

Collagen diseases as a cause of constrictive pericarditis

D. K. C. COOPER¹, W. P. CLELAND, AND H. H. BENTALL

From the Department of Surgery, Hammersmith Hospital and Royal Postgraduate Medical School, Ducane Road, London W12 0HS, UK

Cooper, D. K. C., Cleland, W. P., and Bentall, H. H. (1978). Thorax, 33, 368-371. Collagen diseases as a cause of constrictive pericarditis. Seven patients with constrictive pericarditis associated with collagen disease underwent pericardiectomy with good results in all but one. The collagen disease was confirmed as rheumatoid arthritis in five patients, but in two its nature remained obscure. In one case the illness was marked by a persistent eosinophilia and eosinophilic infiltration of the pericardium. The association of constrictive pericarditis with rheumatoid arthritis and other collagenoses is briefly discussed.

The first reports of constrictive pericarditis occurring in patients with rheumatoid arthritis were published by McMurray and his colleagues (1951) and Gimlette (1959). Since then, the association of rheumatoid arthritis with constrictive pericarditis has been reported in a sufficiently large number of patients to make the aetiological connection extremely likely. By 1966, 15 cases had been reported in the English language (Kennedy *et al.*, 1966). No one institution or author has a large experience of such cases; the five cases reported by Gimlette form the largest series to date.

Present series

Since 1968, 29 patients at the Hammersmith Hospital have undergone pericardiectomy for constrictive pericarditis. In 11 cases the aetiology was considered to be tuberculous, although in not every case was there bacteriological or histological proof. Eight other patients displayed features of a collagen disease, which was positively identified as rheumatoid arthritis in six, the exact diagnosis being less clear in the remaining two. One of the six patients with rheumatoid arthritis was also found to have active tuberculosis, making the cause of her pericardial constriction uncertain. The ages of the patients at the time of onset of the collagen disease and at the time of operation are shown in the Table. Of the remaining ten patients, the constriction was associated with uraemia in one case and with carcinomatous infiltration of

the pericardium in another; in the remainder the aetiology remained unproved but was presumed to be viral.

RHEUMATOID ARTHRITIS

Each of the six patients diagnosed as suffering from rheumatoid arthritis had the typical clinical features of the condition according to the criteria of the American Rheumatism Association (1959). The diagnosis was confirmed by the relevant laboratory tests, notably the latex fixation test for rheumatoid factor and the Rose Waaler, which gave positive results in all cases except one (Table). In no case was there a significant history of viral pericarditis, and in no case except the one already mentioned was there any evidence of infection with the tubercle bacillus. This one patient, in whom tubercle bacilli were cultured from sputum, gastric washings, and urine, and in whom serum antibodies to the tubercle bacillus were present to a titre of 1 in 125, will be excluded from further discussion as the aetiology of the constriction was uncertain. The excised pericardium showed no features of tuberculosis, but by this time the patient was receiving triple chemotherapy.

The remaining five cases had typical clinical and investigative features of constrictive pericarditis and could not be differentiated by any haemodynamic feature from cases not associated with rheumatoid arthritis (Dayem *et al.*, 1967). Clinical features of rheumatoid arthritis had been present for from two to 19 years before operation for constriction of the heart was necessary (Table).

Two of the patients exhibited other complications of rheumatoid arthritis, notably peripheral

¹Present address: Thoracic Unit, Hospital for Sick Children, Great Ormond Street, London WC1.

Table Clinical and serological features of patients developing constrictive pericarditis in association with collagen disease

Case no. and sex	Age at onset of collagen disease	Age at pericardiectomy	Serology				Diagnosis	Extent of collagen disease at pericardiectomy	Activity of collagen disease and medication at pericardiectomy
			LFT	RW	ANF	LC			
1 M	42	58	+	+			RA	Multiple arthropathy. Peripheral neuropathy. Baker's cysts. Subcutaneous nodules	Moderately active. Prednisone 6 mg daily. Ibuprofen
2 F	46	56	+	+	-	-	RA	Multiple arthropathy. Skin ulceration	Almost 'burnt out'. Indomethacin suppositories. DF 118
3 M	59	63	+	+		-	RA	Multiple arthropathy. Soft tissue swelling. Skin ulceration	Active. Prednisone 14 mg daily
4 F	39	47	+	+			RA	Multiple arthropathy. Skin ulceration. Joint effusions	Active. Prednisone 7.5 and 5 mg alternate days. Distalgestic
5 F	52	71	+	-			RA	Multiple arthropathy.	Inactive. No treatment
6 F	48	55	+	+			?RA ?TB	Multiple arthropathy. Soft tissue swelling	Moderately active. Prednisone 5 and 2.5 mg alternate days. Indomethacin 25 mg tds + suppositories
7 F	17	21	+	+	+	-	?SLE	Asthma, rhinitis. (Eosinophilia)	Moderately active. Prednisolone 8 mg daily
8 F	18	23	-	-	-	-	??SLE	Pleural effusions	Moderately active. Prednisone 20 mg daily

RA=rheumatoid arthritis; TB=tuberculosis; SLE=systemic lupus erythematosus; LFT=latex fixation test; RW=Rose Waaler; ANF=antinuclear factor; LC=lupus cells.

neuropathies, Baker's cysts, and peripheral vasculitis.

The histological appearances of the excised pericardium were non-specific cellular infiltration and fibrosis; calcification was not present.

All patients were greatly improved after pericardiectomy, and the improvement has been maintained to date in four cases. The oldest patient (case 5) developed congestive cardiac failure six months after operation and needed considerable medical treatment until the sudden onset of complete heart block caused her death two years later. Necropsy showed evidence of old pulmonary infarctions and myocardial hypertrophy but no residual pericardial constriction.

OTHER COLLAGENOSIS

Two additional patients in the Hammersmith Hospital series of 29 were considered to be cases of constrictive pericarditis associated with collagen disease, although in neither case was the diagnosis absolutely clear (Table). One appears to be the first reported in the UK of pericarditis associated with eosinophilia and eosinophilic infiltration of the pericardium.

The patient was a 17-year-old girl who, in 1964,

developed status asthmaticus which was treated with prednisone and antibiotics. Later the same year, she was found to have arthralgia, ecchymoses, a rash, and pericardial friction. Results of serological tests for rheumatoid arthritis were positive. She subsequently developed a butterfly rash on the face. Antinuclear factor (positive fluorescent antibody for lupus erythematosus) was present in the serum, suggesting a diagnosis of lupus erythematosus, although lupus cells were never identified. One unusual feature was that the eosinophil count was $12\,760/\text{mm}^3$ ($12.7 \times 10^9/l$) out of a total white cell count of $22\,000/\text{mm}^3$ ($22.0 \times 10^9/l$) (58% of the total white cell count). She was again treated with prednisone.

Three years later the patient developed signs of right heart failure with some clinical evidence of constrictive pericarditis, which was supported by cardiac catheterisation studies. The eosinophil count was by now $18\,000/\text{mm}^3$ ($18.0 \times 10^9/l$). At operation, the pericardium was thickened (3–4 mm) and constricted; the myocardium appeared normal. Pericardiectomy was performed. Histologically, the excised pericardium showed fibrous thickening with a mild inflammatory infiltrate mainly of polymorphs and eosinophils. There has been

complete recovery of cardiovascular function, but the eosinophilia has persisted despite steroid therapy.

One other patient was also suspected of having systemic lupus erythematosus, although the diagnosis was never proved. At the age of 18 years she was admitted to another hospital with a febrile illness, bilateral pleural effusions, and abdominal pain. The abdominal symptoms and signs were sufficient to persuade the surgeons concerned to perform a laparotomy, but no abnormality was discovered. A clinical diagnosis of systemic lupus erythematosus was made, although testing for anti-nuclear factor and screening for lupus cells in the blood failed to substantiate this. After operation the patient developed a superior vena caval thrombosis. A high dose of steroid controlled the accumulation of pleural fluid; reduction of the dose caused the effusions to recur.

In 1970, some five years after the onset of her illness, she was referred to the Hammersmith Hospital. The patient displayed signs of constrictive pericarditis confirmed by cardiac catheterisation studies, and hypersteroidism. At operation, the heart was small and encased in an oedematous, thickened (5 mm) pericardium; the epicardium was also thickened (3 mm). Both pericardium and epicardium were stripped off and the heart increased spectacularly in size. After operation, the signs of pericardial constriction disappeared, and it was possible to reduce and eventually discontinue her steroid intake.

Clinical opinion at that time was that the patient's febrile illness had been due to a virus rather than systemic lupus erythematosus, but the control of the pleural effusions over several years with steroids supports the latter diagnosis.

Discussion

The Hammersmith Hospital series almost certainly gives a false impression of the frequency of the collagen diseases as a cause of constrictive pericarditis. The incidence is high because of the proximity of the rheumatology department at the Hammersmith Hospital and the referral of patients from both this unit and that at the Canadian Red Cross Hospital at Taplow.

Constrictive pericarditis is said to occur only in the seropositive form of rheumatoid arthritis, as was the case in the present series (Table). Although rheumatoid nodules have been found in the pericardium at post-mortem examination of patients with rheumatoid arthritis (Bauer and Clark, 1948), we have found no cases reported in which specific rheumatoid changes have been

found in a pericardium excised for constrictive pericarditis.

Gimlette (1959) was of the opinion that patients with constrictive pericarditis associated with rheumatoid disease had severe myocardial involvement and that pericardiectomy did not improve the condition greatly, the patients continuing to be troubled by the myocardial disease. Later authors have not agreed with this opinion, and in the present series four of the five patients have had an excellent result. There therefore seems little evidence for Gimlette's pessimism.

A significant number of patients with rheumatoid arthritis (up to 40% in some studies) develop some form of pericarditis (Connolly and Burchell, 1961; Parker and Cooper, 1961; Wilkinson, 1962) and display non-constrictive adhesions at post-mortem examination (Bauer and Clark, 1948; Bywaters, 1950; Sokoloff, 1953). It is, therefore, only a very small percentage of cases in which the pericarditis progresses to fibrosis and constriction.

Steroid therapy has been given to several patients, both in the present series and in other reported cases, throughout the course of the rheumatoid disease process, yet these patients have still developed chronic constrictive pericarditis. Steroid therapy, therefore, appears to play no part in preventing progression to pericardial fibrosis and constriction (Connolly and Burchell, 1961; Tubbs *et al.*, 1964).

There are also a very few well-documented cases in which pericarditis has been a presenting feature of rheumatoid disease in patients hitherto completely well. This has been followed, sometimes a few weeks after complete clinical resolution of pericarditis, by the typical arthritic features (Gimlette, 1959; Glyn and Pratt-Johnson, 1963).

The exact diagnosis in the case of the patient who showed a persistent eosinophilia remains unclear. Systemic lupus erythematosus was thought to be most likely. However, there have been reports of pericarditis occurring in hyper-eosinophilic states, such as tropical eosinophilia (Vakil, 1961; Singh *et al.*, 1974). The case outlined appears to be the first reported in Britain of constrictive pericarditis associated with such a hyper-eosinophilic state.

Although pericarditis is a common feature of systemic lupus erythematosus, and, as in rheumatoid arthritis, may be symptomatically silent and noted only at necropsy (Jarcho, 1936; Brigden *et al.*, 1960; Shearn, 1959), constrictive pericarditis is an extremely rare complication of this disease. Fibrinous adhesions have been found in the pericardial space at necropsy, but it had

been thought that constriction did not occur (McKusick and Harvey, 1955; Gimlette, 1959; Shearn, 1959) until Yurchak and his colleagues reported one such case in 1965, which appears to remain unique.

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Requests for reprints to: D. K. C. Cooper, FRCS, Thoracic Unit, Hospital for Sick Children, Great Ormond Street, London WC1.