








# Lymphedema secondary to bartonellosis as a differential diagnosis of breast cancer

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## ABSTRACT

In the presence of unilateral axillary lymphadenopathy associated with a breast radiological finding, breast cancer should constitute the main differential diagnosis. This fact is intensified when there is associated lymphedema. We present a case of a patient in these conditions, for whom breast cancer was not confirmed, and a subsequent evaluation showed that it was cat-scratch disease. This report constitutes the second case of association between lymphedema and bartonellosis.

**KEYWORDS:** bartonella henselae; cat-scratch disease; lymphedema; breast neoplasms; lymphadenopathy.

## INTRODUCTION

When axillary lymphadenopathy is the first clinical finding, a wide range of etiologies must be considered – both benign and malignant<sup>1-3</sup>. Malignant etiologies should be ruled out and, when excluded, the etiological diagnosis is not always easy, often being one of exclusion.

Lymphedema is a chronic condition resulting from lymphatic obstruction, usually associated with a malignant condition<sup>4</sup>, or being associated with a rare benign condition. The main diagnostic problem is how to approach a patient with unilateral axillary lymphadenopathy associated with lymphedema whose breast and axillary cancer evaluation was negative.

## CASE REPORT

A female, 47-year-old patient was referred to an oncology service due to a suspicious lesion in the upper exterior quadrant of the right breast, seen in the mammography and ultrasound (BI-RADS V). At the same time, serological tests were made for toxoplasmosis, with negative IgM and reactive positive IgG.

The patient denied having previous comorbidities and autoimmune diseases, and no family history of neoplasm. The physical examination showed absence of palpable breast mass, presence of

a 49 mm axillary adenopathy to the right, associated with lymphedema (2 cm difference in the diameter of the forearm, assessed 10 and 20 cm below the elbow). There were no other peripheral adenopathies. At first, neoplasia was considered the main differential diagnosis, because of the highly frequent association of adenopathy/lymphedema with breast neoplasia.

Mammography detected a nodule in the left breast, and right axillary lymph node enlargement (Figure 1A). An ultrasound showed a cyst in the left breast and confirmed the presence of an expansive formation in the right axilla, with approximate volume of 23 cm<sup>3</sup>, irregular shape, lobulated margins and roughly heterogeneous echotexture, with asymmetric cortical thickening, BI-RADS IV (Figures 1B and C). A venous doppler of the upper right limb (URL) did not show history of thrombosis. Chest computed tomography showed parenchymal enhancement in the upper side of the right breast, associated with heterogeneous axillary lymph node enhancement to the cost of necrotic degeneration, measuring up to 2.4 cm (Figure 1D). Abdominal and pelvic computed tomography showed no changes. The results of the blood test and serology for the human immunodeficiency virus (HIV) were normal.

Fine needle aspiration indicated chronic granulomatous inflammation associated with acute inflammation in the

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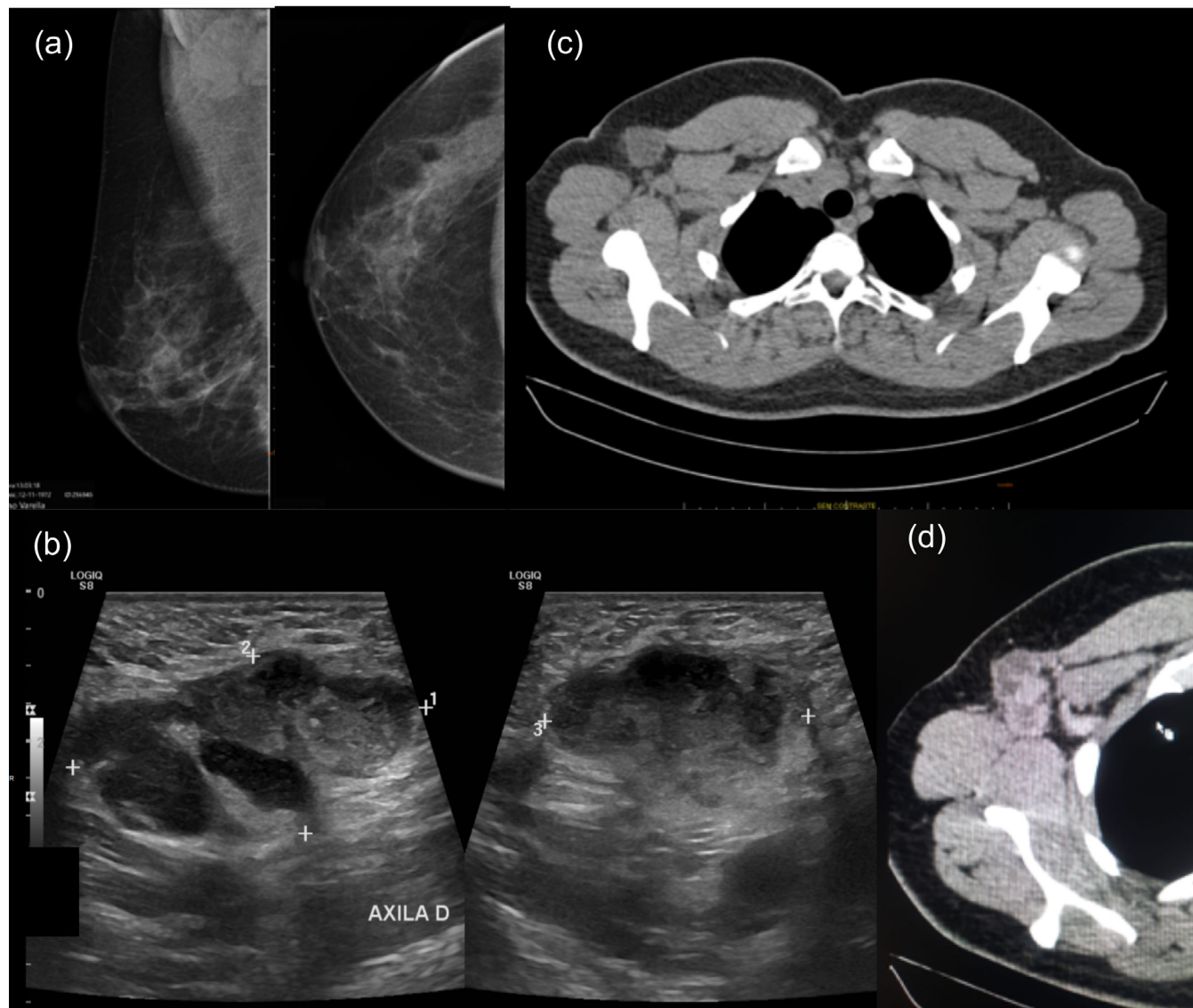
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right axillary region, and core biopsy brought a diagnosis compatible with necrotizing granulomatous lymphadenopathy. The search for Acid-alcohol-resistant bacilli (BAAR) was negative. Due to the conflicting radiological and clinical findings, the choice was to perform an open biopsy, aiming at increasing the sample. Right axillary lymphadenectomy was performed. The anatomopathological examination of the surgical piece identified non-caseating granulomatous lymphadenitis, besides the absence of microorganisms according to the methods used for evaluation (Figures 2a and 2b). The hypothesis of neoplasm had been excluded, so it was necessary to assess other differential diagnoses, as well as to conduct an etiological evaluation aiming at a specific treatment.

In a new appointment, the patient reported working with sick animals (dogs and cats). Then, a test for cryptococcosis and angiotensin converting enzyme was requested to investigate sarcoidosis; the tests were negative. Then, a serology for *Bartonella henselae* was conducted, and showed negative IgM and reactive IgG (1:640). The gene expression analysis using the PCR technique (Polymerase Chain Reaction) in the lymph node was positive<sup>5</sup> in segment of 138pb of the 16S-23S region, intergenic region of the ribosomal ribonucleic acid (rRNA) coding genes of the bacteria, fact that corroborates the lymph node infection by *Bartonella henselae* (Figures 2c and 2d). The treatment was carried out with azithromycin 500 mg (oral administration) for five days. After 12 months, the patients no longer presents with lymphadenopathy, IgG serology 1:320; however, with persistent lymphedema.



(a) Mammography – increased lymph nodes to the right; (b) Ultrasound – heterogeneous axillary adenopathy, with solid and cystic areas, hypervascularization (c,d) axillary lymphadenopathy to the cost of necrotic degeneration.

**Figure 1.** Radiological finding.



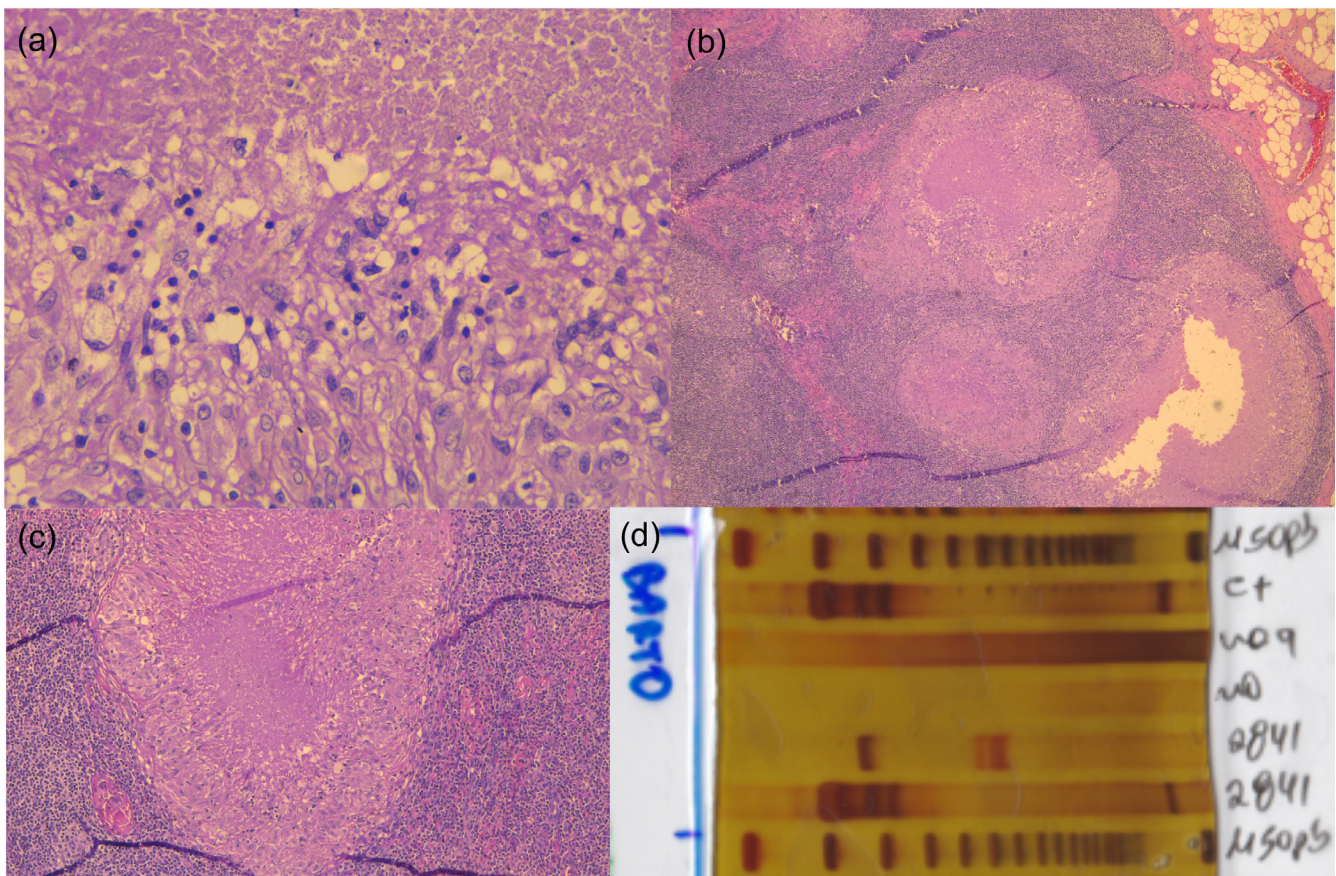
## DISCUSSION

In patients with unilateral lymphadenopathy, when considering the evaluation of unilateral axillary lymphadenectomy, it is important to observe the age, usually associated with inflammatory pathologies in younger patients, and neoplasm<sup>2,6</sup> among the older ones<sup>7,8</sup>. The patient was 47 years old, and at that age the first differential diagnosis to be considered is breast neoplasm<sup>6,7,9,10</sup>. The first image showed a radiological change in the breast, which, due to the adenopathy, was classified as BI-RADS V, fact that is also observed in other studies<sup>7,8</sup>, which led the patient to see a mastologist.

At the presence of neoplasm, immunohistochemistry will often define the primary site, and at the presentation of a possible unknown primary breast disease, associated with axillary metastasis, breast nuclear magnetic resonance becomes an essential test<sup>3,11</sup>. This case has a peculiar characteristic, which is the lymphedema, frequent cause in advanced breast carcinoma and rare in infectious/inflammatory pathologies. The presence of a lymphedema mimics the existence of a carcinoma; however, the data showed an infectious etiology. Such a fact was influenced

by the infrequency of lymphedema associated with benign infectious pathologies; the last known case of bartonellosis associated with unilateral axillary lymphadenopathy and lymphedema was described in the 1960s<sup>12</sup>.

At the presence of non-caseating granulomatous lymphadenitis, tuberculosis should be considered; however, the assessment of the material using the BAAR analysis (Ziehl-Neelsen staining) was negative. Therefore, the possibility of cryptococcosis and *Bartonella* was considered since serology was positive in the second case. The main manifestation of the cat scratch disease is regional lymphadenopathy, often affecting the axilla and the neck. This lymphadenopathy appears approximately two weeks after the cat scratch and can persist for a few months<sup>13</sup>. *Bartonella henselae* is a gram-negative rod that causes the cat scratch disease. Cats are natural reservoirs for this microorganism, developing bacteremia when infected. This bacteria can stay in the host's blood for long periods without causing them any symptom, due to its intraerythrocytic parasitism<sup>14,15</sup>. Even though the patient was treated with antibiotics, the lymphedema remained present after the physical therapy treatment and glove application,



(a) 400XX increase: palisade of histiocytes surrounding necrosis; (b) 40XX increase: microabscesses adjacent to the capsule; (c) 100XX increase: microabscess with histiocytes surrounding necrosis; (d) RT-PCR primer of the study of *Bartonella henselae*. M — molecular marker (50pb); C+ — positive control (DNA extracted from the culture of *B. henselae*); No — negative control (without DNA); T — tested sample. The tested sample (T) presents an amplification 138 pb, suggestive of infection by *B. henselae*.

**Figure 2.** Pathological findings.

potentially associated with lymph node tissue damage. Since the presence of lymphedema was verified at diagnosis, it is possible to say that this is the second report of this type of case published in the literature, thus justifying its exposure<sup>12</sup>.

## CONCLUSION

Although it is a rare condition, bartonellosis may mimicking breast cancer. It must be considered in the differential diagnosis of a benign condition associated with unilateral axillary lymphadenopathy and lymphedema. IgG serology suggest the association, but PCR reaction is necessary to prove this condition.

## AUTHORS' CONTRIBUTION

ACMMF: Data curation, Formal analysis, Methodology, Visualization, Writing – review & editing. BLGM: Data curation, Investigation, Resources, Visualization, Writing – review & editing. PCFJ: Investigation, Resources, Visualization, Writing – review & editing. LCNOF: Investigation, Visualization, Writing – review & editing. HCS: Investigation, Resources, Visualization, Writing – review & editing. LCNO: Data curation, Visualization, Writing – review & editing. CEB: Investigation, Resources, Visualization, Writing – review & editing. RACV: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – review & editing.

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