Constrictive pericarditis in association with rheumatoid arthritis

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Constrictive pericarditis has been regarded as almost invariably tuberculous in origin; in 1948 Andrews, Pickering, and Sellors stated, 'In Great Britain most, perhaps all, of the cases of constrictive pericarditis are due to antecedent acute tuberculous pericarditis'. With the decline in the prevalence of tuberculosis, other causes of constrictive pericarditis may assume greater importance. Recently, Connolly and Burchell (1961) and Robertson and Arnold (1962) have drawn attention to the occurrence of constrictive pericarditis following acute non-specific (possibly virus) types of pericarditis. A few cases have been reported of constrictive pericarditis in association with rheumatoid states (McMurray, Cayer, and Cornatzer, 1951; Gimlette, 1959; Keith, 1962; Partridge and Duthie, 1963). We report here three further cases of constrictive pericarditis in patients with rheumatoid disease.

CASE REPORTS

CASE 1 V. P. was aged 31 at the time of her admission to the Brompton Hospital in May, 1960. At the age of 19 she had developed severe arthritis of all joints, and at 23 she suffered from corneal ulceration. At the age of 30 she had a severe staphylococcal chest infection, for which she was admitted to another hospital. About four months after this she developed dyspnoea on exertion and swelling of the ankles.

On examination in September 1959 at the National Heart Hospital she was obese. Movements were restricted in all joints of both hands; there was fusiform swelling of the wrists with marked ulnar deviation and involvement of both shoulders, knees, ankles, and spine. Many rheumatoid nodules were present over the interphalangeal joints and the olecranon areas. The heart was in sinus rhythm, the blood pressure was 115/85 mm. Hg, and the venous pressure in the neck was 10 cm. above the sternal angle. There was a dominant y descent. There was a loud third heart sound shown on the phonocardiogram to occur 0.14 second after aortic valve closure. There were crepitations at the bases of both lungs. The

liver was palpable two finger-breadths below the costal margin. There was oedema of both ankles.

Investigations The electrocardiogram showed sinus rhythm, low voltage QRS and T waves with T wave inversion in leads 3, AVF, V₁, and V₂. The chest radiograph did not show any cardiac enlargement or pericardial calcification, but there was mottling in the lower two-thirds of both lung fields, suggesting interstitial pulmonary fibrosis. Cardiac catheterization showed the pulmonary artery pressure to be 30/20 mm. Hg rising to 40/30 mm. Hg on exercise. Oxygen saturation was 90% at rest but fell to 77% on exercise. Physiological studies of the lungs showed a forced vital capacity of 1,200 ml., forced expiratory volume (1 sec.) 1,000 ml., and an impaired carbon monoxide diffusion (10.5 ml./min./mm. Hg) at rest and a carbon monoxide extraction of 32%. Sputum examinations were repeatedly negative for *Mycobacterium tuberculosis*. The Mantoux test was weakly positive to 10 T.U. The serum albumin measured 3.5 g./100 ml. and the globulin 3.5 g./100 ml. Electrophoresis revealed a moderate increase in the gamma globulin. Radiographs of the hands (Fig. 1) showed extensive rheumatoid changes. The R.A. latex test was negative, as was the differential agglutination titre (1:16) and anti-nuclear factor test.

Treatment A diagnosis of constrictive pericarditis was made, and the patient was treated with daily streptomycin, P.A.S., and isoniazid for four months before operation, but as the condition subsequently did not seem likely to be of tuberculous origin these were discontinued one month later.

At operation at the Brompton Hospital on 21 June 1960 there was thickening and adherence of the pleura over the lower and middle lobes. The pericardium was thick over the right ventricle and right atrium. It was thin over the left ventricle, except for a very thick constricting band running down from the left atrium in the atrio-ventricular groove. At the site of greatest thickening there was, in some places, yellow serous material between the two layers of the pericardium, and the visceral layer was oedematous and difficult to dissect off the heart. The

FIG. 1. Case 1. A radiograph of the right hand showing gross changes of rheumatoid arthritis.

FIG. 2. Case 1. The microscopic appearances of the pericardium showing gross fibrous thickening.

FIG. 3. Case 1. The microscopic appearances of the lung showing fibrosis of the alveolar walls.

thickened pericardium was excised, and the right lung was decorticated. Examination of the excised pericardium (Fig. 2) showed gross fibrous thickening without calcification (von Kossa's method). Small lymph follicles were normal in size and appearance. The innermost layer consisted of amorphous material containing a large amount of stainable lipoid and many multinucleate giant cells containing crystals of cholesterol. Specific tuberculous lesions were not found. A biopsy taken at operation from the right lung (Fig. 3) showed some slight scattered fibrosis of the alveolar walls. There was striking intimal proliferation in the small arteries.

The patient was seen three years after operation, when the heart condition was satisfactory; the venous pressure was normal, the liver not enlarged, and there was no oedema. The heart sounds were normal and the third sound was not audible. The arthritis remains severe and she is confined to a wheel chair with fixed deformities of the limbs. New subcutaneous rheumatoid nodules continue to appear. The radiological lung mottling remains unchanged, as does the diffusion of carbon monoxide (12.5 ml./min./mm. Hg).

CASE 2 J. B. was aged 29 at the time of her admission to the Brompton Hospital in July 1960. She had had an attack of acute arthritis six years previously,

which had affected the small joints of the right hand. This attack lasted for only two weeks. Four years later she noticed shortness of breath on exertion and complained of pain in the left side of the chest. She was admitted to St. Giles Hospital in March 1958 with fever, tachycardia, and evidence of a left pleural and pericardial effusion. Sputum examination and laryngeal swabs failed to demonstrate *Myco. tuberculosis*, as did the pleural aspirate. The Mantoux test was negative to 100 T.U.

Two weeks later she developed pain and swelling in the joints of the fingers of both hands. The R.A. latex test at this time was negative and L.E. cells were not found.

She was treated with streptomycin, isoniazid, and prednisone for two weeks. The pleural effusion cleared. The heart size returned to normal and the arthritis improved.

Two months after stopping the prednisone the arthritis recurred in the right hand and left ankle. Cortisone was given with improvement in the joint symptoms and was continued up to the time of admission to the National Heart Hospital two years later, when she complained of shortness of breath on exertion and swelling of the abdomen.

On examination in 1960 at the National Heart Hospital, the heart was in sinus rhythm, the blood pressure was 105/90 mm. Hg, and the venous pressure in the neck veins was 8 cm. above the sternal angle with a dominant x descent. The Kussmaul sign was positive. A third heart sound was heard at the left sternal border. Dullness and weak breath sounds were present at the bases of both lungs. The liver was palpable two finger-breadths below the costal margin, and there was considerable ascites. There was wasting and weakness of the shoulder muscles, spindle-shaped swelling of the proximal interphalangeal joints, and swelling with limitation of movement in both wrists and in the left ankle joint. No subcutaneous nodules were found.

Investigations An E.C.G. showed sinus rhythm, low voltage QRS and T waves with T wave inversion in leads 3 and V₁.

Radiographs of the chest showed a small heart outline and pleural thickening at the left base. There was no pericardial calcification. Radiographs of the wrists and hands showed bone erosions in several metacarpals. On investigation of the lung function, the forced vital capacity measured 2,000 ml. and forced expiratory volume (1 sec.) 1,800 ml. The carbon monoxide diffusion was normal (21.5 ml./min./mm. Hg) and carbon monoxide extraction was 58%. The R.A. latex test was positive as was the differential agglutination titre (1:64). The serum albumin measured 4.1 g./100 ml., and the serum globulin 3.5 g./100 ml. Electrophoresis showed a slight increase in the gamma and alpha 2 globulins.

Treatment Pericardiectomy was performed at the Brompton Hospital on 12 August 1960. There was

FIG. 4. Case 2. The microscopic appearances of the pericardium showing dense featureless fibrosis.

extensive fibrous thickening of the pericardium, measuring 3 to 4 mm. in some places. It stripped off the heart fairly easily. There was a small left pleural effusion with adhesions over the left lower lobe.

Histological examination of the excised pericardium showed dense featureless fibrous tissue (Fig. 4).

After operation the patient progressed well, and, when seen in June 1963 (three years later), she was not breathless, and the jugular venous pressure was normal, as were the heart sounds. There was no oedema, and the liver was not palpable. The joints remained unchanged.

CASE 3 R. H. was aged 58 at the time of his admission to the Brompton Hospital in January 1962. Two years earlier he had developed painful swelling in the small joints of both hands. This subsided in about one month but recurred for a few weeks seven and 10 months later. At this time he developed shortness of breath on exertion and was admitted to the North Middlesex Hospital. He was found to have painful swollen joints of both wrists and of the fingers. A subcutaneous nodule was palpable over the right olecranon. The venous pressure in the neck was raised 10 cm. above the sternal angle. A pericardial friction rub was audible. The liver was enlarged and there was sacral oedema. There was a pleural effusion

on the right side. The aspirated fluid contained many lymphocytes and mesothelial cells, but on culture *Myco. tuberculosis* was not grown. The Mantoux test was negative to 10 T.U. The R.A. latex test and antinuclear factor were negative. No L.E. cells were found.

He was treated with rest, digitalis, diuretics, and prednisone. The arthritis subsided and the pleural effusion and sacral oedema cleared, but he became increasingly short of breath over the next four months.

On admission to the Brompton Hospital in January 1962 the heart was in sinus rhythm; the pulse was paradoxical and the blood pressure was 125 to 110/90 mm. Hg. The jugular venous pressure was raised about 15 cm. above the sternal angle with the patient at 90°. The Kussmaul sign was positive. The heart sounds were normal. A third heart sound was present on inspiration only. High-pitched expiratory rhonchi were present on both sides of the chest. The liver was enlarged three finger-breadths below the costal margin. There was slight ankle oedema.

Investigations Radiographic examination of the chest showed some pleural thickening at the right base. An E.C.G. showed sinus rhythm with flat T waves. Phonocardiography confirmed the presence of

a third heart sound 0.11 second after aortic valve closure. At cardiac catheterization the pulmonary artery pressure measured 27/13 mm. Hg.

The right atrial pressure was the same as the pulmonary capillary venous pressure, with a mean of 10 mm. Hg. The arterio-venous oxygen difference was 54 mm. Hg. and a square wave response was obtained on the Valsalva manoeuvre. The serum albumin measured 3.8 g./100 ml. and the serum globulin 2.9 g./100 ml. The electrophoretic pattern was normal.

Treatment Pericardiectomy was performed on 20 March 1962. The pericardium was thick, fibrous, and adherent, particularly over the right ventricle and in the atrio-ventricular groove.

Pathological examination of the excised pericardium showed gross fibrous thickening without calcification (Fig. 5). The superficial fatty layer contained a striking infiltration by plasma cells with some polymorphs.

When seen 14 months after operation (17 May 1963), the patient had returned to full work as a printer and was only slightly breathless if he walked more than a mile. The heart sounds were normal. No third sound was audible. He had had no recurrence of joint pains, but the differential agglutination titre at this time was positive (1:32). The R.A. latex test and antinuclear factor remained negative and the radiographs of the hands were normal.

DISCUSSION

It is suggested that the cause of the constrictive pericarditis in these three patients is related to their rheumatoid disease and is not due to tuberculosis.

Proof that a case of chronic constrictive pericarditis is due to antecedent tuberculosis is never easy to obtain. In 65 patients treated by operation, Connolly and Burchell (1961) isolated *Myco. tuberculosis* in only six instances, and Effler (1961) had positive findings in only two of 26 cases. The histological features in the excised pericardium are more likely to show the changes characteristic of tuberculosis when the operation is done in the subacute rather than in the chronic phase of the disease. In a population with a high incidence of positive reactions, the Mantoux test is only of value when it is negative, i.e., indicating that the patient has not been infected with tubercle bacilli. Wood (1956) regarded pericardial calcification as strong evidence for tuberculosis; calcification was present in 75% of the cases in his series.

During the period when these three patients with constrictive pericarditis and rheumatoid disease were seen, 17 other patients with pericarditis were treated by operation at the Brompton

FIG. 5. Case 3. The microscopic appearances of the pericardium showing fibrous thickening without calcification.

Hospital. Fourteen of these 17 had pericardial calcification. Of the 14 with calcification, two had acid-fast bacilli in the sputum and three had typical tuberculous appearances in the excised pericardium. Of the three patients without pericardial calcification, one had histological features of tuberculosis in the pericardium; in the other two patients there were no clues as to the cause of the disease. None of these 17 patients had any evidence of associated diseases.

None of the three patients with constrictive pericarditis and rheumatoid arthritis reported here had pericardial calcification. None had evidence of tuberculosis in the excised pericardium. In two patients the Mantoux reaction was negative and in the third it was positive. In the latter (V.P.) no evidence of tuberculous granulation tissue was found in the pericardium although it was oedematous and in a subacute state of inflammation, a stage at which the microscopic appearance of tuberculosis is most commonly found.

There is, on the other hand, good evidence that these patients had rheumatoid arthritis, and the features are summarized in Table I. It will be seen that in each case many of the criteria set out by the American Rheumatism Association (1959) are satisfied. The clinical features of tenderness, stiffness, pain on movement, soft tissue swelling in at least one joint extending to swelling in many joints within an interval of less than three months, and symmetrical joint swelling were present in all three patients. Subcutaneous rheumatoid nodules were present in two. Typical radiographic

changes, including joint deformity and subluxation, periarticular decalcification, and bone erosions, were present in varying severity in two patients. The R.A. latex test was positive in one patient and the differential agglutination titre was positive in two patients at some stage of the disease. The patient with the persistently negative R.A. latex and negative differential agglutination titre was in fact the patient with the most advanced arthritis assessed clinically and radiologically. In this patient numerous olecranon rheumatoid nodules are present. It is well recognized that about 10% of patients with undoubted rheumatoid arthritis run their entire course with negative serological reactions (Plotz and Singer, 1956). There was no demonstrable evidence of disseminated lupus erythematosus in any of these patients: L.E. cells were looked for on several occasions and were never found, and the antinuclear factor was always negative.

Non-constricting adhesive pericarditis is a common post-mortem finding in cases of rheumatoid arthritis. Sokoloff (1953) found the condition in 40 out of 101 cases, Graef, Hickey and Altman (1952) in half of 66 cases, Young and Schwedel (1944) in 19 of 38 cases, and Bywaters (1950) in two of 24 cases. Bauer and Clark (1948) found pericarditis in 44% of 445 necropsies and in two of these cases found rheumatoid nodules in the pericardium, histologically similar to skin nodules.

Clinically, acute pericarditis as a complication of rheumatoid arthritis has been reported by

TABLE I
A SUMMARY OF SOME CLINICAL FEATURES

	Patient		
	J.B.	R.H.	V.P.
Arthritis	Mild, 4 years; intermittent pain and swelling L. carpophalangeal joint, L. wrist, L. ankle, L. shoulder, neck	Moderate, 2 years; intermittent swelling and pain hands, knees, ankles, elbows, neck	Severe, 10 years; pain and swelling hands, wrists, ankles, elbows, shoulders; increasing deformity 5 yr.; now confined to chair
Nodules	None	Olecranon nodules 2 years ago	Multiple subcutaneous nodules—still appearing
Radiological changes ..	Rarefaction, narrowed joint spaces, erosions L. hand	Normal	Gross radiological changes (Fig. 1)
R.A. latex	Positive	Negative	Negative
Differential agglutination titre ..	Positive 1 : 64	Positive 1 : 32	Negative 1 : 16
Antinuclear factor	Negative	Negative	Negative
Serum proteins (g./100 ml.) ..	Albumin, 4.3; globulin, 3.4; γ slightly increased	Albumin, 4.3; globulin, 2.8; α_2 and β slightly increased; γ slightly decreased	Albumin, 3.5; globulin, 3.5; γ moderately increased
Mantoux	Negative, 100 T.U.	Negative, 10 T.U.	Positive, 10 T.U.
Pericardial calcification ..	None	None	None
Other features	Pleurisy when arthritis started	Pleurisy with effusion 1 year after arthritis	Interstitial pulmonary fibrosis confirmed by lung biopsy; corneal ulceration

Parker and Cooper (1951), Connolly and Burchell (1961) and Wilkinson (1962). Wilkinson (1962) has, however, stated that rheumatoid pericarditis does not seem to be harmful. The cases reported here and other published reports by Glyn and Pratt-Johnson (1963), Partridge and Duthie (1963), McMurray *et al.* (1951), Gimlette (1959), and Keith (1962) suggest that some patients with acute rheumatoid pericarditis may later develop cardiac constriction.

There are other interesting points of similarity between the cases presented here and those in the literature. Pleural effusion was present at the stage of active pericarditis in the case reported by Partridge and Duthie, by Glyn and Pratt-Johnson, and in two of the four cases reported by Wilkinson. Pleural effusion was present in two of the three cases studied here. In two of our patients the joint pains were not severe and occurred intermittently for a relatively short time before evidence of pericarditis appeared. This mild type of rheumatoid arthritis was present in the cases reported by McMurray *et al.* (1951), Keith (1962), and Partridge and Duthie (1963). Steroids do not seem to have been helpful in preventing progression to constriction (Connolly and Burchell, 1961; Partridge and Duthie, 1963). Two of our three patients received long-term steroids but progressed to constriction. The absence of specific rheumatoid appearances on microscopy in the excised pericardium was noted in all three of our patients and appears to be the experience of other authors; indeed we were unable to find in the literature any instance in which specific rheumatoid changes had been found in a pericardium excised for constrictive pericarditis.

Our patient with the most advanced arthritis had pathological changes in the lungs in addition to the pericardial lesion. Radiologically, these looked like interstitial pulmonary fibrosis; this diagnosis was supported by the demonstration of a defect in diffusion and confirmed by histological examination of a lung biopsy. These lung changes have been reported in patients with rheumatoid arthritis (Ellman and Ball, 1948).

Gimlette (1959), reporting five cases of pericarditis associated with rheumatoid arthritis, suggested that there was usually an important myocardial factor and that these patients did not improve on pericardiectomy. In all three of our cases we found at operation that the thickened pericardium could be separated from the heart

more easily than in many cases of tuberculous aetiology, and all have had a completely satisfactory result from the cardiac point of view. Successful pericardiectomy has also been reported by others.

SUMMARY

Three cases of constrictive pericarditis associated with rheumatoid arthritis are reported.

The part played by rheumatoid disease in the aetiology of constrictive pericarditis is discussed.

Pericardiectomy gave satisfactory relief of the cardiac symptoms in all three cases.

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