showed focal necrosis. Talc crystals were not demonstrable within the heart. Microscopic pathologic examination of the lungs resembled that of the biopsy reported above. There was marked central lobular congestion of the liver; scattered birefringent crystals with associated lymphocytic and histiocytic infiltrate were present within the portal areas.

**DISCUSSION**

Magnesium trisilicate (talc) is commonly used as a filler in medicines manufactured for oral use; when such drugs are dissolved and injected intravenously, localization of the talc within the pulmonary vessels results in formation of intravascular and extravascular granulomas involving the alveolar septa, and also arteries. Hypertensive pulmonary vascular disease with cellular intimal proliferation, fibroelastosis, and medial hypertrophy of muscular pulmonary arteries and arterioles follows. Experimental production of identical lesions by intravenous injection of tripelennamine hydrochloride containing talc has been demonstrated by Puro and co-workers.\(^2\)

Diffuse vascular injury results in pulmonary hypertension; clinical investigation of the patient presented here showed a low diffusion capacity and a restrictive defect, which may not all be accounted for by the vascular occlusive effects. Macklem and Becklake\(^3\) demonstrated that pulmonary interstitial fibrosis was characterized by a reduction in diffusion and overall lung compliance. Diffuse involvement by granulomas could function in a similar manner.

In this patient, there was slight evidence of left heart dysfunction. It is of interest that in Szwed's report\(^4\) of a case of "blue velvet" abuse, the left ventricular end-diastolic pressure was elevated. In the case reported by Wendt's group,\(^5\) both ventricular walls were grossly and microscopically hypertrophied. Whether these observed left ventricular abnormalities were due to talc, to some other toxic effect, or to some unrecognized cause is unclear. It seems unlikely that they contributed significantly to the severe clinical disturbance.

In one series, talc granulomatosis made up less than 1 percent of pulmonary complications of drug abuse.\(^6\) The victims are young people who receive talc unknowingly in the course of drug administration.\(^7\) Histologic studies have usually resembled those reported here. In addition to our case, there is at least one other report of death after open lung biopsy; one patient tolerated trephine biopsy, suggesting that the latter may be safer.\(^5,6\) A newer procedure, transbronchial lung biopsy, offers promise of more safety.\(^8\) When the diagnosis of talc granulomatosis is made, a trial of corticosteroid therapy seems warranted.\(^9\)

While it is realized that talc granulomatosis makes up but a small portion of the total side effects of drug abuse, some of the risk of illicit drug use could be avoided if a soluble substance were to replace talc in selected oral preparations.

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**Pleural Effusion Associated with Aortitis Syndrome**

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A patient with aortitis syndrome had a pleural effusion which subsided but reappeared with an exacerbation of aortitis symptoms while under antituberculosis treatment. The character of the fluid was that of an exudate, and the glucose concentration was normal. Clinical and laboratory features of the case suggest that the effusion was part of the aortitis syndrome per se.

There are many diseases which present with pleural effusions as a prominent clinical manifestation. The current report illustrates a case of aortitis syndrome with recurrent pleural effusions associated with disease activity. The initial pleural effusion disappeared once but recurred together with a pericardial effusion concomitant with exacerbation of the aortitis symptoms; the patient was under antituberculosis treatment with isoniazid and paraaminosalicylic acid at the time of the recurrence. The character of the fluid was that of an exudate, and the pleural effusion was thought to be a clinical manifestation of the aortitis syndrome.

**CASE REPORT**

A 32-year-old man developed pain in the left side of his chest and in his back with a temperature of 37.5°C (99.5°F)

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in September 1968. He was admitted to the Keio University Hospital, Tokyo on Oct 22, 1968. The chest x-ray film on admission disclosed a small amount of left pleural effusion without other abnormalities. Only a few drops of turbid and yellowish pleural effusion were aspirated by thoracicocentesis. A pleural needle biopsy was attempted without success.

Streptomycin, paraaminosalicylic acid, and isoniazid with alternate-day corticosteroid therapy (prednisone, 20 mg/day) were administered. Fever and chest pain continued, but the pleural effusion was no longer noted on the chest x-ray film taken 16 days after admission. The patient's temperature returned to normal, and corticosteroid and streptomycin therapy was discontinued.

In the early spring of 1969, while still receiving isoniazid and paraaminosalicylic acid therapy, the patient again noted left hypochondriacal pain. A chest roentgenogram taken on April 4, 1969 revealed a recurrent left pleural effusion with enlargement of the cardiac shadow, suggesting an associated pericardial effusion (Fig 1). At that time, radial artery pulsations were undetectable bilaterally. Systolic murmurs were audible over both carotid arteries and at the left subclavicular artery. Aortography confirmed obstruction of the subclavicular arteries bilaterally. The character of the pleural fluid was that of an exudate, with specific gravity of 1.018, a positive Rivalta reaction, a protein concentration of 3.9 gm/100 ml, and a cholesterol concentration of 33 mg/100 ml. Culture of pleural fluid was negative for bacterial pathogens, including acid-fast bacilli. Pleural biopsy revealed swelling of mesothelial cells (Fig 2) and scattered small numbers of mononuclear cells (Fig 3). There was no evidence of definite inflammation or granulomatous lesions. An elevated erythrocyte sedimentation rate of over 100 mm/hr was observed with an antistreptolysin O titer of 333 Todd units, a C-reactive protein reaction of +++, a serum IgG level of 2,818 mg/100 ml, a serum IgA level of 610 mg/100 ml, and a serum IgM level of 86 mg/100 ml. Neither antinuclear antibody nor anti-DNA antibody was detected by immunofluorescence. After readministration of corticosteroid, streptomycin, and ethambutol therapy, the pleural effusion disappeared in late May of 1969, but numbness of the right arm and loss of radial artery pulsations continued, and extracardiac sounds were audible in the right supravacicular fossa, over the carotid arteries, and in the epigastrium. These vascular murmurs gradually became faint, and other symptoms abated by May of 1970, at which time the patient was discharged and returned to work.

**DISCUSSION**

Aortitis syndrome is known as Takayasu's disease, pulseless disease, branchial arteritis, brachiocephalic arteritis, and aortic arch syndrome. It is well known that the incidence of this disease is far more frequent in Japan than in the United States or European countries. Although the etiology of this disease is still obscure, a past history of tuberculosis is relatively common (43 of 197 cases and 22 of 84 cases in two Japanese studies1-2). Participation of tuberculosis in this disease has been suggested not only in view of this high incidence of past history, but also from the histopathologic findings, especially the appearance of giant cells in lesions. In our case of aortitis syndrome associated with pleural effusion, the clinical manifestations of aortitis were not characteristic initially. After administration of antituberculosis drugs and corticosteroid therapy, the

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**FIGURE 1.** Chest x-ray film showing pleuropericardial effusion (April 4, 1969).

**FIGURE 2.** Pleural section showing swollen mesothelial cells at center (Hematoxylin and eosin, original magnification × 350).

**FIGURE 3.** Pleural section showing small numbers of scattered mononuclear cells (Hematoxylin and eosin, original magnification × 100).

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pleural effusion soon disappeared. Seven months later, symptoms of active aortitis became evident, and at the same time a pleuropericardial effusion reappeared despite continuation of isoniazid and paraaminosalicylic acid therapy. This fact indicates that the pleural effusion was probably not tuberculous in origin. There was also no evidence of infection or valvular heart disease to account for the pleuropericardial effusion, and the character of the fluid was that of an exudate, which did not support the presence of cardiac failure. With the initial pleural effusion, cardiac size was normal on chest roentgenogram, but the second episode was associated with definite pericardial effusion. Based on these observations, pericarditis was not thought to be the cause of the pleural effusion.

There is only one report dealing with the coexistence of aortitis syndrome and pleural effusion;1 in that report, nine out of 197 cases revealed pleural effusion as a clinical manifestation. The pathogenesis, etiology, and character of the pleural effusion were not mentioned in the report. Cardiac failure with valvulitis is known to be present in some cases of aortitis syndrome, and some of the reported cases might be directly related to heart failure. The similarities between aortitis syndrome and some diffuse connective tissue diseases have been discussed,2,4 and pleural effusion is one of the prominent extraarticular manifestations of rheumatoid arthritis. The character of the pleural effusion in the present case differed, however, from that of rheumatoid arthritis with regard to glucose concentration.5,6

In view of the previously mentioned clinical and laboratory features of our case, we feel that the pleural effusion was likely a clinical manifestation of the aortitis syndrome per se rather than a secondary manifestation of an underlying undiagnosed infectious, autoallergic, or related disease.

References


Rheumatoid Spondylitis, Aortic Insufficiency, and Coronary Artery Disease

An Operable Combination

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A case of rheumatoid (ankylosing) spondylitis with aortic insufficiency and arteriosclerotic coronary heart disease is presented. Surgical replacement of the aortic valve and aortocoronary bypass grafts were successfully accomplished.

The interrelation between rheumatoid (ankylosing) spondylitis, aortitis, and aortic valvulitis is well recognized. In addition, varying degrees of heart block have also been associated with rheumatoid spondylitis.1,2 The distinctive cardiovascular abnormalities have also been associated with rheumatoid spondylitis.1,2 The distinctive cardiovascular abnormalities in rheumatoid spondylitis have been described and the unique features of the cardiovascular lesions illustrated (Fig 1). We report the clinical findings and surgical results in a patient with rheumatoid spondylitis, aortic insufficiency, and intermittent complete heart block, as well as severe coronary artery disease. The coronary artery obstructions were successfully bypassed with saphenous vein aortocoronary grafts; we, therefore, suggest that this procedure is technically feasible in patients with rheumatoid spondylitis.

Case Report

The patient was a 54-year-old man with a 20-year history of rheumatoid (ankylosing) spondylitis (still quiescent). He was initially admitted to Hahnemann Hospital, Philadelphia, on Jan 3, 1972 after a severe bout of precordial chest pain. The patient had first-degree heart block and had been taking a digitalis preparation.

On admission, physical examination revealed an early diastolic murmur heard best along the left sternal border; an electrocardiogram showed complete atrioventricular (AV) heart block. The patient was treated with temporary transvenous pacing, and the digitalis therapy was discontinued. On the second day, complete heart block was intermittent. On the third day, sinus rhythm returned, with the first-degree heart block still present. The patient was then discharged and instructed to return for further evaluation.

The patient was readmitted to Hahnemann Hospital in February 1972. Cardiac catheterization revealed 3+ aortic insufficiency and triple-vessel coronary artery disease: left main coronary artery, 50 percent occlusion; the left anterior descending artery, 95 percent occlusion; the left circumflex artery, 80 percent narrowing; and the right coronary artery, 75 percent occlusion. During the course of the catheterization, intermittent AV dissociation occurred several times. After catheterization, a demand pacemaker was inserted without difficulty. The patient was discharged shortly afterward.

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