Four faces of acute myopericarditis

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Sixty patients with acute myocarditis or pericarditis or a combination of the two lesions, without endocarditis, were encountered by the authors in hospital and domiciliary consulting practice over a period of seven years. Similar cases have been reported under a variety of names; e.g. Cocksackie myopericarditis, acute nonspecific pericarditis, Bornholm disease, isolated myocarditis, Fiedler's myocarditis, and cardiomyopathy of pregnancy.

The clinical presentation fell into 4 groups. I: 19 patients presented with classical symptoms of acute pericarditis. II: 24 presented as coronary mimics, with severe substernal pain unaffected, or only slightly affected, by respiration, posture, or movement. III: 3 presented with progressive heart failure. IV: 14 presented with miscellaneous symptoms, most frequently resembling influenza.

Evidence of concurrent viral illness was found in 15 patients, 9 being Cocksackie infections. Other specific diseases were identified in 3 patients; but in 42, including 3 who died and were examined at necropsy, the nature of the disease could not be established.

Three patients died of heart failure, and in 10 others the electrocardiogram remained abnormal over 3 months after the onset; the remaining patients made a complete recovery. Nine patients relapsed, 7 of them being in the group presenting with acute pericarditis. No specific treatment was found to be of value.

The term myopericarditis has been used (Smith, 1966; *British Medical Journal*, 1971) to cover a group of cases with pericarditis or myocarditis or both, without any evidence of endocarditis. The grouping of myocarditis and pericarditis together is of value clinically in that both layers of the heart tend to be involved in the same types of acute disease process, and particularly in the common Cocksackie virus infections.

There is at the present time great confusion surrounding this group of cases. Much of this arises from the number of possible agents which may damage the myocardium and pericardium, and the fact that it is often impossible to establish the aetiology during life, and even at necropsy. This confusion is reflected in the nomenclature. For example, patients with Cocksackie B myopericarditis have been reported as acute nonspecific pericarditis or benign idiopathic pericarditis when symptoms of pericarditis have predominated; or as isolated myocarditis, idiopathic myocarditis, or Fiedler's myocarditis when myocardial damage has predominated; or as pregnancy cardiomyopathy when heart failure has developed during pregnancy.

Acute myopericarditis is important on account of its global frequency, and the difficulty it often presents in diagnosis. Most physicians encounter one or two cases of acute pericarditis each year – cardiologists and specialists in respiratory medicine see more – though these are often mistaken initially for myocardial infarction. At the Mayo Clinic, 269 cases of acute nonspecific pericarditis were diagnosed over a period of 10 years (Connolly and Burchell, 1961). Acute myocarditis is probably commoner than acute pericarditis, but more often overlooked; it is frequently found at necropsy when it has been missed during life. Gore and Saphir (1947) were able to record over 1000 cases from postmortem material submitted to the United States Army Institute of Pathology during the 1939-46 War. A considerable proportion of these cases was due to specific infections such as typhus and diphtheria, which are not commonly seen in civilian life; nevertheless, there were 43 in association with virus pneumonia, and 30 diagnosed as 'idiopathic'.

In this paper we attempt to resolve the current confusion on the basis of our experience of the problem as it presents in hospital and domiciliary consulting practice among adults in the North-East of Scotland, an area with a population of approximately 500,000.

Subjects and methods

We became interested in the problem of acute myopericarditis in 1964 after seeing a series of patients in whom the family doctor had suspected a coronary attack. We decided to collect all cases of acute myocarditis and acute pericarditis without evidence of endocarditis coming under our observation from this time, closing the series at the end of October 1971.

To qualify for inclusion, a patient must have been examined by one of us personally and have shown evidence of acute cardiac involvement, either by the development of a pericardial rub or serial electrocardiographic abnormalities. It was also essential that acute myocardial infarction could be reasonably excluded. At first we were inclined to omit any patient who gave a history of effort angina or previous infarction, but this might have given the impression that acute myopericarditis did not occur in patients with coronary heart disease. We therefore decided to accept patients with acute pericarditis provided the pain was different in site and quality from any previous coronary pain, and provided there was no electrocardiographic or enzymic evidence suggestive of recent infarction. There is good evidence that acute infarction is only complicated by pericarditis if the infarct is large (Thadani *et al.*, 1971); so this simplifies the problem of differential diagnosis.

During the seven-year period from November 1964 to October 1971 we saw 60 patients who fulfilled the criteria laid down above. Forty-eight were admitted directly to hospital as emergencies and the remaining 12 were seen initially in their home or in urgent outpatient consultation. The age and sex of the patients are shown in Fig. 1. Since our work was practically confined to adults the youngest patient in the series was aged 13 years.

In an attempt to establish the aetiology, the following screening tests were performed: the antistreptolysin O titre, *Brucella abortus* agglutinins, immunopathology, and the Paul Bunnell test; in many patients the toxoplasma dye test was also carried out. Virus isolation was attempted by inoculating throat swabs and stools into

FIG. 1 Age and sex distribution of 60 patients with acute myopericarditis.

cultures of secondary monkey kidney, human embryonic kidney, and HeLa cells. Sera were tested for the presence of antibodies to Coxsackie B1-6 viruses by means of the neutralization test in HeLa cells. Complement-fixation tests were carried out using the following antigens: influenza A, influenza B, parainfluenza, adenovirus, respiratory syncytial, psittacosis, Q fever, and *Mycoplasma pneumoniae*. Criteria for recent infection were either a fourfold rise in antibody titre or a 'high' titre; 256 or greater in the case of the Coxsackie B and influenza viruses, 128 or greater in the others. For parainfluenza and adenovirus a 'high' titre was not considered sufficient without epidemiological evidence or virus isolation.

Virological tests were not undertaken in 10 patients, either because a non-viral cause such as systemic lupus erythematosus or rheumatic fever was obvious, or because the patient was afebrile and an infection was not suspected at the time.

Clinical spectrum

Four distinct clinical presentations were encountered in this group of 60 patients, and though some patients had features of more than one group, it was possible to assign each case to one of the four groups by reference to the presenting symptom (Fig. 2).

I: *Classical acute pericarditis*: 19 patients presented with praecordial pain which was strikingly affected by respiration or posture (sometimes by both factors), and who were found to have a pericardial rub, a classical electrocardiographic pattern of pericarditis, or both features.

II: *Coronary mimic*: 24 patients presented with praecordial pain strongly suggestive of myocardial infarction. In these patients, the pain was unaffected, or only slightly affected, by respiration or posture, and the electrocardiogram showed abnormalities consistent with early myocardial infarction.

III: *Progressive heart failure*: 3 patients presented with heart failure which pursued a relentless course to a fatal termination.

IV: *Febrile and miscellaneous*: 14 patients presented with miscellaneous symptoms, most commonly an influenza-like illness, characterized by fever, sweating, pains in muscles or joints, and headache. None presented with praecordial pain suggestive of pericarditis or coronary disease, and none developed heart failure.

As indicated above, the groups overlap to some extent. Each group contains patients with objective evidence of pericarditis; a number of patients in Group I had febrile symptoms and one developed transient heart failure; several patients in Group II

FIG. 2 Clinical features of the four groups. Presenting symptoms are indicated by the black bars. Note: fever, temperature over 37.5°C on at least 2 days; tachycardia, pulse over 90 a minute on at least 2 days.

had praecordial pain which was slightly affected by respiration and movement; some patients in Groups III and IV had slight praecordial pain, though it was never a presenting feature.

Aetiology

Evidence of recent infection with one of the Cox-sackie B viruses was found in 9 cases; B4 in 3 cases, B2 in 3, B3 in 2, and B4 and B2 in 1 case. There were also 2 cases of influenza A, 2 of adenovirus infection, and 1 each of brucellosis and glandular fever. In addition there were 2 cases of systemic lupus erythematosus and 1 of rheumatic fever. In 42 cases the aetiology could not be established; 3 of these patients died, and the presence of acute myocarditis was confirmed histologically, but in each case the cause of the disease remained unexplained.

Group I - Classical acute pericarditis (19 patients)

Age and sex The age and sex distribution in this group was similar to that in the series as a whole (Fig. 3).

Presenting symptom Every patient in this group presented with a history of anterior midline chest pain. It was usually situated at midsternal level, occasionally above or below this point, and was invariably aggravated by respiration; in 12 patients, it was also affected by change of position. The pain was frequently referred to the left shoulder; occasionally to the back or the left side of the

neck, and a few patients also complained of tingling or heaviness in the left arm. The pain was frequently described as being very severe, and 12 patients required morphia or pethidine for its relief.

Other symptoms These were common (Fig. 2); notably sweating (12 patients), headache (9),

FIG. 3 Age and sex distribution in the four groups.

muscular aching (9), shivering (7), cough (6), and sore throat (6). Less common symptoms included dyspnoea (4), coryza (4), syncope (2), and nausea with or without vomiting (2).

Abnormal physical signs Nine patients exhibited dyspnoea, 9 were febrile (temperature over 37.5°C on at least 2 days), and 11 had a tachycardia (pulse rate over 90 a minute on at least 2 days). Two had soft systolic murmurs, 2 had enlarged lymph glands, and 1 developed right heart failure. The most striking sign, however, was a pericardial rub which was heard at some time during the course of the illness in 16 patients. In several cases, the rub was evanescent, and in 2 patients it was heard on a single occasion only.

Investigations Ten patients had an erythrocyte sedimentation rate of over 20 mm in the first hour at some time during the course of the illness, and six had a leucocyte count in excess of 12,000/mm³. Two patients had slight or moderate rises in aspartate aminotransferase without any rise in alanine aminotransferase; 63 international units (IU) in one case, and 26 IU in the other.

Chest x-ray In 2 patients, a large cardiac silhouette decreased significantly during recovery, suggesting the resolution of a pericardial effusion.

Electrocardiogram – see below.

Virology Four of the patients in this group showed evidence of recent infection with a virus of the Coxsackie group. Virus studies were negative in the remaining patients, one of whom showed characteristic features of systemic lupus erythematosus.

Relapse In several patients, symptoms showed a tendency to fluctuate in severity, sometimes strikingly, during the course of the illness; 7 patients suffered a distinct relapse between 3 months and 2 years after apparent complete recovery. The relapse was usually less severe than the initial illness, but in one case it was more severe. Two patients relapsed after 2 months, 1 after 3 months, 2 after 6 months, 1 after a year, and another after 2 years.

Group I: illustrative cases

Coxsackie B3 myopericarditis A 38-year-old steel erector complained of severe pain across the epigastrium followed two weeks later by pain across the upper chest which persisted for four weeks. The pain was aggravated by walking, and he was unable to take a deep breath. He also became tired easily.

On examination, there was evidence of severe right heart failure, and a pericardial rub was audible over the lower end of the sternum. The electrocardiogram showed extensive T wave flattening, with inversion in leads I, II, and V4. The initial ESR was 25 mm but fell to normal after a week. The heart failure subsided after two weeks, and the electrocardiogram became normal 4 months after the onset. Convalescent serum showed a high titre (1/1280) to Coxsackie B3 virus.

Pericarditis of unknown aetiology A 39-year-old works manager developed severe generalized headache, stiffness of the neck, and general malaise. Two days later he had a rise of temperature to 39°C accompanied by profuse sweating and shivering. On the following day he developed a gripping and burning pain in the centre of the sternum radiating down both arms to the elbows; this was aggravated by deep breathing and was so severe that it required morphia for its relief. The following day he had another similar attack.

On clinical examination, the only abnormality was a regular tachycardia of 110 a minute. No pericardial rub was heard at any time. Symptoms subsided rapidly, though fever persisted for 3 days. The maximal ESR was 52 mm on the fourth day, and the initial aspartate aminotransferase level was 63 IU (alanine aminotransferase 17 IU). All these fell to normal within 10 days.

The electrocardiogram taken on admission showed ST elevation in leads I, II, VL and V3, with reciprocal ST depression in VR. By the following day, the T wave was inverted in I, and 2 days later it was inverted in all the anterior leads and so remained until discharge from hospital 3 weeks later. Three months later, at outpatient review, the T waves had become positive and were merely somewhat low in leads II and V6. Seven months from the start of the illness the electrocardiogram had returned to normal.

Virological studies were negative, but it may be relevant that the patient's eldest daughter had developed mumps 10 days before the onset of her father's illness.

Group II: coronary mimics (24 patients)

Age and sex The mean age of patients in this group was higher than that in the series as a whole, and there was a greater preponderance of males (Fig. 3).

Presenting symptom Every patient in this group presented with severe central chest pain which raised in the mind of the family doctor a suspicion of acute myocardial infarction. Most were sent to hospital with this diagnosis; one doctor stating explicitly 'I am certain he has had an infarction'. The patients described their pain as crushing, gripping, tight, or vice-like; sometimes they volunteered that it was aggravated by effort, and in one case it was said to be relieved by trinitrin. No patient in this group stated that his pain was affected by respiration or movement, but on close questioning 9 admitted that it was aggravated both by breathing and

by a change of position or twisting movements; 3 more had noted an aggravation by change of posture and 2 by respiration. In 8 cases, the pain was so severe as to require morphia, pethidine, or dihydrocodeine.

Other symptoms These were relatively few and slight (Fig. 2). Nine patients complained of muscular pains which were separate from the central chest pain which formed the primary complaint; 4 experienced a syncopal attack, usually at the height of the pain; 4 complained of weakness, fatigue, or exhaustion, and a similar number of shivering or nausea. Other less frequent complaints were of coryza (4 patients), sore throat (3), cough (3), dyspnoea (3), headache (3), and sweating (2).

Abnormal physical signs Abnormal physical signs were likewise infrequent. Three patients exhibited dyspnoea, 4 were febrile, and 3 had a tachycardia. Six had a pericardial rub, another 3 a soft systolic murmur, and 1 a pleural effusion. Ten patients had no abnormal signs whatsoever.

Investigations Eight patients had a raised ESR at some time during the course of the illness, but none had a leucocytosis. Three had a slight rise of both aspartate and alanine aminotransferase (27/27, 40/32, 29/48 IU) and one an increase of alanine aminotransferase only (47 IU).

Electrocardiogram – see below.

Virology Two patients in this group showed evidence of recent infection with a virus of the Coxsackie group, one with an adenovirus, and another with brucellosis. Another patient was diagnosed as systemic lupus erythematosus. In the remaining patients, the nature of the illness remained uncertain.

Relapse Only one patient in this group suffered a relapse. She had 2 recrudescences of symptoms within 6 months of the original illness.

Group II: illustrative cases

Coronary mimic of unknown aetiology A 23-year-old long-stay patient in a mental hospital, previously physically fit, complained of sudden severe gripping central chest pain accompanied by profuse sweating and dyspnoea. The pain lasted 12 hours and was not affected by posture or respiration. The pulse was regular but very rapid (140 per minute) and the blood pressure was unrecordable. No pericardial rub was heard. The electrocardiogram showed flattened or diphasic waves in the anterior leads. The chest x-ray was normal. The aspartate aminotransferase was 40 I.U., and the alanine amino-

transferase 32 IU. Over the next 3 days, the tachycardia subsided and the blood pressure rose to 115/85 mmHg. The ESR remained normal throughout. The chest pain did not return, but the patient complained of being easily fatigued for 2 months. The electrocardiogram gradually returned to normal over a period of 4 months. Viral studies were negative.

Another coronary mimic of unknown aetiology A 36-year-old housewife complained of pain in the upper chest with slight radiation to the left shoulder on and off for 5 days. The pain was not induced by effort or affected by respiration, but was increased by twisting the neck, for example when reversing the car. Her mother had had a small myocardial infarct the previous year.

Clinical examination was essentially negative apart from slight tenderness to the right of the sternum. Five days later, the pain which had persisted mildly since the first examination suddenly became much more severe and was localized in the centre of the chest, radiating through to the back between the scapulae; morphia was required for its relief. The electrocardiogram showed slight ST depression proceeding to flattening of the T waves in leads II, VF, and V6. The first aspartate aminotransferase was 30 IU and five days later 27 IU.

Attacks of pain and syncope recurred over a period of two weeks, by the end of which time, the electrocardiogram and transaminases had returned to normal. Ten weeks later there was a relapse of pain and slight electrocardiographic abnormality lasting 2 weeks. Seven months from the onset, the patient was still experiencing a dull ache in the lower ribs especially when tired, though the electrocardiogram remained normal. One year from the onset the patient was well. No evidence of virus infection was obtained in this case.

Group III: relentless heart failure (3 patients)

Age and sex See Fig. 3.

Presenting symptom Each of the patients in this group presented with dyspnoea. One also complained of cough, another of nausea and exhaustion, and the third of slight praecordial pain unaffected by respiration, position, or movement. All showed signs of right and left heart failure associated with tachycardia, and the patient with the praecordial pain had a pericardial rub. None of these patients had fever, leucocytosis, or a raised ESR. One had a very slight rise in aspartate aminotransferase (23 IU). Two showed radiological evidence of cardiac enlargement, but in the third, the cardiac silhouette remained well within normal limits (cardiothoracic ratio 44%) up to the time of death. All 3 pursued a relentless downhill course, dying between 1 and 6 months after the onset of symptoms.

Electrocardiogram In each case, the abnormalities were remarkably slight. In the patient with pericarditis, the T waves were inverted; but in the other 2 cases, they were merely flat.

Necropsy This confirmed the diagnosis of acute myocarditis in each case, without revealing the nature of the disease.

Virology This was negative in all 3 cases.

Group III: illustrative cases

Acute carditis in a young man A 29-year-old engineer attended the outpatient clinic on account of increasing dyspnoea on effort followed by the appearance of oedema. Two years previously he had been off work for three months on account of an illness which was diagnosed as acute rheumatism.

On examination, the heart rhythm was regular, 90 a minute, and there was no evidence of cardiac enlargement or failure; the electrocardiogram, however, showed flattening of the T waves in the inferior and lateral leads. Two weeks later, the patient was admitted to hospital as an emergency with rapidly increasing oedema and breathlessness. On this occasion, raised jugular venous pressure was noted and the chest x-ray showed slight enlargement of the heart by comparison with the previous examination, though the cardiothoracic ratio was still only 44 per cent. The signs of heart failure subsided with intensive diuretic therapy, but reappeared whenever the therapy was reduced. One month later, the patient was admitted in acute pulmonary oedema and died.

Necropsy showed acute myocarditis without any clue as to its aetiology. All the valves were normal, and none of the histological stigmata of rheumatic disease was observed. Viral studies were negative.

Acute heart failure developing at end of pregnancy A 21-year-old woman was admitted to the maternity hospital at term with a 7-day history of increasing dyspnoea, and orthopnoea culminating in an attack of acute pulmonary oedema. On examination, she was severely dyspnoeic and grossly oedematous. The heart rhythm was regular, 160 a minute, and the blood pressure 120/80 mmHg. The chest x-ray showed moderate cardiac enlargement and bilateral pulmonary oedema. The electrocardiogram showed a pulmonary P wave, and flattening of the T waves in leads I, II, and VL, though not in the precordial leads.

On the day after admission, caesarean section was performed on account of placenta praevia. Cardiac arrest developed immediately after the operation and though the heart was restarted manually permanent arrest soon followed.

Necropsy showed diffuse myocarditis with disseminated microscopical foci of necrosis. Viral studies were negative.

Group IV: miscellaneous (14 patients)

Age and sex There was a preponderance of younger patients in this group (Fig. 3).

Presenting symptoms By contrast with the previous groups, these patients had a noncardiac presentation. In none was precordial pain a promi-

ent symptom, and none showed evidence of heart failure. The commonest symptoms (Fig. 2) were sweating or shivering (13 patients), muscular aching (9), headache (8), sore throat (7), pleurisy (5), and joint pains (3). One patient (Coxsackie B4 infection) presented with hemiplegia, and another (unknown aetiology) with haematemesis. Most patients had three or more presenting symptoms, the general picture frequently resembling influenza.

Abnormal physical signs Signs of infection were frequent in this group: 10 had tachycardia, 9 fever, and 9 dyspnoea; 6 had a pericardial rub, and 4 others a systolic murmur; 3 had enlarged lymph glands, 1 a pleural effusion, and 1 pneumonia.

Investigations Eleven patients had a raised ESR and 7 a leucocytosis. Two showed a rise in aspartate aminotransferase (over 125 IU and 32 IU, respectively). In none did the x-ray suggest pericardial effusion.

Electrocardiogram – see below.

Virology Three patients in this group showed evidence of recent Coxsackie infection, 2 showed evidence of influenza, 1 of glandular fever, 1 of adenovirus infection, and 1 of rheumatic fever.

Relapse Only one of the patients in this group relapsed – three weeks after discharge from hospital after the original illness.

Group IV: illustrative cases

Acute myocarditis associated with infectious mononucleosis A 24-year-old housewife developed a confluent erythematous maculopapular rash and severe oral and pharyngeal ulceration, followed by swollen salivary glands and tender cervical and axillary lymph nodes. One week later, she developed aching retrosternal pain and discomfort along the rib margins which was aggravated by coughing and deep breathing. The pain was severe and recurrent, and necessitated her admission 2 weeks after the onset of symptoms.

On examination, the patient looked very ill, and was febrile, with necrotic ulcers on tongue and palate, and tender enlarged salivary, cervical, and axillary glands. The pulse was regular, 120 a minute, and the blood pressure 120/80 mmHg. The liver was enlarged and tender, and the day after admission the patient became jaundiced. No pericardial rub was heard at any time. The ESR on admission was 24 mm, later rising to 45 mm. The electrocardiogram showed ST elevation in the lateral chest leads. The aspartate aminotransferase was over 125 units on admission, and the serum alkaline phosphatase 71 units. Atypical lymphocytes and glandular fever cells were seen in blood films. Over the following 2 weeks, symptoms subsided, the electrocardiogram and

TABLE 1 *Clinical picture correlated with infective agent*

Aetiology	Cases	No. with pericarditis	Presentation			
			I Acute pericarditis	II Coronary mimic	III Heart failure	IV Febrile and miscellaneous
Coxsackie B	9	8	4	2	0	3
Adenovirus	2	0	0	1	0	1
Brucellosis	1	0	0	1	0	0
Influenza A	2	1	0	0	0	2
Infectious mononucleosis	1	0	0	0	0	1
Rheumatic fever	1	0	0	0	0	1
Systemic lupus erythematosus	2	2	1	1	0	0
Unknown	42	31	14	19	3	6
Total	60	42	19	24	3	14

aminotransferase returned to normal, but the ESR and serum alkaline phosphatase remained high. One month later, all investigations were normal.

Acute myocarditis associated with adenovirus infection A 24-year-old teacher became vaguely unwell with tiredness, anorexia, aching discomfort behind the eyes, and stiffness of the neck, followed two days later by low backache and discomfort in the centre of the chest. The following day she developed stiffness and pain in several joints, particularly the ankles, knees, right shoulder, and fingers, accompanied by headache, photophobia, and rigors. On examination, the temperature was raised to 38°C, and the pulse rate was 110 a minute. The finger joints were swollen, red, and tender, the throat was inflamed, and there was a maculo-papulo-vesicular rash on the shins. No cardiac abnormality was detectable on auscultation, but the electrocardiogram showed generalized flattening of the T waves, with improvement, though not complete recovery, by the time of discharge 11 days after the onset. The aminotransferase levels remained within normal limits, and the highest ESR recorded was 22 mm. Complement-fixation tests were positive for adenovirus infection.

Correlation between infective agent and clinical picture

An infective agent was incriminated in only 15 of the 60 patients. No clear-cut correlation was noted between a specific virus and any particular clinical picture (Table 1). Two trends may, however, be noted; 8 of the 9 patients with Coxsackie infection had objective evidence of pericarditis; and 4 out of 6 patients with other virus infections presented with generalized rather than cardiac symptoms.

Electrocardiogram

The electrocardiogram was abnormal at some time in the course of the illness in every patient except one, who had a pericardial rub. In one patient – with rheumatic carditis – the only abnormality was transient prolongation of the PR interval.

Three types of QRST abnormality were encountered during the acute stage (Table 2); ST elevation (21 patients), ST/T depression (35 patients), and left bundle-branch block (2 patients). Abnormal Q

TABLE 2 *Correlation between electrocardiogram and clinical presentation*

	No. of patients	Clinical presentation				Electrocardiogram					
		I Peri- carditis	II Coronary mimic	III Heart failure	IV Miscel- laneous	ST elevation		ST/T depression		LBBB	Normal
						Major	Minor	Major	Minor		
<i>Pericarditis</i>											
Pericardial rub	30	16	7	1	6	13	3	6	5	2	1
Pericardial pain	12	3	8	0	1	5	0	4	3	0	0
<i>Myocarditis</i>	18	0	9	2	7	0	0	10	7	0	0
Totals	60	19	24	3	14	18	3	20	15	2	1

waves were not seen in any patient. ST elevation was classified as 'major' if over 1 mm in any lead except aVR and V₁ to 3 (18 patients), and 'minor' if 0.5 to 1.0 mm in these leads (3 patients). ST/T depression was classified as 'major' if the ST segment was depressed more than 0.5 mm or if the T wave was flat, diphasic, or inverted in any of the leads I, II, aVF, V₃ to 6 (20 patients), and 'minor' if the ST segment was depressed 0.25–0.5 mm or the T wave was less than one-tenth the height of the preceding R wave (Short, 1972) (15 patients).

ST elevation was only seen in patients in whom a pericardial rub was heard, or who had chest pain which was much increased by respiration. Out of 30 patients with a pericardial rub, 13 had major and 3 a minor degree of ST elevation; and out of 12 patients without a rub, but with pain much increased by respiration, 5 had major ST elevation. ST elevation was an early and transient manifestation of pericarditis, and only twice was it found more than one week after the onset of symptoms (Fig. 4). It was usually followed by ST/T depression in the second and third weeks and then by a gradual return to normal. Sometimes, however, ST elevation subsided without any recorded T wave abnormality; and in many patients, T wave abnormalities persisted for several months after clinical recovery.

In the 21 patients with signs or symptoms of pericarditis in whom ST elevation was not recorded, it is possible that the pattern was missed; though in 9 of the cases, the first electrocardiogram was recorded within 3 days of the onset of symptoms.

FIG. 4 Electrocardiogram in 42 patients with pericarditis related to time after onset.

ST/T depression with or without T wave inversion was characteristic of patients with myocarditis without pericarditis; but a similar pattern was seen in many of the patients with pericarditis. In the majority, complete recovery of the electrocardiogram took place within two months.

Complete left bundle-branch block In 2 patients with a pericardial rub, the first electrocardiogram showed left bundle-branch block, and in both the pattern persisted unchanged; in one case for 6 months and in the other for 5 years.

Discussion

During the first half of this century, with the steadily increasing recognition of coronary heart disease and the decline in severity of rheumatic fever, myocarditis and pericarditis went into eclipse; but during the past two decades, the frequency of both has been increasingly recognized. However, the pattern has changed; rheumatic fever and tuberculosis, the historic enemies of the myocardium and pericardium, now only account for a small number of cases in the more prosperous countries, and their place has been taken by the viruses, especially those of the Coxsackie B group, and other factors as yet unidentified. The present scene is one of confusion in classification and nomenclature, and of difficulty in diagnosis; and this report attempts to clarify the situation.

It may be thought that pericarditis and myocarditis should be considered separately. But a joint consideration is justified by the fact that both layers of the heart are frequently involved in the same disease process. Thus, patients presenting with pericarditis usually show evidence of myocardial involvement (Woodward *et al.*, 1967) and a significant proportion develop heart failure (Smith, 1970).

Aetiology

Ideally, a survey of acute myopericarditis should be based on aetiology; but this is not possible at the present time because in a majority of cases the aetiology is unknown. Thus Woodward *et al.* (1967) found evidence of a specific infection in only 23 of their 82 cases. Our success rate was similar with a probable cause identified in only 18 out of the 60 cases. It is possible that more intensive investigation would have yielded more frequent evidence of infection. The patients might have been screened for a wider range of potential pathogens; but the number of infective agents which have been incriminated in cases of acute myocarditis and pericarditis is great, and such a search would be laborious, expensive, and moreover purely academic, because there is at present no specific antiviral treatment available.

The fact that no infective agent can be incriminated in the majority of cases of myopericarditis has led to the suggestion that this condition may represent an autoimmune reaction to a variety of agents (Friedberg, 1966; Lewis, 1969). Robinson and Brighden (1968) were able to demonstrate anti-heart antibodies in 6 out of 15 patients with recurrent idiopathic pericarditis. It is, however, still uncertain whether such antibodies are the cause or the result of injury to the heart (Fowler, 1971).

At the present time, in the absence of any specific treatment, a correct aetiological diagnosis is unimportant; all that matters is the recognition that the heart has been involved and that the disease is inflammatory and not ischaemic.

Recognition of cardiac involvement – the four faces

It is important to recognize cardiac involvement in an acute illness, because, where this is present, patients should logically have more prolonged rest than would otherwise be indicated. Acute myopericarditis may present in four different ways – as pericarditis, as a coronary mimic with unexplained heart failure, or as a febrile influenza-like illness. Clues to the presence of heart disease may be provided by the history, clinical examination, and the electrocardiogram.

Severe central chest pain must always raise a strong suspicion of heart disease. If the pain is affected by respiration or posture, this is very suggestive of acute pericarditis; and this diagnosis may be confirmed by the presence of a pericardial rub, or by characteristic changes in serial electrocardiograms. If the pain is not affected by respiration or posture, the possibility of myocardial infarction will be suggested, and an electrocardiogram will be recorded and the appropriate serum enzymes measured.

On clinical examination, the features which suggest cardiac involvement are persistent tachycardia out of proportion to any fever that may be present, evidence of cardiac failure, and a pericardial rub; the latter is, however, frequently transient and may therefore be missed.

The electrocardiogram is usually of considerable help in the diagnosis of myopericarditis. In patients with pericarditis, it often shows ST elevation if the recording is made within the first few days. As the ST elevation subsides, the T waves usually become low, flat, or inverted, returning to normal over a period of weeks or months. There is, however, much variation (Spodick, 1971), and the ST elevation may disappear without the development of any T wave abnormality. In a considerable proportion of patients with pericarditis (almost 50% in this series)

the earliest abnormalities are ST/T depression or bundle-branch block; occasionally the electrocardiogram remains normal throughout. In patients with myocarditis without pericarditis, the electrocardiogram usually shows ST/T depression, but even in fatal cases there may be merely T wave flattening without inversion.

Differentiation between myopericarditis and coronary heart disease

The greatest problem in the diagnosis of myopericarditis is the differentiation from myocardial infarction. The severe praecordial pain, unaffected by respiration or posture, seen in some patients may closely mimic that of infarction – and a substantial proportion of these patients are men over 50 years of age. The suspicion of coronary disease may be supported by the finding of ST/T depression in the electrocardiogram similar to that found in some cases of early infarction (Short, 1970), and occasionally by a rise in the aspartate aminotransferase level. The differentiation between coronary disease and carditis may be very difficult, and can frequently be made only by repeated examination (Table 3). A history of recent infection such as coryza or diarrhoea is commoner in carditis than in infarction but this is not by itself decisive in an individual case. The presence of symptoms other than chest pain is an important point of distinction. In a patient with myocardial infarction, the chest pain (with or without radiation) is predominant, and the only other symptoms as a rule are nausea with or without vomiting, sweating, palpitation, and dyspnoea (Short and Stowers, 1972). A complaint of extraneous symptoms such as headache, shivering, or muscular pain unrelated to the site and radiation of the chest pain, or pain that flits from one area of the chest to another is strong evidence against myocardial infarction. The other important piece of evidence concerns the time relation of the chest pain. In myocardial infarction, the duration of the pain varies widely – from minutes to days – but it rarely, if ever, takes the form of brief ‘stabs’ lasting only a few seconds. Furthermore, there is, as a rule, a close relation between the duration of the pain and the extent of the electrocardiographic changes (Short and Stowers, 1972). In carditis, the pain is often too short to be ischaemic; or too long to be consistent with the relatively slight electrocardiographic abnormalities. A pericardial rub is seldom, if ever, found in myocardial infarction unless the infarct is transmural (Thadani *et al.*, 1971). Thus, the presence of a rub in association with an electrocardiogram showing only slight ST/T abnormalities is inconsistent with infarction but typical of myopericarditis. A rise of aspartate aminotransferase may be

TABLE 3 *Differentiation between acute myopericarditis and acute myocardial infarction*

	<i>Myopericarditis</i>	<i>Myocardial infarction</i>
<i>History</i>		
Respiratory or gastrointestinal infection within previous month	Common	Coincidental
Recent effort angina	Rare	Common
Pain aggravated by respiration or posture	Common	Rare
Headache, muscular pain, shivering	Common	Rare
<i>Examination</i>		
Pericardial rub	Common, appears early, without electrocardiographic evidence of extensive myocardial damage; often transient but may be persistent	Uncommon, appears later, invariably associated with extensive myocardial damage; usually transient
<i>Electrocardiogram</i>		
ST elevation – over 5 mm	Rare	Common
ST elevation – convex upward	Rare	Common
ST elevation – with reciprocal ST depression in standard leads	Rare	Common
T inversion over 7 mm	Rare	Common
Abnormal Q waves	Never	Common
<i>Serum transaminase rise</i>	Sometimes slight or moderate rise which may be persistent; alanine aminotransferase often as high as aspartate aminotransferase	Very common transient rise of aspartate aminotransferase without corresponding rise of alanine aminotransferase

found in both conditions; but in infarction the peak occurs 24 to 36 hours after the onset and declines rapidly, the alanine aminotransferase being low at the time when the aspartate aminotransferase is maximal. In myopericarditis, on the other hand, a transaminase rise is unusual, and if it does occur it tends to have a later peak, the rise persists longer, and often affects both transaminases.

The origin of the chest pain in myocarditis without pericardial involvement is uncertain. The fact that it is rarely if ever referred to the arms, the throat, the jaw, or the back between the scapulae, is an argument against an origin from the myocardium; and so is the fact that patients with identical pain sometimes show no electrocardiographic abnormality. It seems likely that in these patients the pain arises from skeletal muscle as in Bornholm disease or pleurodynia.

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