

Aetiology of chronic constrictive pericarditis

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SUMMARY In a consecutive series of 32 cases of chronic constrictive pericarditis treated by pericardiectomy during the past 25 years, four were attributable to rheumatoid disease, two to trauma, one to sarcoidosis, and four, at a maximum, to tuberculosis. In the remaining 21 cases of undetermined aetiology there was no evidence of tuberculosis. It appears, therefore, that tuberculosis was not a common cause of chronic constrictive pericarditis during the period under review, which included the 1950s and early 1960s when tuberculosis was widespread.

Specific antituberculous chemotherapy came into wide use in the 1950s (isoniazid was introduced in 1952), but it was almost another decade before there was an appreciable reduction in the incidence of tuberculosis. During those years constrictive pericarditis was generally regarded as due mainly to tuberculosis.¹⁻⁴ An article by Andrews *et al.* published in 1948¹ appears to have been a major influence in establishing this belief. More recently, with the decline in tuberculosis, other causes have come to be recognised with greater frequency,⁵⁻⁷ but even in the past there were authors who had reservations about the general view.^{2,8,9}

In the course of a study of a series of cases of chronic constrictive pericarditis, submitted to pericardiectomy at this hospital, evidence for extracardiac tuberculosis was notably uncommon. The series dates back to the 1950s, the earliest operation being in 1958. In many patients symptoms of constriction were already present for some years before surgery and any preceding acute tuberculous pericarditis would have occurred earlier still. Since tuberculosis was widespread in the 1950s and 1960s it prompted the question of whether, even then, it was the predominant cause of constrictive pericarditis. To explore this question further we studied the whole series, deciding to analyse only those cases coming to pericardiectomy since these might be expected to provide valuable evidence from examination of the excised pericardium.

Patients and methods

Since 1958, 32 patients with chronic constrictive

pericarditis have been submitted to pericardiectomy. Table 1 shows their distribution in time. They were studied with particular reference to (a) a history of earlier acute tuberculous pericarditis, (b) evidence of tuberculosis other than pericardial, (c) the result of Mantoux testing, and (d) the findings in the pericardium at surgery and at subsequent examination.

FINDINGS

As shown in Table 2, a definite non-tuberculous aetiology was present in seven cases, leaving 25 for further analysis. Of these 25 patients, three had evidence of tuberculous pericarditis. In one, operated on in 1961, tubercle bacilli were reported on direct examination of the excised pericardium; the tissue was not cultured and there were no typical granulomatous lesions. In a second, who also underwent surgery in 1961, pericardial fluid aspirated during an attack of acute pericarditis three years before surgery was reported to be positive for tubercle bacilli on direct examination but failed to grow the bacillus on culture. In a third, operated on in 1970, pericardial fluid obtained six years earlier was reported as growing tubercle bacilli on culture. Two further patients had a history of acute pericarditis 11 months and 10 years earlier; the illness was not severe and necessitated admission to hospital for only two and three weeks. Pericardial fluid was negative for tubercle bacilli both on direct examination and on culture in one patient but was not examined in the other. Antituberculous chemotherapy was not given to either patient. They came to surgery in 1966 and 1968. In the remaining 20 patients, there was no previous history of acute pericarditis or indeed of any serious acute illness. In one of these a chest x-ray examination

Table 1 *Chronic constrictive pericarditis*

Years:	1956-60*	1961-65	1966-70	1971-75	1976-80	1981-85
No. of cases:						
Total	3 ⁺	5	5	9	4	6 ⁺
Of unknown aetiology	2	2	3	7	3	4

*Series began during this quinquennium.

+Incomplete quinquennia.

at the time of surgery in 1960 showed a small area of shadowing at one lung apex consistent with tuberculosis. Tubercle bacilli could not, however, be isolated from sputum, throat swab, or gastric aspirate. There was no record of a Mantoux test. In one of the two patients with a previous history of a tuberculous pericardial effusion the chest x-ray film at the time of surgery showed a lesion suggesting old healed pulmonary tuberculosis, but in all the other patients the lung x-ray findings were normal.

Excluding the seven patients with a non-tuberculous aetiology (Table 2), the three with evidence of tuberculous pericarditis, and the one with a pulmonary shadow on the x-ray film, there were 21 patients with no direct evidence of aetiology (Table 1). They ranged in age from 16 to 70 years with a mean of 42 years. Symptoms and signs did not differ notably from those of the remaining patients. The interval between the onset of symptoms and eventual surgery ranged up to nine years with a mean of 2.4 years. A Mantoux test was carried out in 12 patients on admission for surgery; the first strength test (at 1/10,000) was positive in four and negative in eight. Of the eight negative cases, four were positive and four negative on second strength testing (at 1/1000). At surgery the pericardium was thickened in all cases. In 12 cases it consisted of fibrocalcific tissue rigidly encasing the heart. In five cases calcification was so dense that the tissue could be excised only with difficulty. In four cases the surgeon reported finding caseous like material, which to him suggested a tuberculous aetiology, and it probably provides one reason for this widespread belief. Subsequent histological examination did not, however, support such a diagnosis and it is noteworthy that "caseous material" was present in two of the four cases of rheumatoid disease. Clearly, it represents a non-specific reaction.

The results of histological examination of the

excised pericardium were available in 30 of the 32 patients but could not be traced in two who underwent surgery in 1962 and 1969. Apart from the single case in which tubercle bacilli were reported on histological examination there was no evidence of tuberculosis in the remainder. In nine cases there was a non-specific inflammatory reaction in the form of foci of lymphocytes and plasma cells scattered through a fibrous tissue stroma, while in 20 there was dense hyalinised connective tissue frequently interspersed with amorphous material and variable amounts of calcification. In the two cases in which the result of the histological examination could not be found, anti-tuberculous treatment was not given postoperatively, suggesting that the histological findings were not indicative of tuberculosis.

Discussion

The crucial test for tuberculous infection rests either on a positive sputum test result in the case of a pulmonary lesion or a positive biopsy result in other tissue disease. In this series the tissue in question was pericardium, and examination of the excised pericardium yielded a non-specific result in all but one instance. Undoubtedly, acute tuberculous pericarditis may eventually heal completely leaving only a featureless fibrosis,^{1,3} but if tuberculosis was the predominant cause of disease in this series a specific tuberculous picture would be expected in some instances. A similar experience has been reported in most published series of chronic constriction.^{1,3,7}

In those patients in whom the Mantoux test was performed the first strength was negative in two thirds and in these the second strength was negative in half. This frequency of a positive Mantoux reaction was if anything lower than would be expected in the general population during the period in question.

It was the finding on chest x ray examination that first drew attention to the problem of the aetiology of constrictive pericarditis. It seemed surprising that only two patients showed a pulmonary lesion consistent with tuberculosis, if in fact tuberculosis was a frequent cause. Equally, it was unexpected that there was no history of previous or current extracardiac tuberculosis.

In 19 of the 21 patients with no evidence of aetiol-

Table 2 *Aetiology of chronic constrictive pericarditis*

Aetiology	No. of cases
Rheumatoid	4
Traumatic	2
Sarcoid	1
Other	25
Total	32

ogy in this series, there was no previous history of acute pericarditis or other notable illness. Before the advent of specific antituberculous chemotherapy in the early 1950s the mortality rate from acute tuberculous pericarditis was about 90%.^{10 11} If tuberculous pericarditis was the predominant cause of pericardial constriction in the present series it would be most unlikely that such a serious illness would not be a predominant feature in the history. There is no convincing evidence for such an entity as subclinical acute tuberculous pericarditis leading to chronic constrictive pericarditis some years later. If there was, there would also of necessity be cases of subclinical tuberculous pericarditis without any clinical sequelae whatsoever since all cases of acute tuberculous pericarditis do not lead to constriction. Such a diagnosis has never been postulated much less proved. On the other hand, subclinical rheumatoid¹² and viral¹³ pericarditis may occur both without clinical sequelae and with eventual constriction. Undoubtedly, acute tuberculous pericarditis may progress to chronic constriction and there may be an interval of several years without symptoms between the two presentations. Where such a progression has been observed, however, it has usually spanned several months rather than years, and the process of constriction has occurred essentially as a continuation of the acute illness.^{1 10 14}

The belief that tuberculosis was the predominant cause of constrictive pericarditis originated at a period when tuberculosis was common. At that time other causes of pericarditis such as disseminated lupus erythematosus and viral infections were poorly recognised,¹ so that a diagnosis of tuberculosis was often made on meagre evidence. In fact, on reviewing the early cases in this series it is clear that a common attitude was to accept a diagnosis of tuberculosis in cases of serosal effusions until proved otherwise. It is understandable then that pericarditis would often be regarded as tuberculosis on quite inadequate evidence. The present series of cases dates from the 1950s, and since then there has been a progressive decline in the incidence of tuberculosis so that if constrictive pericarditis was due mainly to tuberculosis its incidence would have declined steadily over the years. This, in fact, has not occurred in our experience (Table 1).

It is tempting to seek a uniform mechanism for all cases of chronic constrictive pericarditis except those caused by pericardial infiltration with neoplastic tissue. In this series of 32 cases, four were associated with rheumatoid disease and one with sarcoidosis. This raises the possibility that the pathogenesis may be in the nature of an immune reaction. Pericardial trauma was responsible for constriction in two cases in the present series. Clearly, however, pericardial con-

striction occurs in only a few traumatic cases so that these must possess some special characteristics. At first sight an immune mechanism may not be obvious. A recent report of a series of five cases of constrictive pericarditis after cardiac surgery may, however, throw light on this.¹⁵ In four of the five patients, a postpericardiotomy syndrome followed the operation. Perhaps then constriction develops only when the pericardial trauma gives rise to an immune response. Such an immune reaction may not always be recognised at the time of its occurrence, its manifestations being confused with those produced directly by trauma. Again, it is noteworthy that constrictive pericarditis may follow the Dressler syndrome, which is generally accepted as being an immune disorder.¹⁶ There can be no doubt that an immune disorder may indeed give rise to serosal fibrosis as demonstrated for instance by the retroperitoneal fibrosis reported with practolol administration.¹⁷

It seems feasible then that any type of pericardial damage may go on to constriction if it initiates an immune reaction. Tuberculous infection would represent one type of damage and it is possible that it may cause an immune reaction with particular readiness. Where it is so common as to be endemic it could be the main cause of constrictive pericarditis,⁴ but this does not appear to have been the case in a Western country such as Britain, at least during the past 30 years or so.

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