

Constrictive pericarditis following Coxsackie virus infection

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Infection with Coxsackie B₂ virus is described in a 49-year-old farmer in whom myopericarditis and pneumonitis was followed over a period of 10 months by constrictive pericarditis.

The differentiation between restrictive cardiomyopathy and constrictive pericarditis was not achieved without exploratory thoracotomy. The adherent pericardium was successfully excised with complete relief.

The literature is reviewed and it is suggested that the development of constriction following Coxsackie pericarditis must be considered at subsequent examinations of the patient.

CASE REPORT

The patient, a farmer born in 1920, was well until October 1967, when he developed a feverish illness with an ache in the right chest and shoulder, a dry cough, generalized myalgia, and lassitude. The illness subsided after two days, with persistence of the dry cough for a few weeks. A week after the onset there was a mid-systolic click, widely heard over the precordium, followed at the apex by a short systolic murmur. A chest radiograph was normal and an electrocardiogram showed non-specific T wave flattening from inferior leads.

He remained well until June 1968, when he developed epigastric discomfort, a feeling of fullness in the neck, an unproductive cough, pyrexia, profuse night sweats, and increasing dyspnoea on effort. There was an elevation of the jugular pressure to 10 cm., persistent sinus tachycardia, a blood pressure of 100/70 mm. Hg, low-grade pyrexia, pericardial friction, fine inspiratory pulmonary basal crepitations, ankle and sacral oedema, and tender liver enlargement. The ESR was 38 mm./hour, rising to 72 mm./hour during the next 10 days. The WBC was 11,600/cu. mm., neutrophils 78%, lymphocytes 18%, and monocytes 4%, and haemoglobin 11.9 g./100 ml. Blood cultures and tests for antinuclear factor were negative. The aspartate aminotransferase was 115 units/ml. and hydroxybutyrate dehydrogenase 333 units/ml. Both enzymes were normal 14 days later. Mantoux tests at dilutions of 1/1,000 and 1/100 were negative and the antistreptolysin O titre was less than 100 Todd units/ml. A serial electrocardiogram showed no change. The chest radiograph showed cardiac enlargement, pulmonary congestion, and consolidation in the right lower lobe.

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Digoxin and frusemide had no effect during the first five days. A right pleural effusion developed, and a cellular yellow fluid was aspirated with a protein content of 2.8 g./100 ml. A diuresis began and a slow improvement occurred with disappearance of the signs of congestive cardiac failure. The ESR fell to 16 mm./hour after three and a half weeks. He was discharged after five weeks and digoxin and frusemide were continued for some weeks thereafter.

On 1 August 1968 he was tired and had a persistent unproductive cough with twinges of pain in the right lower chest posteriorly where there was pleural friction. Follow-up chest radiographs showed no abnormality apart from slight cardiac enlargement with left ventricular prominence. A soft mid-systolic murmur was heard at the apex. Results of earlier viral antibody studies showed significantly elevated neutralization titres to Coxsackie B₂ virus (Table I).

TABLE I

COXSACKIE B₂ NEUTRALIZATION TITRES
(tested in parallel)

2 July 1968	512
18 July 1968	1,024
26 February 1969	512
1 July 1969	256
19 September 1969	256

There was no significant level with Coxsackie B₁, B₃, B₄, and B₆. There were no antibodies to Q fever I and II and complement fixation tests were negative for adenoviruses, psittacosis, mumps, and chicken-pox.

In September 1968 he was much improved, apart from slight breathlessness on effort, and had returned to supervisory farm work. The jugular venous pressure was not raised. The blood pressure was 120/70 mm. Hg. The mid-systolic murmur remained maximal at the lower left sternal edge and it was louder than

before. He was discharged to the care of his general practitioner with the diagnosis of a Coxsackie B₂ infection, involving pericardium, myocardium, right lung, and pleura.

In January 1969 there was a recurrence of dry cough, discomfort in the right chest, and increasing breathlessness. The pulse was in sinus rhythm at 76/minute. The jugular venous pressure was elevated to 6 cm. He had ankle oedema, liver enlargement, inspiratory basal crepitations, and coarse right pleural friction. The mid-systolic murmur had not altered, but wide splitting of the second heart sound was heard. There was again no change on the ECG. The chest film showed the reappearance of pulmonary venous congestion and slight cardiac enlargement. The ESR was 5 mm./hour, WBC 7,800/cu. mm., and the serum transaminase enzymes normal.

He was treated again with digoxin and frusemide, with only partial improvement and without a return to normal health. The jugular venous pressure remained elevated and by May 1969 the wave form had become abnormal with unduly prominent 'a' and 'v' waves and a conspicuous 'y' descent. A soft third heart sound was heard in addition to the systolic murmur. An apex cardiogram and phonocardiogram showed a retracting apex beat with confirmation of a mid-systolic murmur and third heart sound.

He was admitted for cardiac catheterization (Table II). The findings were in keeping with pericardial

Within 24 hours the jugular venous pressure had returned to normal. The post-operative course was uneventful and the patient has gradually resumed a normal life without requiring drugs. He has been aware of occasional right-sided pleural friction. Neutralization titres to Coxsackie B₂ have fallen (Table I).

DISCUSSION

Acute 'benign' pericarditis was recorded by Hodges (1854). The Coxsackie virus was first isolated by Dalldorf and Sickles (1948). The first adult case of acute pericarditis was shown by Fletcher and Brennan (1957) to be due to Coxsackie B₃ infection, and the following year they reported a further case due to B₄ infection (Fletcher and Brennan, 1958). Weinstein (1957) reported a patient with pericarditis due to B₅ and Smith (1966) gave the first account of a B₂ infection causing pericarditis.

Constrictive pericarditis is a rare complication of acute 'benign' pericarditis and in many series no cases of constriction have been reported (Levy and Patterson, 1950; Scherl, 1956; Wood, 1961; Bradley, 1964; Robinson and Brigden, 1968). Sporadic cases, however, are to be found in the literature (Freilich, 1952; Krook, 1954; Rabiner, Specter, Ripstein, and Schlecker, 1954; Connolly and Burchell, 1961; Azar, 1963; Harrold, 1968). The suggestion that constriction may follow Coxsackie infection came from Robertson and Arnold (1962, 1965). They studied an epidemic in Vancouver in which 125 cases of acute pericarditis were seen and evidence of Coxsackie B₃ infection was obtained from some of these cases. Twelve patients developed constriction requiring surgery and, although it seems likely that the Coxsackie virus was the cause, it was not in fact demonstrated in any of the patients who developed constriction. The first definite case was that of Gibbons, Goldbloom, and Dobell (1965), who reported a child in whom Coxsackie B₃ was implicated. Another child with pericardial constriction after Coxsackie A₁ infection was mentioned by MacCallum (1966). The first adult case of constriction was that of Howard and Maier (1968), when Coxsackie B₃ was the agent.

In our case, evidence has been presented for Coxsackie B₂ infection as the cause of myopericarditis and the immediate result of operation demonstrated constrictive pericarditis. Myocarditis was diagnosed because there was an initial elevation of myocardial enzymes without electrocardiographic change and the patient developed congestive cardiac failure.

TABLE II
CARDIAC CATHETERIZATION
(R + L heart studies)

Site	Phasic Pressures (mm. Hg)	Mean Pressure (mm. Hg)
Superior vena cava	20/10	15
Right atrium	a 22 c 16	12-14
Right ventricle	x 2 y 8	
Mean pulmonary artery ..	34/8-14	
Pulmonary artery wedge ..	28/12	14
Left ventricle	18/8	
Aorta	95/18-25	
	95/58	

constriction or a restricted myocardium and it was decided that an accurate diagnosis could only be made by thoracotomy in spite of the opinions of a distinguished panel of cardiologists to whom the patient was presented.

At operation on 20 June 1969, there was dense fusion between the pericardium and the epicardium, but no calcification. The pericardium was mobilized and excised from the diaphragm to the termination of the main pulmonary artery and from the left pulmonary vein to the pericardial reflection of the right pleura. Microscopic examination of a myocardial biopsy was normal. The pericardium showed dense white fibrous tissue with numerous small blood vessels on both surfaces. There was very little lymphocytic infiltration and no giant cells or follicle formation.

Constriction developed later during a period of 10 months. The physical signs, the results of cardiac catheterization, apex cardiography and phonocardiography failed to differentiate constrictive pericarditis from restrictive cardiomyopathy, and the diagnosis was in doubt until thoracotomy was undertaken. At operation it would be of value to try to isolate the virus by tissue culture from the affected area of pericardium. It is important to know of the possibility of pericardial constriction after Coxsackie virus infection, otherwise the clinical signs of constriction may be attributed to cardiomyopathy and surgery may not be considered.

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