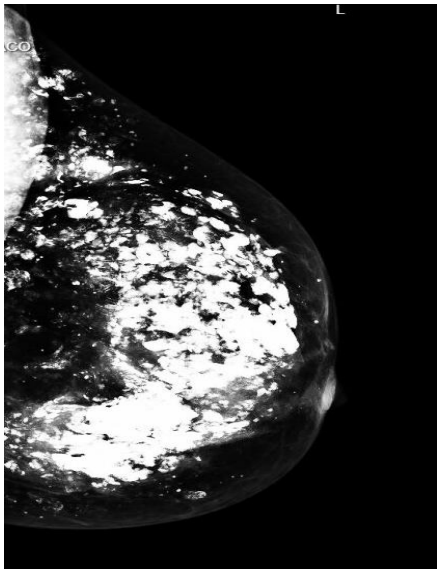

Figure 1: Mammogram showing extensive calcifications suggestive of breast amyloidosis

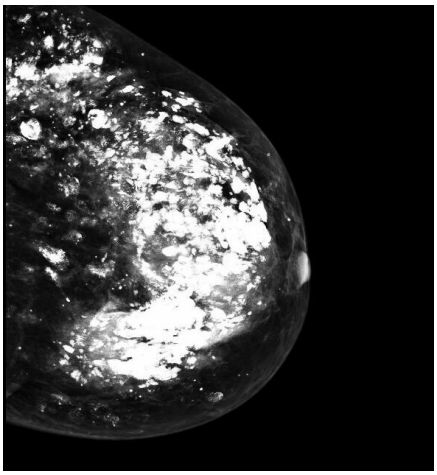

Figure 2: Additional mammogram view with diffuse calcifications typical of amyloidosis

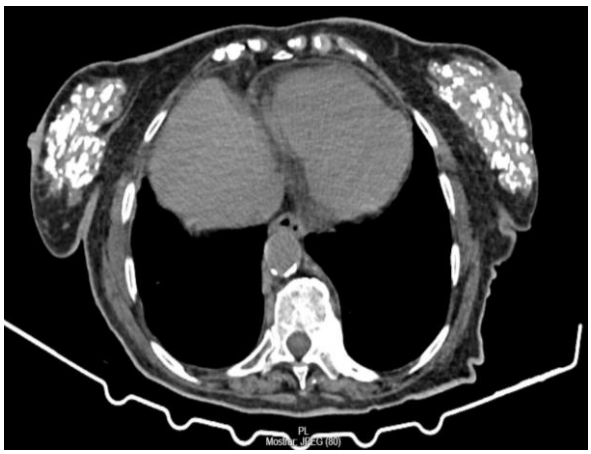

Figure 3: Axial CT showing calcified deposits in breast tissue, indicating amyloidosis

DISCUSSION

Localized breast amyloidosis presents unique diagnostic and management challenges due to its rarity and nonspecific presentation. In this case, the patient's history of gynecological malignancy and subsequent treatments likely played a role in the pathogenesis. Chronic inflammation induced by chemotherapy and radiotherapy has been implicated in the misfolding and deposition of amyloid fibrils. Although systemic amyloidosis is often associated with organ dysfunction and worse outcomes, localized forms, such as this one, typically have a more benign course [1, 6]. The masses found in this case were painless and often mimic other benign or malignant tumors. This makes amyloidosis a challenging diagnosis to consider without histopathological confirmation, especially in patients with a history of cancer [4, 7].

The standard diagnostic method for amyloidosis is histopathological examination. Imaging, while helpful in identifying calcifications and masses, is insufficient to differentiate amyloidosis from other conditions. Congo red staining, the gold standard, provides definitive evidence of amyloid deposits, as demonstrated in this case. Differentiating localized from systemic amyloidosis is critical, as the treatment and prognosis differ significantly [5].

Management of localized breast amyloidosis varies depending on the patient's symptoms and overall health. As in this case, conservative management is often appropriate for asymptomatic or minimally symptomatic patients, particularly those with significant comorbidities. Surgical intervention, ranging from limited excision to mastectomy, may be warranted in cases where the masses cause pain, cosmetic concerns, or diagnostic uncertainty. Recent literature underscores the importance of individualized care, particularly in elderly patients with complex medical histories [8].

Medical treatment for amyloidosis depends on the underlying etiology of fibril production. While systemic amyloidosis may require targeted therapies such as anti-CD38 monoclonal antibodies or novel investigational agents, localized amyloidosis typically does not warrant systemic therapy. In cases where systemic amyloidosis is suspected or identified, combination therapies involving daratumumab, cyclophosphamide, bortezomib, and dexamethasone remain the cornerstone of treatment. For localized cases like this, the emphasis is placed on monitoring and addressing local symptoms.

Surgical management of breast amyloidosis should be carefully tailored to the individual. Given that localized breast amyloidosis is a benign condition with no reported cases of progression to systemic disease, routine excision is not always necessary. When excision is desired, either for symptom relief or patient preference, the risks of potential complications, such as scarring, dimpling, or ductal damage, should be carefully communicated. For patients requiring mastectomy due to concurrent breast cancer, reconstruction decisions should consider the unique risks posed by amyloid deposits, including potential vascular complications and the possibility of amyloid deposition in autologous tissue transfers. Abdominal fat pad biopsy prior to autologous reconstruction is a valuable tool to minimize unexpected outcomes and inform surgical planning.

When implant-based reconstruction is performed, particular attention must be given to mitigating risks such as capsular contracture, which may be exacerbated by amyloid-related vascular abnormalities. The use of acellular dermal matrices can reduce such risks and enhance reconstructive outcomes. For cases requiring post-mastectomy radiation therapy, a staged reconstructive approach may optimize both aesthetic and functional results while minimizing complications.

This case highlights the importance of considering amyloidosis in the differential diagnosis of breast masses, particularly in patients with a history of malignancy or chronic inflammation. Recognizing this rare condition can prevent unnecessary interventions and improve patient outcomes. It also raises awareness about the potential long-term effects of cancer therapies, emphasizing the need for ongoing vigilance in the care of cancer survivors [9, 10].

CONCLUSION

Breast amyloidosis is a rare and underdiagnosed condition that must be considered in the evaluation of breast masses, especially in patients with a history of malignancy or cancer treatment. In this case, the patient's chemotherapy and radiotherapy likely contributed to the localized amyloid deposition in the breasts. Diagnosis was confirmed through biopsy and Congo red staining, and conservative management was chosen due to the patient's advanced age and minimal symptoms.

The growing understanding of amyloidosis highlights the importance of a multidisciplinary approach to patient care. For localized breast amyloidosis, monitoring with annual mammograms and physical exams provides a non-invasive means of managing asymptomatic cases. In contrast, patients presenting with concurrent malignancies require tailored surgical strategies that address both the oncological and reconstructive challenges posed by amyloid-related complications.

This report underscores the importance of histopathological confirmation in diagnosing breast amyloidosis and highlights the need for individualized management strategies. Further research is needed to better understand the pathophysiology of localized breast amyloidosis and its association with chronic inflammation and cancer therapies [6][8]. Moreover,

ongoing investigations into the implications of amyloid deposits in reconstructive surgery may refine surgical techniques and patient counseling, contributing to improved care for individuals with this rare condition.

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DECLARATIONS

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Ethical Approval: Not required

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