
Amyloid Infiltration of the Diaphragm as a Cause of Respiratory Failure*

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Respiratory involvement with amyloidosis typically involves the tracheobronchial tree or lung parenchyma. We describe a patient with systemic amyloidosis who was respiratory-dependent because of extensive amyloid infiltration of the diaphragm, with no evidence of other pulmonary amyloidosis. Diaphragmatic myopathy from amyloid should be considered in respiratory failure in amyloidosis.

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Respiratory involvement with amyloidosis typically involves the tracheobronchial tree or lung parenchyma. We describe a patient with systemic amyloidosis who could not be weaned from mechanical ventilation because of extensive amyloid infiltration of the diaphragm, with no evidence of amyloid in the remainder of the respiratory system.

Case Report

A 55-year-old black man was admitted to the hospital because of cough and dyspnea. Despite his having smoked, chest x-ray findings were normal five years previously. One year prior to admission he noted arthralgias, and six months before admission noted a sore tongue. Three months prior to admission he developed dysphagia, diarrhea, and malaise. Ten days before admission his cough became productive, and he suffered pleuritic chest pain and dyspnea.

On admission, his tongue was enlarged and his breath sounds were diminished at both lung bases. He had bilateral knee effusions, diffuse muscular atrophy, and a sensory deficit in stocking distribution. His serum bicarbonate level was 26 mEq/L, and room air arterial blood gas levels showed: Po2, 72 mm Hg; Pco2, 51 mm Hg; and pH, 7.33. Chest x-ray examination demonstrated bilateral lower lobe infiltrates and left pleural effusion (Fig 1). Sputum stains showed Gram-positive diplococci and no acid-fast bacilli. Left thoracocentesis yielded transudative fluid with negative findings on Gram stain. He was treated for presumed pneumococcal pneumonia with cefoxitin. Gentamicin was added on the third hospital day after the pleural fluid culture grew Acinetobacter anitratus. Two subsequent pleural fluid cultures gave negative results. Group D Streptococcus was grown from his sputum, but was not thought to be pathogenic. His knee joint effusions contained amorphous congophilic material consistent with amyloid, and a biopsy of his tongue also showed amyloid. Biopsies of his rectum, esophagus, stomach, and bone marrow were negative for amyloid. No increase in plasma cells was seen in his marrow. Serum antinuclear antibody and rheumatoid factor were negative, and serum protein electrophoresis showed a total protein of 5.1 g/100 ml (normal 6.0-8.5), albumin 2.6 g/100 ml (normal 3.1-5.4), and gamma globulin 0.5 g/100 ml (normal 0.7-1.7), with no evidence of an abnormal paraprotein spike. Urine electrophoresis was not done because of anuria.

The patient’s principal problem was progressive mechanical respiratory failure requiring mechanical ventilation on the seventh hospital day. His chest x-ray appearance improved (Fig 1), and he was

Figure 1. Left: AP chest film on admission shows bilateral lower lobe infiltrates and left pleural effusion. Right: AP film on the ninth day of hospitalization. Despite marked clearing of infiltrates, the patient remained ventilator-dependent.
Discussion

The patient had extensive amyloid infiltration in the esophagus, tongue, rectum, and diaphragm, manifested by positive Lugol’s iodine reactions on fresh tissue. Histologically, these organs contained dense accumulations of congophilic amorphous material, associated with extensive replacement and entrapment of muscle fibers. The diaphragmatic thickness was 0.5 to 0.8 cm (normal 0.2-0.3 cm), with extensive homogeneous amyloid infiltration and variable degrees of fibrosis accounting for the increased thickness (Fig 2). There was no amyloid in other organs, including lungs, kidneys, phrenic nerves or skeletal muscle. New pulmonary infiltrates were from disseminated Herpes hominis (simplex) I infection of the lungs, liver, pharynx, esophagus, and stomach. One sputum culture from the ninth hospital day grew Mycobacterium tuberculosis, but cultures of six other sputum specimens, bone marrow, knee fluid, and pleural fluid were negative for tuberculosis at eight weeks.

Post-mortem Observations

The patient had extensive amyloid infiltration in the esophagus, tongue, rectum, and diaphragm, manifested by positive Lugol’s iodine reactions on fresh tissue. Histologically, these organs contained dense accumulations of congophilic amorphous material, associated with extensive replacement and entrapment of muscle fibers. The diaphragmatic thickness was 0.5 to 0.8 cm (normal 0.2-0.3 cm), with extensive homogeneous amyloid infiltration and variable degrees of fibrosis accounting for the increased thickness (Fig 2). There was no amyloid in other organs, including lungs, kidneys, phrenic nerves or skeletal muscle. New pulmonary infiltrates were from disseminated Herpes hominis (simplex) I infection of the lungs, liver, pharynx, esophagus, and stomach. One sputum culture from the ninth hospital day grew Mycobacterium tuberculosis, but cultures of six other sputum specimens, bone marrow, knee fluid, and pleural fluid were negative for tuberculosis at eight weeks.

Discussion

This patient suffered almost total replacement of his diaphragmatic musculature with amyloid. Superimposed pneumonia undoubtedly further compromised his respiratory function. However, we believe that his ventilator dependence was caused by diaphragmatic weakness from amyloid infiltration. We were unable to test phrenic nerve function, but no evidence of amyloid in these structures was seen at autopsy. There was no evidence of an underlying disorder leading to secondary amyloidosis, except the one positive culture for tuberculosis. This patient may represent a case of primary systemic amyloidosis.

Respiratory failure from amyloidosis is generally associated with direct involvement of the upper and/or lower respiratory tract. The usual patterns include: tracheobronchial, parenchymal nodular, diffuse interstitial, pleural, and hilar amyloidosis. Unusual presentations of pulmonary amyloidosis have been reported in association with a mediastinal mass, hilar adenopathy, a nodular parenchymal pattern with bronchiectasis, and diffuse alveolar septae involvement. To our knowledge, mechanical respiratory failure from extensive amyloid infiltration in the dia- phragm has not been reported. We suggest that diaphragmatic myopathy from amyloid be considered when respiratory failure occurs in the setting of systemic amyloidosis.

References

5. Thompson P, Jewkes J, Corrin B, Citron KM. Primary bronchopulmonary amyloid tumour with massive hilar lymphadenopa-
Sarcoidosis Developing during Therapy for Breast Cancer*

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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 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 supravacuclavicular 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 supraclavicular 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 cyclophosphamide, 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 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 pathologic 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...