A 36-Year-Old Woman With a Unilateral Breast Mass

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A 36-year-old Hispanic woman presented to University Hospital for further evaluation of a mass in her left breast. The mass had been present for 5 months and was painful. The past medical history was significant for human immunodeficiency virus disease, end-stage acquired immunodeficiency syndrome (CD4 count of 99 cells/mm³ and a viral load of 200,000 copies/µL), hepatitis B and C, syphilis, cytomegalovirus infection, left-sided blindness, and multiple lung nodules. There was no family history of breast cancer. Physical examination revealed a palpable 2-cm mass in her left breast. The initial workup, including mammography and a core biopsy of the mass, was performed at another hospital. The mammogram revealed a suspicious asymmetrical density at 7 o’clock. An excisional biopsy was performed at our institution and the specimen was submitted for pathologic and microbiologic evaluation.

Gross examination revealed adipose tissue containing a 2.5 × 1.0 × 1.0-cm circumscribed mass that was firm and gray-tan in color. Histologic examination showed breast tissue with necrotizing granulomatous inflammation (Figure 1). The lobules contained necrotic debris and were diffusely infiltrated by epithelioid histiocytes, lymphocytes, plasma cells, occasional multinucleated giant cells, and polymorphonuclear leukocytes. Histiocytes containing multiple intracellular organisms with peripheral clearing were identified with hematoxylin-eosin stain (Figures 2 and 3). Yeast forms with narrow-based buds and nonbudding yeast forms measuring 2 to 4 µm were noted with Grocott-Gomori methenamine-silver stain (Figure 4). A similar granulomatous process was found in a biopsy of lung nodule samples. The histologic findings were confirmed with microbiologic cultures.

What is your diagnosis?
Pathologic Diagnosis: Necrotizing Granulomatous Mastitis Secondary to Budding Yeast Forms Morphologically Consistent With Histoplasma capsulatum

Abstract

Histoplasma capsulatum is a thermal dimorphic fungus found primarily along the major river valleys in parts of North America. It is contracted by the inhalation of fungal spores, and infrequently causes clinical disease. Histoplasma capsulatum is an extremely rare cause of granulomatous mastitis. The organism causes a necrotizing granulomatous inflammation of the breast lobules; 2- to 4-μm yeast forms of the organism are seen within histiocytes. The definitive diagnosis is made by several mechanisms, including microscopic examination, microbiologic culture, antigen detection, and serologic tests. The main differential includes other fungal infections, Mycobacterium tuberculosis, sarcoidosis, and idiopathic granulomatous mastitis. Treatment of \( H \) capsulatum granulomatous mastitis is complete excision followed by antibiotic therapy.

Granulomatous mastitis secondary to Histoplasma capsulatum is an infrequently reported entity that has been documented in women ranging from 21 to 74 years of age. Typically, the patient presents with a history of a gradually increasing unilateral breast mass. There may be overlying skin retraction and/or inflammation. There has been a report of 1 patient who also presented with axillary lymphadenopathy. A common mammographic finding is an asymmetrical density with a thickening of overlying skin. This dense area may be clinically and radiographically difficult to distinguish from breast cancer. The definitive diagnosis of \( H \) capsulatum is made by several mechanisms, including antigen detection in body fluids, microscopic examination of tissue and blood, isolation and characterization of the fungus in culture, and serologic tests.

The gross examination shows a firm, whitish tan, and focally necrotic mass with surrounding adipose tissue. Histologic examination reveals a necrotizing granulomatous inflammatory process involving breast lobules. The inflammatory infiltrate is composed of polymorphonuclear leukocytes, mononucleated and multinucleated epithelioid histiocytes, lymphocytes, and, occasionally, eosinophils. Histiocytes containing intracellular fungi that are morphologically consistent with \( H \) capsulatum are seen with Grocott-Gomori methenamine-silver stain, are not identified with mucicarmine staining, and occasionally demonstrate a periodic acid–Schiff reaction. The organism may exhibit a peripheral clearing fixation artifact on hematoxylin-eosin stain. The definitive diagnosis is made by several mechanisms, including antigen detection in body fluids, microscopic examination of tissue and blood, isolation and characterization of the fungus in culture, and serologic tests.

The main differential diagnosis of granulomatous mastitis secondary to \( H \) capsulatum includes other fungal infections, Mycobacterium tuberculosis, sarcoidosis, and idiopathic granulomatous mastitis. Clinical correlation as well as laboratory and radiographic studies are important in determining the correct diagnosis. Fungal organisms likely to be confused with \( H \) capsulatum in tissue sections include yeast forms of Torulopsis glabrata and Blastomyces dermatitidis. Torulopsis glabrata is primarily an extracellular organism and does not exhibit a peripheral clearing fixation artifact with hematoxylin-eosin stain. Blastomyces dermatitidis is a multinucleated fungal spore that demonstrates broad-based budding. Necrotizing granulomas are present in \( M \) tuberculosis. Acid-fast organisms are identified by Zielh-Neelsen stain, microbiologic culture, or molecular techniques. In sarcoidosis, there are nonnecrotizing, well-circumscribed small granulomas with an associated lymphocytic infiltrate and a lack of abscess formation.

Idiopathic granulomatous mastitis has also been described as granulomatous lobular mastitis. In 1972, Kessler and Wellcho introduced the term granulomatous mastitis to describe nonspecific lobular granulomatous inflammation occurring in the absence of a known contributory cause. Since then, approximately 120 cases of granulomatous mastitis have been reported worldwide. Some proposed causes of this disease include autoimmunity, undetected organisms, oral contraception use, and a localized immune response to extravasated secretions associated with parturition and lactation.

Treatment of \( H \) capsulatum granulomatous mastitis is complete excision followed by initial treatment with amphotericin B. Continued maintenance treatment with itraconazole, fluconazole, or amphotericin B is necessary for the treatment of disseminated histoplasmosis to decrease relapse.

References