

> **THE PATIENT**  
44-year-old woman  
from Afghanistan

> **SIGNS & SYMPTOMS**

- Firm, non-tender mass in right breast
- Worsening, nonproductive cough
- Pleuritic pain

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## > THE CASE

A 44-year-old woman with a 15-year history of type 2 diabetes sought care for a firm, non-tender mass in the medial lower quadrant of her right breast. She hadn't experienced any skin changes or axillary lymphadenopathy. The patient had immigrated to California from Afghanistan 22 years earlier, at which time she was briefly married to an Afghan man suffering from a chronic cough.

Mammography revealed a 3.5 x 4 x 4 cm lesion at the chest wall, which was highly suspicious for carcinoma (FIGURES 1A AND 1B). Sonography showed a heterogenous hypoechoic and isoechoic mass with posterior acoustic enhancement (FIGURE 1C). An excisional biopsy was performed.

One week postoperatively, the patient presented to the emergency department for a worsening nonproductive cough that intensified when supine, and was associated with subscapular pleuritic pain. She denied fever or weight loss. Biopsy results were pending.

## THE DIAGNOSIS

Chest x-rays revealed a large right pleural effusion that was presumed to be malignant (FIGURES 1D AND 1E). Thoracentesis yielded 1.5 liters of tea-colored exudate containing 2800 nucleated cells/mL—63% lymphocytes and 37% neutrophils—and a pleural fluid to serum protein ratio >0.5. Adenosine deaminase was <1 U/L. Fluid Gram stain, acid-fast bacillus (AFB) fluorescent antibody testing, AFB cultures, and cytology were negative. Computed tomography (CT) subsequently demonstrated recurrent effusion without hilar or mediastinal lymphadenopathy or pleural enhancement (FIGURE 1F).

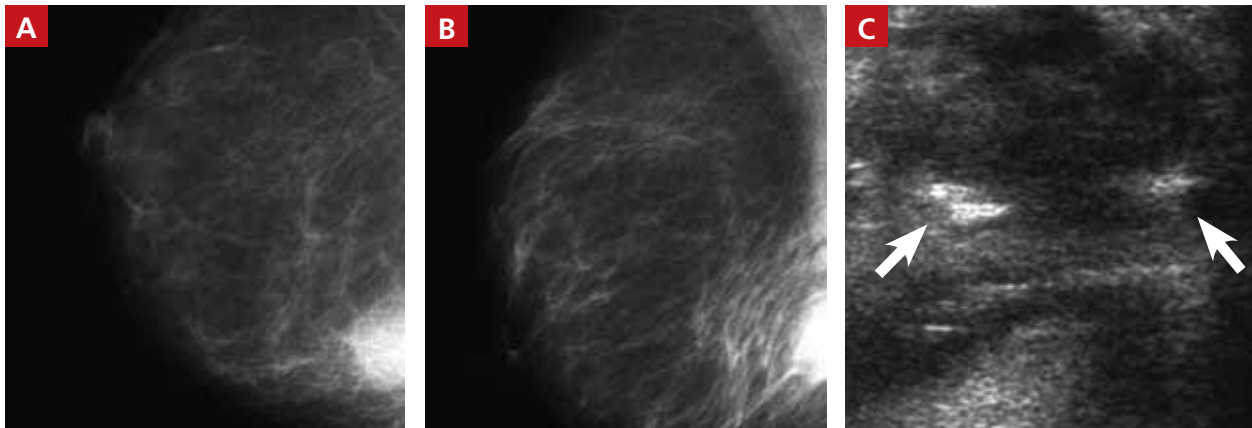
Histologically, the breast mass showed caseating granulomatous inflammation (FIGURES 1G AND 1H). An AFB stain was negative. Polymerase chain reaction (PCR) performed on DNA extracted from the formalin-fixed, paraffin-embedded biopsy material was positive for *Mycobacterium tuberculosis*.<sup>1</sup> A CT-guided pleural biopsy showed only normal tissue. A follow-up tuberculin skin test (purified protein derivative [PPD]) yielded a 10-mm indurated reaction.

## DISCUSSION

Granulomatous lesions, such as foreign body granuloma, idiopathic granulomatous mastitis (IGM), and sarcoidosis can mimic breast carcinoma.<sup>2,3</sup> IGM is associated with elevated prolactin (eg, pregnancy or oral contraceptive use) and is usually subareolar.<sup>2</sup> Infection, however, is also commonly subareolar. Sarcoidosis rarely exhibits unilateral pleural effusion and usually manifests with bilateral interstitial lung disease, hilar lymphadenopathy, and non-necrotizing granulomas.<sup>3,4</sup>

FIGURE 1

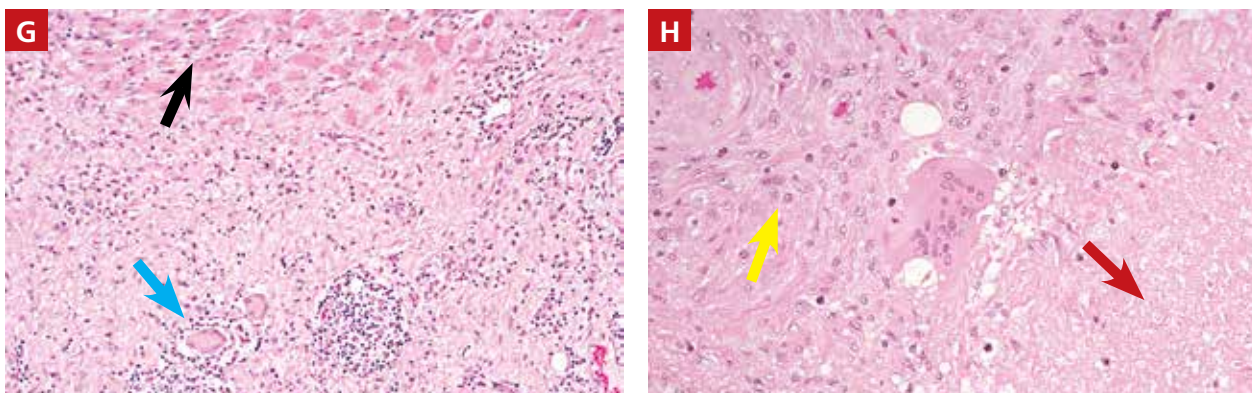
## Multiple testing modalities showed the presence of a breast mass and pleural effusion



Craniocaudal (A) and mediolateral oblique (B) mammogram images of the right breast showing a high-density mass with irregular trabeculated margins in the medial inferior aspect of the breast. Right anti-radial ultrasound (C) showing a heterogeneous hypoechoic and isoechoic lobulated lesion, demonstrating partial posterior acoustic enhancement (arrows). Posterior acoustic enhancement is more common in benign cystic and solid lesions (eg, fibroadenoma or granuloma), but may also be present in carcinoma.



Anterior-posterior (D) and lateral chest x-rays (E) demonstrating a partially loculated, right lower and upper lateral pleural effusion. Computed tomography (F) subsequently showed reformation of the pleural effusion, which was drained. Postoperative fluid changes of the right breast and anterior chest wall were also apparent. No pleural enhancement or lymphadenopathy was noted. Pleural biopsy was negative.



Histopathology of the excised breast mass (G), showing granulomatous inflammation (blue arrow) extending to the chest wall skeletal muscle (black arrow). A hematoxylin and eosin stain at 400x (H), showing granulomatous inflammation (yellow arrow) and surrounding caseating necrosis (red arrow). An epithelioid giant cell is visible in the center of the photomicrograph.

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**This case emphasizes the need for increased awareness of extrapulmonary TB by physicians in developed countries.**

*M tuberculosis* and other granulomatous infections may also feign breast cancer.<sup>5-13</sup> Breast TB, which is highly uncommon in the developed world, often demonstrates imaging similar to that which was seen in this case. Breast TB may appear nodular with ill-defined contours. Masses are sometimes attached to the chest wall and usually lack microcalcifications on mammography; they are also typically hypoechoic and heterogeneous on ultrasound, often showing posterior enhancement.<sup>5,7,8</sup> Like other breast infections, tuberculosis may show cutaneous sinus tract formation, which is seen in about one-third of patients.<sup>6,7</sup> Alternatively, it may manifest as a diffuse mastitis with skin thickening and axillary lymphadenopathy.<sup>8</sup>

Primary breast TB without chest disease comprises up to 86% of mammary tuberculosis.<sup>6,7</sup> Infection may occur via contamination of the skin or nipple.<sup>5-7</sup> Lactation, pregnancy, and other causes of immunosuppression (especially human immunodeficiency virus) have been associated with an increased risk of breast infection.<sup>6-8</sup> This patient was at risk for immunosuppression from longstanding diabetes.<sup>14</sup>

Many patients from TB-endemic areas have received the bacille Calmette-Guerin (BCG) vaccine and may exhibit equivocal or false-positive PPD results. Because interferon-gamma release assay TB blood tests (eg, QuantiFERON-TB Gold or T-SPOT.TB) are not affected by BCG, they are not associated with false-positive repeat testing results.<sup>15</sup>

### **Biopsy is necessary to rule out malignancy and diagnose breast TB**

A pleural fluid to serum protein ratio  $>0.5$  is consistent with infection, but also with sarcoidosis or malignancy.<sup>3,16</sup> Elevated pleural fluid adenosine deaminase ( $>40$  U/L) is sensitive, albeit nonspecific, for the presence of TB microorganisms. If a lymphocyte-dominant exudate is also present, however, its reliability greatly increases.<sup>16,17</sup> Increased pleural fluid interferon-gamma is also sensitive and specific for TB pleurisy.<sup>18</sup> Culture, along with drug sensitivity testing, should be performed on all unexplained pleural effusions.

A biopsy is often required to diagnose breast TB and should be performed on all

suspicious lesions to exclude malignancy.<sup>5-7,9</sup> AFB stains and cultures of aspirate fluids or tissue are often negative.<sup>7,9</sup> PCR or other nucleic acid amplification tests of sputum, body fluids, or biopsy material may be positive in culture-negative cases and can rapidly confirm *M tuberculosis* infection.<sup>17,19</sup> No testing modality offers 100% sensitivity or specificity; therefore, an additional confirmatory test is desirable.

Possible routes of transmission include activation of latent pulmonary tuberculosis and direct, lymphatic, or hematologic extension to the chest wall and breast.<sup>5-7</sup> In this patient, we believe that activation of a latent breast granuloma may have resulted in a secondary or “sympathetic” pleural effusion, possibly triggered by surgical manipulation. This is compatible with her negative pleural adenosine deaminase result, negative culture, absence of pulmonary parenchymal disease, and negative pleural biopsy. Although we conducted a PubMed search, reviewing material as far back as 1966, we were unable to find a previous case of apparent sympathetic effusion associated with breast TB.

■ **Our patient** was treated with daily oral isoniazid, rifabutin, pyrazinamide, and ethambutol for 2 months, followed by isoniazid and rifabutin for 4 months. She has been disease-free for over 10 years.

### **THE TAKEAWAY**

We describe a rare case of breast TB mimicking carcinoma that was associated with unilateral pleural effusion in a woman who had emigrated from Afghanistan. Patients at particular risk for breast TB include immigrants from endemic regions—especially parous females,<sup>6,7</sup> those with a history of TB contacts, and those who are immunosuppressed.<sup>8</sup> This case emphasizes the need for increased awareness of extrapulmonary TB by physicians in developed countries. **JFP**

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