Pulmonary Diffuse Amyloidosis and Ankylosing Spondylitis*
A Rare Association
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We report herein the association of primary pulmonary amyloidosis and ankylosing spondylitis. To our knowledge, this rare association has never been reported. This case reemphasizes that not all pulmonary complications that appear in the course of ankylosing spondylitis are related to the seronegative spondyloarthropathy. Primary pulmonary amyloidosis should be considered in patients with interstitial pulmonary disease. (Chest 1992; 106:960-10)

Amyloid substance may infiltrate the lungs in a variety of forms. The most common is the infiltration of airways, a condition called tracheobronchial amyloidosis.1 It produces nonspecific symptoms such as cough, dyspnea, or hemoptysis. Other patients exhibit a parenchymatous deposition of amyloid substance, such as in nodular or diffuse form (interstitial).2 These patients are usually asymptomatic. Less frequent patterns are pleural or lymph node infiltration.3

Diffuse interstitial amyloidosis constitutes an uncommon condition. It has been described in primary amyloidosis, both in its systemic or localized form4 and in cases of secondary amyloidosis.5

We are reporting herein a case of diffuse interstitial pulmonary amyloidosis, diagnosed by means of a transbronchial lung biopsy specimen in a patient with ankylosing spondylitis, monoclonal gammapathy, and interstitial pulmonary disease.

CASE REPORT
A 61-year-old man was admitted to the hospital because of increasing dyspnea. He had been a long-term smoker. Two years before hospital admission, he began to experience mild effort dyspnea and cough. Fifteen days before hospitalization, he presented with dyspnea and cough that gradually increased with purulent sputum production and low-grade fever. History was unremarkable except for a progressive dorsal kyphosis noticed by the patient's wife. The patient denied any history of arthralgia and/or arthritis.

Physical examination indicated a patient in no respiratory distress. Axillary temperature was 37.4°C. There was no clubbing. Rhonchi and wheezing were detected in both lungs, as were a few scattered crackles. Articular examination indicated marked dorsal kyphosis and rigidity of the cervical spine. Sacroiliac joints were not tender. Peripheral joints appeared to be normal.

Results of hematologic and biochemical tests were normal. ESR was 102 mm. Test for RF, ANA, anti-DNA antibodies, ACE, and serum complement levels disclosed normal results. Arterial blood gases (FIO₂ = 0.21) indicated PO₂ of 57 mm Hg, Pco₂ of 36 mm Hg, pH of 7.40, and HCO₃⁻ of 38 mmol/L. Serum total protein level was 84 g/dl with 22.6 percent of γ-globulin. Immunoelectrophoresis revealed a monoclonal IgG gammapathy with κ light chains and the

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FIGURE 1. Thoracic CT of the patient that shows the interstitial pulmonary pattern.

quantification of immunoglobulins were as follows: IgG, 2.098 mg/dl (N:660 to 1,360); IgA, 355 mg/dl (N:100 to 300); IgM, 65 mg/dl (N:42 to 162); IgE, 38 mg/dl (N:<100). Repeated urine examinations showed no proteinuria. HLA B27 disclosed a positive result. Bone marrow examination indicated 0.2 percent of plasma cells.

Chest roentgenogram showed a diffuse reticulonodular pattern, suggestive of interstitial pulmonary disease. Thoracic CT confirmed this finding and failed to demonstrate enlargement of mediastinal lymph nodes (Fig 1). Gallium 67 scanning of the lungs was reported to be normal. A roentgenographic examination of the spine indicated calcification of the anterior vertebral ligament. Sacroiliac joints were blurred.

Electrocardiogram and two-dimensional echocardiogram were normal. The pulmonary function values were as follows: FVC, 62 percent; FEV₁, 55 percent; FEV₁/FVC percent, 75; TLC, 71 percent; VR, 103 percent; Dco, 80 percent; and KCO, 67 percent.

Results of fiberoptic bronchoscopy were normal. The bronchoalveolar lavage recovered 2,640 cells per milliliter with 88 percent of macrophages, 10 percent of lymphocytes, and 2 percent of polymorphonuclear cells. Bronchial and transbronchial biopsies were performed. Bronchial biopsy specimens indicated no amyloid deposition. Microscopic examination of transbronchial lung biopsy specimens showed deposition of amyloid substance within the wall of blood vessels (hematoxylin-eosin × 250) (Fig 2) and focal amyloid deposition that thickened some areas of the alveolar septa (Congo

FIGURE 2. Deposition of amyloid within the wall of blood vessels (hematoxylin-eosin, × 250).
red staining \( \times 250 \) (Fig 3). When the samples were treated with potassium permanganate and reexamined under polarized lamp, green birefringence persisted. Congo red stain of rectal, abdominal fat, and bone marrow biopsy specimens showed no amyloid deposits.

After one year of follow-up, a chest roentgenogram and pulmonary function tests remain unchanged. Because of persistent cough, another bronchoscopic procedure has been performed showing discrete nodules in the carina and main bronchial tree from which biopsy specimens were taken. Microscopic examination indicated infiltration by amyloid substance, which was resistant to potassium permanganate staining. The samples were also stained with anti-AA and anti-transthyretin antisera indicating a negative result.

DISCUSSION

The patient whose case was reported met criteria of ankylosing spondylitis and primary pulmonary amyloidosis. This case poses, however, some interesting questions related mainly to pulmonary disease.

The first one is the possible relationship between ankylosing spondylitis and pulmonary disease. Interstitial pulmonary disease may appear in the course of ankylosing spondylitis. It is usually asymptomatic and limited to the upper lobes of both lungs, in a fibrous sheet form. The pattern found in the chest roentgenogram of the patient whose case was reported was not suggestive of pulmonary involvement by ankylosing spondylitis, and that is the reason because other studies were performed directed to investigate other causes of interstitial pulmonary disease. Results of the diagnostic tests indicated the presence of diffuse interstitial pulmonary amyloidosis, and, later, slight infiltration of the bronchial wall by amyloid substance.

Second, since secondary amyloidosis may complicate ankylosing spondylitis in 4 percent of patients, the interstitial pulmonary disease of the patient reflects a secondary amyloidosis or is primary form. Some details favor the presence of a primary amyloidosis. One is the exclusive deposition in lung tissue, since amyloid substance was not detected in any other organ examined and there was no clinically demonstrable renal amyloidosis. Previous reports of secondary amyloidosis complicating ankylosing spondylitis have indicated that amyloid substance infiltrates the kidney and the rectum rather than the lung alone. Moreover, secondary amyloidosis in ankylosing spondylitis usually appears when extravertebral joints are affected, a condition not found in our patient. Second, the persistence of birefringence in Congo red stain after potassium permanganate treatment of the sample, although not specific, suggests strongly that the patient whose case was reported had a type AL amyloidosis. Also, the negative result when bronchial biopsy tissue was stained with anti-AA and anti-transthyretin clearly favors the presence of a type AL amyloidosis.

Pulmonary interstitial disease due to amyloid deposition may exhibit two different patterns: a focal deposit with vascular infiltration and a diffuse alveoloselotomat form. Unlike the latter, the former is characterized by normal results of pulmonary function tests. In early reports, this condition was usually diagnosed by means of an open lung biopsy specimen or postmortem examination. Recently, some works have reported the value of transbronchial lung biopsy as a diagnostic tool in diffuse amyloid infiltration. Whereas clinically significant bleeding has been associated with the procedure, our patient did not present this complication.

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Figure 3. Focal amyloid deposition thickening some portions of the alveolar septa (Congo red, \( \times 250 \)).
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**Early Congestive Heart Failure due to Origin of the Right Coronary Artery from the Pulmonary Artery**

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We describe a two-month-old infant with early congestive heart failure due to anomalous origin of the right coronary artery from the pulmonary artery. The diagnosis was made by two-dimensional and color flow Doppler echocardiography, confirmed by angiocardiography, and the case was successfully corrected at surgery. As opposed to the more frequent anomalous origin of the left coronary artery from the pulmonary trunk, this anomaly generally does not cause any typical clinical finding, often becoming an autopic or surgical surprise after infancy or in adult age.

**CDE = color Doppler echocardiography; RCA = right coronary artery**

Anomalous origin of the right coronary artery (RCA) from the pulmonary trunk is a very rare malformation described for the first time by Brooks.1 In the 43 cases reported in the literature (Table 1), the anomaly was recognized at autopsy, during surgery due to other cardiac malformations, at angiography, and recently at two-dimensional echocardiography (2DE), and using Doppler color flow echocardiography (CDE).4 As opposed to the more frequent anomalous origin of the left coronary artery from the pulmonary trunk, this anomaly generally does not cause any typical clinical finding, often becoming an autopic or surgical surprise after infancy or in adult age.5 However, some cases of cardiac arrest and sudden death are reported.7,8

Our report concerns the diagnosis by echocardiography (2DE and CDE) and the surgery in a two-month-old infant with early congestive heart failure due to anomalous origin of the RCA.

**CASE REPORT**

The patient was admitted to our department for severe cardiac failure with gallop rhythm and a 2/6 loud murmur at the apex. An electrocardiogram (ECG) showed sinus tachycardia and signs of lateral ischemia with deep Q waves in the inferior leads, and chest roentgenogram showed cardiomegaly. At 2DE there was a marked dilatation with severe hypokinesia of the left ventricle and reduced ejection fraction (31 percent). There was severe mitral valve regurgitation, the left coronary artery was dilated (Fig 1), while the RCA appeared to course anterior to the aorta to join the pulmonary trunk (Fig 2). The CDE showed a diastolic retrograde flow pattern without indicating a trivial “steal effect” from the coronary circulation into the pulmonary artery (Fig 3). Origin of the RCA from the pulmonary artery with poor intercoronary collateral system was subsequently confirmed by cineangiography. A minimal left-to-right shunt (Qp/Qs = 1.3/1) was also demonstrated. The anomaly was successfully corrected by a direct reimplantation of the RCA together with a cuff of the adjacent pulmonary artery into the aorta.

**FIGURE 1.** Short axis parasternal view demonstrating the dilated left coronary artery (LCA) normally arising from the aorta (AO), and the right coronary artery (RCA) arising from the pulmonary trunk (PT). AO = aorta.

**FIGURE 2.** Short axis parasternal view showing the anomalous origin of the right coronary artery (RCA) from the pulmonary trunk (PT). AO = aorta.

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