tion between the two entities may be artificial. Smyth and Edwards¹⁵ have presented this argument, citing the presence of a localized ridge of medial tissue projecting into the aortic lumen in classic coarctation and in several cases of pseudocoarctation which they examined. However, surgical and pathologic material from other cases has not confirmed the universal presence of such a ridge in pseudocoarctation.¹⁶ Dungan et al¹⁴ reported the absence of any intraluminal obstructing lesion in several cases of pseudocoarctation in which pressure gradients were identified. The gradient is presumably due to the kinking of the aorta; amelioration of pressure gradients after surgical relief of the kinking has been reported.¹⁴,¹⁵

Pseudocoarctation appears to be a congenital, rather than an acquired anomaly. Its appearance in infants¹⁵ and its association with other forms of congenital heart disease strengthen this conclusion. Souders and associates,² in their original description, suggested that traction on the aorta by an abnormally short ductus might be the cause of pseudocoarctation. Patterson and Grainger¹⁷ postulated that failure of normal embryologic compression of the third to seventh segments results in pseudocoarctation. Lavin et al¹⁷ proposed that failure of the distal right arch to atrophy and its subsequent incorporation into the distal left arch might be the embryologic basis of pseudocoarctation.

The unusually cephalad course of the aortic arch, extending both to the left and right of the sternum, suggests that the third, rather than the fourth embryologic arch may have persisted in this patient. The coincidence of this finding, together with the mid-arch coarctation and the pseudocoarctation itself, supports the contention that pseudocoarctation represents a congenital anomaly. It is possible that the tortuosity and dilatation of the aorta distal to the coarctation might merely represent post-stenotic dilatation. However, this degree of post-stenotic change is rarely observed in mid-arch coarctation. The relationship between coarctation and pseudocoarctation remains conjectural.

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Interstitial Pneumonitis Complicating Rheumatoid Arthritis

Sustained Remission with Azathioprine Therapy*

James M. Cohen, M.D.;** Albert Miller, M.D., F.C.C.P.† and Harry Spiera, M.D.‡

A patient with classic rheumatoid arthritis developed biopsy-proven diffuse interstitial pulmonary fibrosis and ventilatory insufficiency which appeared to be irreversible. The administration of azathioprine coincided with significant immediate improvement in pulmonary function and clinical status. During five years of continuous azathioprine therapy, progressive improvement in lung function has been accompanied by marked deterioration of the rheumatoid joint disease, suggesting that the pulmonary and joint lesions of rheumatoid disease may not be mediated by the same pathways.

Although arthritis is the most common manifestation of rheumatoid disease, involvement of other organ systems has been described. Ellman and Ball¹ first noted diffuse interstitial pneumonitis with fibrosis at autopsy of two rheumatoid patients. While the association of interstitial pneumonitis with fibrosis to rheumatoid dis*

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CHEST, 72: 4, OCTOBER, 1977

INTERSTITIAL PNEUMONITIS 521
ease has been questioned, a number of studies have confirmed it.

Interstitial pneumonitis complicating rheumatoid disease varies from mild pulmonary involvement associated with little functional abnormality and a stable or slowly progressive clinical course, to a fulminant disease which rapidly causes severe hypoxemia, cor pulmonale, and death. Treatment of these critically ill patients has been disappointing. Corticosteroids do not significantly alter the course of the disease. Lorber reported three patients in whom penicillamine may have been beneficial, but this observation has not been confirmed. Recently, azathioprine and cyclophosphamide have been used in the treatment of progressive rheumatoid joint disease. We report a patient with rheumatoid arthritis and fulminant interstitial pulmonary fibrosis in whom a remission of the lung disease coincided with the institution of azathioprine therapy.

**Case Report**

The patient, a 47-year-old white woman, noted bilateral wrist swelling in 1963. In 1966, this recurred together with pain in her right ankle. In April, 1970, she was hospitalized for shortness of breath. She improved with administration of ampicillin and prednisone (80 mg per day), but regressed when the prednisone was tapered and did not respond when it was reinstated.

Upon transfer to The Mount Sinai Hospital, New York, physical examination revealed an acutely ill cyanotic woman in respiratory distress. Temperature was 37°C, blood pressure 110/78 mm Hg, pulse 150 per minute and regular, and respiratory rate 40 per minute. She had Cushingoid features, diffuse fine rales and moderate synovial thickening of the proximal interphalangeal joints.

On laboratory evaluation, hemoglobin was 10.1 grams percent with hypochromic, microcytic red cells; erythrocyte sedimentation rate was 80 mm/hr (Westergren) and leukocyte count was 6,500/cu mm with a normal differential. Latex fixation titer was 1:5,120. Lupus cell preparations and antinuclear antibody determinations were negative. Protein electrophoresis and immunoglobulin levels were normal. Bone marrow aspiration revealed erythroid hyperplasia with decreased iron stores. Serum iron was 35 mg percent and total iron binding capacity 363. Serum folate, vitamin B12, haptoglobin and direct and indirect Coombs tests were normal.

On skin testing, PPD (5 TU) was negative and mumps antigen was positive. Electrocardiogram revealed sinus tachycardia and left ventricular hypertrophy. Chest x-ray film on admission (Fig 1) showed diffuse interstitial infiltrations and diminished lung volumes. Cultures of blood, sputum and urine gave negative findings.

Pulmonary function tests revealed a vital capacity (VC) of 960 ml, 30 percent of the predicted value of Bates et al., maximum voluntary ventilation (MVV) of 50 L/min, 60 percent of the predicted value of Baldwin et al. and a forced expiratory volume in one second (FEV1) which was 81 percent of the forced VC. On breathing room air, PaO2 was 29 mm Hg, Pco2 40.5 mm Hg, pH 7.49 and O2 saturation was 62 percent. On inhalation of 100 percent O2, PaO2 increased to 528 mm Hg and PaCO2 to 45.5 mm Hg with a decrease in pH to 7.43 (Table 1). The patient was too ill to undergo further testing. These values are consistent with a severe restrictive ventilatory impairment, with marked hypoxemia and combined metabolic alkalosis and respiratory acidosis indicated by the response to oxygen inhalation.

Lung tissue from open biopsy revealed thickening of the alveolar septa with fibrous tissue progressing to gross fibrosis with loss of tissue architecture. Terminal air spaces were dilated (Fig 2). All cultures of lung tissue were negative.

During the next two weeks, the patient's respiratory status worsened; the PaO2 remained about 32 mm Hg despite supplemental O2. Since there was no response to other therapeutic modalities, including antibiotics, intravenous diuretics, high dose corticosteroids, azathioprine was instituted at a dose of 100 mg per day. After one week, the patient was improved. Since her illness had not responded to any other therapy, and her inexorably downhill course made a spontaneous remission unlikely, this improvement was considered to result from the azathioprine. She was discharged four weeks later with a VC of 1170 ml (an increase of 210 ml (23 percent over the pretreatment value) and a PaO2 of 58 mm Hg on room air.

During the following five years, the patient's lung function progressively improved while azathioprine was continued and prednisone tapered (Fig 3). Roentgenograms of the chest after two and one half years of therapy showed an increase in lung volume and moderate clearing of the interstitial infiltrates. The VC was 1870 ml (twice its initial value), the

**Figure 1.** Admission roentgenogram (PA), August, 1970, showing reduced lung volumes and diffuse lower zone infiltrations.

**Figure 2.** Photomicrograph of lung removed at open thoracotomy (Hematoxylin-eosin, original magnification X 100) showing fibrotic thickening of alveolar septa and focal dilatation of terminal air spaces.
On breathing room air, PaO₂ was 60 mm Hg and PaCO₂ 41 mm Hg after one minute of exercise. Despite continued pulmonary improvement, the patient’s arthritis progressed. She developed ulnar deviation of the hands, active synovitis of the elbows, knees, and feet, and rheumatoid nodules. Demineralization and joint space narrowing were seen on x-ray examination of the hands.

In February, 1974, four weeks after an emergency cholecystectomy, the patient was readmitted with a presumptive diagnosis of pulmonary embolism. Since then, on anticoagulant therapy as well as azathioprine, she has felt well despite her progressively disabling arthritis.

**Discussion**

The diagnosis of rheumatoid arthritis in this patient was established by progressive symmetrical polyarthritis, joint space narrowing, ulnar deviation, rheumatoid nodules and high titer rheumatoid factor. Interstitial pneumonitis with fibrosis was documented by roentgenography, pulmonary function tests and open lung biopsy. Although there had been no response to antibiotics, diuretics or high dose corticosteroids, the patient’s pulmonary function, blood gas levels and clinical course improved within a week after initiation of azathioprine therapy. This improvement has continued for five years, demonstrating improved quality of life and progressive increase in vital capacity and oxygen tension.

Spontaneous remission of rapidly progressive pulmonary interstitial fibrosis in rheumatoid disease, while reported, is contrary to most experience. Azathioprine appeared to reverse this patient’s pulmonary disease at the same time that the joint disease progressed. Although the etiology of rheumatoid arthritis is unknown, it is believed that joint and lung impairment are mediated by similar immune mechanisms. The disparity in

**Table 1—Sequence of Pulmonary Function Findings**

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<th>Date</th>
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(Numbers in parentheses indicate percent of predicted values; see text)
clinical response between the joint and pulmonary lesions in this patient suggests that they may not be mediated by the same pathways.

References


Rate-Dependent Variation in the Duration of the QRS Complex with Left Anterior Fascicular Block

David M. Mirvis, M.D.; Jack F. Bandura, M.D.; and Daniel A. Brody, M.D.

The case of a 67-year-old man with combined ischemic and valvular heart disease is presented. Electrocardiographic abnormalities included left anterior fascicular block with a variable duration of the QRS complex. The width of the QRS complex was dependent on the length of the cycle, being broader with short than with long preceding R-R intervals. This is interpreted as a tachycardia-dependent focal block coexisting with a fixed delay in fascicular conduction.

Delays in conduction within the fascicular components of the left bundle-branch system have become associated with characteristic aberrations in the morphology of the QRS complexes. These abnormalities are typically restricted to changes in the electrical axis, with only minor alterations in total duration of the QRS complex. When depolarization is lengthened beyond 0.12 second, other abnormalities of conduction are assumed to coexist with the fascicular blocks. These include delays in other major conducting bundles producing complete right or complete left bundle-branch block or delays in distal specialized conducting or myocardial tissue. The width of the QRS complex has also been related to cardiac size, with prolongation of depolarization directly related to the anatomic distance between the bases of the two left ventricular papillary muscles and to the length of the bundle branches themselves.

We report here an example of yet another cause of widening of the QRS complex, ie, tachycardia-dependent prolongation of the QRS complex with fixed left anterior fascicular block.

Case Report

The patient, now a 67-year-old black man, was first seen in 1971 shortly after the onset of severe retrosternal pain in the chest. Physical examination revealed a murmur of aortic insufficiency. An electrocardiogram demonstrated a normal P-R interval, duration of the QRS complex, and mean electrical axis. Elevation of the S-T segment was present in leads 2, 3, and aVF, which evolved in a manner typical of transmural inferior myocardial infarction.

Two months later, the patient was readmitted for cardiac catheterization. Results demonstrated severe aortic regurgitation. A Starr-Edwards prosthesis was implanted at that time. Subsequent ECGs revealed axis deviation (−45°) in the frontal plane with a QR complex in lead 1 and Rs complexes in leads 2, 3, and aVF, all consistent with a diagnosis of left anterior fascicular block.

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524 Mirvis, Bandura, Brody

CHEST, 72: 4, OCTOBER, 1977