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Sarcoidosis Developing during Therapy for Breast Cancer

Richard Whittington, LCDR, MC, USNR, Angeline Lazarus, CDR, MC, USN; Stacy Nerenstone, M.D., and Alison Martin, M.D.

Two women with breast carcinoma developed bilateral hilar adenopathy, with pulmonary infiltrate in one, during treatment for breast carcinoma. There was strong suspicion of metastatic disease from breast carcinoma. However, biopsy of a mediastinal node in first patient and transbronchial specimen biopsy in the second patient proved the diagnosis to be sarcoidosis. In one patient improvement was noted without therapy, and in the other improvement was noted with steroid treatment.

Sarcoidosis and breast carcinoma are two diseases that occur most commonly in young and middle-aged women. Clinical presentation of sarcoidosis is so variable that it is included in the differential diagnosis of many conditions. Coexistence of other diagnoses can frequently complicate the diagnosis of sarcoidosis, as the abnormalities may be attributed to conditions other than sarcoid. We report two women undergoing potentially curative radiation therapy and chemotherapy for breast carcinoma who developed abnormal findings on chest roentgenograms during treatment. The final diagnosis in each case was sarcoidosis, although the initial radiographic diagnosis was metastatic breast carcinoma. The occurrence of sarcoidosis has not been previously reported in women treated for breast carcinoma.

Case Reports

Case 1

A 51-year-old caucasian woman was noted to have a right breast mass on routine gynecologic examination. Mammographic film was suspicious for malignancy, and a 1.5 x 1.5 cm mass was excised in September 1983 and found to be infiltrating ductal carcinoma. She was four years post-menopause with no history of hormone use. Chest roentgenographic film, liver and bone scan results were normal. She elected to be treated with definitive radiation and underwent re-excision of the biopsy site and axillary lymph node dissection. A small focus of residual carcinoma was excised from the breast and two of 25 axillary lymph nodes contained microscopic deposits of breast carcinoma. Breast and supravacular lymph nodes were treated with a dose of 5,040 rads using cobalt 60 radiation for six weeks. A three-field technique with two tangential fields was used to treat the breast and an en face supravascular field. Biopsy site was boosted to a total dose of 7,000 rads using a 12 MeV electron beam. The patient was started on adjuvant cyclogammadine, methotrexate and five fluorouracil (CMF) chemotherapy concurrent with her radiation therapy, and completed therapy on April 5, 1984.

On April 10, 1984, a routine chest x-ray examination demonstrated bilateral hilar adenopathy with right paratracheal lymphadenopathy (Fig 1). Computed tomographic examination confirmed the presence of lymphadenopathy and demonstrated no other abnormality. Liver-spleen scan, liver enzyme test, bone scan, and mammogram results were normal. A diagnosis of metastatic carcinoma of the breast was made. Tissue was obtained through mediastinoscopy that showed only non-caseating granulomas. The patient was observed without therapy. In the ensuing months, the lymphadenopathy resolved. Lungs have remained clear and the patient is asymptomatic and without evidence of recurrent breast carcinoma.

Case 2

A 42-year-old premenopausal caucasian woman presented to the Bethesda Naval Hospital with a 7 x 5 x 5 cm mass in the upper half of the right breast and a palpable 1 x 1 cm right axillary lymph node. Bone and liver-spleen scan results were normal. Chest roentgenographic film was unchanged from 1979. Mammographic examination suggested that there was diffuse involvement of the right breast with tumor. The patient underwent a right modified radical mastectomy and pathology showed tumor throughout the breast with tumor on the pectoral fascia and 15 of 25 lymph nodes containing tumor. There was involvement of dermal lymphatics and axillary fat with tumor. Because of the overall poor prognosis with a high risk of both local and distant recurrence, the patient was treated

Figure 1. Bilateral hilar adenopathy with right paratracheal lymphadenopathy.

*From the Radiation Oncology Branch, Division of Pulmonary Medicine, and NCI-Navy Medical Oncology Branch, Naval Hospital Bethesda, Bethesda, Maryland.

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Reprint requests: Dr. Lazarus, Portsmouth Naval Hospital, Portsmouth, Virginia 23708

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concurrently with adjuvant chemotherapy and radiation therapy to the right anterior chest wall. The patient received 12 cycles of CMF chemotherapy and radiation therapy. Chest wall, axilla, and internal mammary and supraclavicular lymph nodes were treated with a dose of 5,000 rads during 5½ weeks. Tangential fields were used to treat the chest wall with an en face supraclavicular field and a posterior axillary boost field, all using cobalt 60. An enface 12 MeVp electron field was used to treat the internal mammary lymphatics.

In 1978, the patient was noted to have hilar lymphadenopathy and bilateral apical interstitial infiltrates. Bronchoscopic examination transbronchial biopsy showed noncaseating granulomas. A diagnosis of sarcoidosis was made. The patient remained asymptomatic and pulmonary function test results were normal. Chest x-ray examination in June, 1979 demonstrated no hilar node enlargement, and clearing of no interval change in chest roentgenographic films from 1979 until her mastectomy in November, 1983. Chest roentgenographic examination after four cycles of chemotherapy in March, 1984 showed right hilar adenopathy with bilateral interstitial infiltrates. A clinical diagnosis of metastatic breast cancer was made. The patient had a nonproductive cough but was otherwise asymptomatic. There was no eosinophilia, and liver enzyme test and bone scan results were normal. Bronchoscopic examination with transbronchial biopsy again showed non-caseating granulomas. Pulmonary function test results showed restrictive changes. She continued to receive chemotherapy and was treated with a two-month course of prednisone. The lymphadenopathy resolved and the infiltrates regressed and stabilized. The patient completed chemotherapy in October, 1984 and is currently without evidence of relapse without therapy. Chest roentgenographic film is unchanged.

**DISCUSSION**

The two patients reported here were undergoing therapy for breast carcinoma with curative intent. Because both patients were at high risk for metastases, the initial clinical diagnosis in both cases was recurrence of tumors. In retrospect, both patient's clinical and radiographic findings are typical of sarcoidosis. The presenting abnormality in each case was asymptomatic lymphadenopathy involving hilum and mediastinum and in one patient, bilateral pulmonary infiltrates were noted, too. There are series that have attempted to assess the risk of metastases to these lymph nodes. In an autopsy series, Abrams et al found that 66 percent of patients had lymph node involvement and 77 percent had pulmonary parenchymal involvement. In a series of women with known metastatic breast carcinoma, the incidence of hilar or mediastinal lymphadenopathy was 24 percent. In an unselected series of women treated for breast cancer, the incidence of hilar or mediastinal lymphadenopathy was 1 percent.

Sarcoidosis has been reported previously in patients treated for osteosarcoma and testicular tumors who had received chemotherapy. Israel has suggested several mechanisms by which the tumor or the immunosuppressive effects of therapy might contribute to the development of sarcoidosis. Methotrexate has been used to treat sarcoidosis, but both our patients developed their abnormalities while receiving methotrexate for breast cancer. Bilateral hilar adenopathy in both, and the pulmonary infiltrate away from the radiation field in the second case, are not commonly seen in either radiation or chemotherapy injury to the lung.

We cannot explain why sarcoidosis recurred in the second patient. As Israel suggested, it could be related to chemotherapy but would not explain the occurrence in the first case. It could be related to the fact that both sarcoidosis and breast cancer are diseases that commonly occur in women. These patients again call attention to the need to consider non-malignant diagnoses in those with prior malignancies, and the need to document whenever possible the first recurrence of a tumor following potentially curative therapy.

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