CURRENT SURVEY

Acute non-specific pericarditis

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Incidence

Acute non-specific pericarditis (acute benign pericarditis; acute idiopathic pericarditis) has been recognized for over 100 years (Christian, 1951). In 1942 Barnes & Burchell described fourteen cases of the condition and since then several series of cases have been published (Krook, 1954; Scherl, 1956; Swan, 1960; Martin, 1966; Logue & Wendkos, 1948).

Until recently Swan's (1960) series of fourteen patients was the largest collection of cases in this country. In 1966 Martin was able to collect most of his nineteen cases within 1 year in a 550-bed hospital. The disease is thus by no means rare and warrants greater attention than has previously been accorded it, despite its usually benign course.

Clinical features

Acute non-specific pericarditis can occur at any age but is most common in the third and fourth decades (Bradley, 1964). The sex incidence has been variously reported as equal (Bradley, 1964), M/F 3 : 1 (McGuire, Kotte & Helm, 1954) and M/F 8.5 : 1 (Martin, 1966). A history of an upper respiratory tract infection about 2 weeks before is common (McGuire *et al.*, 1954). The onset is almost always acute and pain the almost universal presenting symptom. The pain is usually severe and may be accompanied by shock and hypotension (Martin, 1966). It may be sharp and stabbing and aggravated by respiration, or dull and aching. It is unrelated to exertion though may be prolonged and aggravated by the patient's failure to rest. The pain is very often aggravated by rotating the trunk (McGuire *et al.*, 1954), by bending forward at the waist (Bradley, 1964), or in extreme recumbency and lying on the left side (Friedberg, 1966). The site of the pain is frequently retrosternal and if also dull and pressing may result in a wrong diagnosis of myocardial infarction. It may radiate to one or both shoulders and arms, to the

neck, to either flank and frequently through to the back. Occasionally pain is experienced on swallowing (McGuire *et al.*, 1954) and this was the presenting symptom in one of our own patients. Mild attacks of premonitory chest pain may occur up to 4 weeks before the main onset of symptoms (Martin, 1966). Malaise is very common, and is often severe and accompanied by listlessness and depression. The latter symptom is especially common in patients suffering multiple relapses or prolonged attacks, but is only partly related to the length of the illness and fluctuates markedly from day to day with the patient's general condition.

Tachycardia occurs in almost every patient at some stage of the illness. It is usually sinus in origin and may outlast all other symptoms and signs by several months (Dressler, 1966). James (1962) has shown that because of the close proximity of the sinus node to the epicardium it is usually involved in pericarditis. Sinus tachycardia in pericarditis thus indicates irritation of the sinus node. Other dysrhythmias, e.g. atrial fibrillation (Soffer, 1960), supraventricular and ventricular ectopics and tachycardia, and atrial flutter may occur. Pyrexia of more than 100°F is present in most patients at the onset of the illness but a few patients remain afebrile throughout.

A pericardial friction rub is probably present in most patients at some stage of the illness. However, it may be extremely transitory and may disappear completely within a matter of hours or be replaced by a pericardial click. Auscultation of the heart several times a day during the acute stages is, therefore, advisable to detect it. The behaviour of the pericardial rub is independent of the intensity of pain. The effect of respiration on the intensity of the pericardial rub is very variable and occasionally the patient's position is crucial, the rub only being heard, for example, when the patient bends forward (Bradley, 1964). The heart sounds are otherwise normal apart from being dulled at times by pericardial effusion.

The occurrence of pericardial effusion in acute non-specific pericarditis is extremely variable, the

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reported incidence ranging from 20% (Martin, 1966) to 73% (Bradley, 1964). Pericardial tamponade should be suspected if there is marked elevation of the jugular venous pressure with a systolic descent in the wave form (Gibson, 1960) accompanied by pulsus paradoxus. The presence of a third heart sound does not indicate pericardial tamponade or constriction but is a sign of underlying myocardial failure (Gibson, 1960). A positive Kussmaul's sign (elevation of the mean jugular venous pressure on inspiration) is likewise misleading and can occur in any situation producing marked elevation of the jugular venous pressure, notably cardiac failure. Pleural effusion and/or pneumonitis occur not infrequently and produce the corresponding physical signs in the lungs.

Special investigations

Since the diagnosis of acute non-specific pericarditis is largely one of exclusion, special tests are as much directed at ruling out other causes of pericarditis, e.g. bacterial infection, including tuberculosis; collagen disease, notably systemic lupus erythematosus and peri-arteritis nodosa; and infectious mononucleosis, as in confirming the diagnosis.

Chest X-ray may be completely normal. Its principal value is to rule out tuberculous or malignant foci, or other causes of pericarditis which could result from direct spread and to establish the presence and follow the course of significant pericardial effusions. Bradley (1964) points out that 250 ml of fluid may be present in the pericardium in the adult before the heart appears enlarged radiologically, and suggests a lateral film with the patient leaning forward to show fluid in the pericardium below and in front of the heart shadow. The most significant radiological finding is a sudden change in heart size in the absence of clinical evidence of heart failure. Rapid increase in heart size associated with clinical evidence of a raised jugular venous pressure with a systolic descent in its wave form and pulsus paradoxus should suggest the development of cardiac tamponade. Conversely, progressive reduction in heart size without resolution of these clinical signs should suggest that the patient may be developing pericardial constriction. Pleural effusions are present in two-thirds of the patients with pericardial effusions (Bradley, 1964).

Fluoroscopy is of limited value but may show some diminution in the pulsation of the heart in pericardial effusion or constriction.

Cardiac catheterization and angiography are seldom justified except where pericardial constriction is suspected, when injection of contrast medium into right atrium with cine-angiography

may demonstrate pericardial thickening and loss of mobility of the right heart border. At the same time the right atrial pressure wave form may show the systolic descent characteristic of pericardial tamponade or constriction (Gibson, 1960).

Pericardiocentesis should be performed as a therapeutic measure where cardiac tamponade is suspected and as a means of obtaining fluid for bacteriological, virological and cytological study where the diagnosis is in doubt. The pericardial fluid may be serous or, especially when anticoagulants have been given for a mistaken diagnosis of myocardial infarction, blood stained (Liu & Garcia, 1965).

The *electrocardiogram* is frequently unrewarding in acute non-specific pericarditis. It may range from normal to the type of tracing suspicious of acute or chronic coronary artery disease (Bradley, 1964). In one of our patients whose illness lasted 4 months the only electrocardiographic abnormality was intermittent mild ST segment depression in several leads coinciding with clinical exacerbations of her illness. The classical pattern in pericarditis of raised ST segment, retaining its natural concavity, returning within a few days to the isopotential level or becoming depressed with subsequent flattening or inversion of the T wave, was first described by Porte & Pardee (1929). The variations of this pattern in acute non-specific pericarditis have been comprehensively reviewed by Soffer (1960).

Blood. Anaemia, if present at all, is never more than mild. The erythrocyte sedimentation rate is usually moderately elevated in the early stages, generally between 20 and 30 mm/hr, Westergren (Martin, 1966). However, as in our patient who had been ill for 8 months, the ESR may be normal throughout. A return to normal from a previously high reading must not be used as an indication for ambulation of the patient, especially if steroids are being used (Bradley, 1964). Leucocytosis with absolute neutrophilia is present in about half the patients on admission to hospital (Johnson *et al.*, 1961). Most of the remainder have a normal total white cell count with or without some relative neutrophilia (Bradley, 1964). In two of our own patients and in one of Martin's (1966), neutropaenia was observed. Serum transaminases are universally normal in uncomplicated acute non-specific pericarditis (Bradley, 1964) and are a useful means of distinguishing between post-myocardial infarction syndrome and an extension of the original myocardial infarction.

Virus studies. A search for evidence of recent virus infection particularly with the Coxsackie B group should be made in every suspected case of acute non-specific pericarditis. The virus may be

cultured from faeces or from throat washings, and its association with the current illness confirmed by the demonstration of a rising titre in the appropriate neutralization tests on the patient's blood. In the event of failure to grow the virus, examination of paired sera is seldom practicable due to the multiplicity of strains of the Coxsackie virus.

Differential diagnosis

Other forms of pericarditis. In acute *bacterial pericarditis* the patient is usually much more severely ill than with acute non-specific pericarditis. The patient's history or physical examination may reveal the source of such an infection and cultures of blood and purulent pericardial fluid will usually disclose the specific cause.

Tuberculous pericarditis is much more insidious in onset. Pericardial effusion is almost always present and pain is uncommon. Pericardiocentesis should be performed for culture and guinea-pig inoculation of the pericardial fluid.

Spirochaetal, fungal and parasitic pericarditis are all rare in this country.

Malignant pericarditis is seldom of such acute onset as acute non-specific pericarditis. It results from direct spread of the process from the surrounding structures. The site of origin may be revealed by chest X-ray. Blood-stained pericardial effusion is usual and cytological examination of this will often reveal the true aetiology.

Post-traumatic and post-operative pericarditis can usually be eliminated by their association with recent operation or trauma. However, the post-pericardiotomy syndrome may occur 3 months or more after the operation, when the distinction becomes more difficult. As most authorities now regard acute non-specific pericarditis, post-pericardiotomy syndrome and post-myocardial infarction syndrome as representing the same disease process, whose treatment is the same in each case, the distinction is largely academic.

Rheumatic pericarditis is frequently associated with other serious rheumatic manifestations, in particular carditis and cardiac failure. The patient is usually much more seriously ill. The ESR is usually higher and the anti-streptolysin titre raised. Prolongation of the PR interval in the electrocardiogram is common in rheumatic pericarditis but is not seen in acute non-specific pericarditis.

Collagen diseases, in particular systemic lupus erythematosus, may exhibit pericarditis as part of a much more generalized disease process. Abnormal findings in other systems, e.g. hepatic or renal involvement, the finding of LE cells in the blood, and muscle biopsy will help to reveal the true cause of the pericarditis.

Myocardial infarction. The distinction between this and uncomplicated acute non-specific pericarditis is usually not difficult provided adequate attention is paid to the history. A history of pain related to breathing, sudden changes of posture and swallowing should militate strongly against a diagnosis of myocardial infarction. The pericardial friction rub of either condition may be evanescent. That of myocardial infarction is usually so while the rub of pericarditis usually persists several days. The second sound occasionally shows reversed splitting (i.e. splitting on expiration instead of inspiration) in acute coronary insufficiency or myocardial infarction but is always normal in pericarditis. The electrocardiogram will usually differentiate between the two conditions. The QRS complex is never affected in pericarditis whereas conduction defects are not uncommon with infarction. The distinction between myocardial infarction and post-myocardial infarction pericarditis is more difficult as the fever, raised ESR and leucocytosis of the infarction may still be present at the time when the pericarditis develops. The changing T waves and ST segments of a healing infarct may mask those of pericarditis. Pain of different character from the original infarct and pericardial in quality occurring 1 or more weeks after the infarction favours a diagnosis of post-myocardial infarction syndrome (Dressler, 1959a).

Aetiology

The cause of acute non-specific pericarditis remains unknown. Its association with Bornholm disease was described by Bing in 1933. Since 1957, when the first cases of pericarditis associated with Group B Coxsackie virus infections were described (Fletcher & Brennan, 1957; Weinstein, 1957), there have been numerous reports strengthening the association between infections with this virus and pericarditis (Smith, 1966). However, association does not necessarily mean direct causation and it is difficult to explain the 2 weeks' delay frequently noted between the development of the infection and the onset of pericarditis on the basis of direct infection of the heart and pericardium with the virus. Furthermore, an identical clinical picture of acute non-specific pericarditis can be seen following other infections such as Reiter's disease (Csonka & Oates, 1957), infectious mononucleosis (Gardner, 1959) and lymphogranuloma venereum (Sheldon *et al.*, 1948). Likewise in pericarditis following heart operations (Engle & Ito, 1961); following myocardial infarction (Dressler, 1959a); gunshot wounds to the heart (Wood, 1956); following traumatic haemopericardium (Tabatznik & Isaacs, 1961); as a result of drug therapy (Costa, Holland & Pickren, 1961; Shafar,

1965) and with penicillin hypersensitivity (Schoenwetter & Silber, 1965), the clinical features are the same. This suggests that an autoimmunity reaction rather than direct causation by all the various agents may be responsible. Anti-heart antibodies have been found in the post-pericardiotomy and post-myocardial infarction syndromes (van der Geld, 1964) and in one of our patients with an 8-month history of smouldering non-specific pericarditis the titre of anti-nuclear factor rose to 1 : 320 after being negative on two occasions 8 months previously. This patient also gave a previous history of recurrent attacks of the same symptoms over the previous 7 years. A similar course has been described in many patients (Swan, 1960 ; Dressler, 1962) and this time interval renders purely viral causation unlikely.

Treatment

The epicardium is always involved to a greater or lesser degree in pericarditis and it is this involvement which is responsible for the ECG changes. Occasionally the myocarditis may be greater than the pericarditis (Smith, 1966). Because of this, and because complete bed rest is the most important measure in minimizing the degree and duration of the acute attack (Bradley, 1964), the patient should be kept in bed for at least a few days after pain, fever and the pericardial rub have subsided, and convalescence should then be gradual. Simple analgesics such as aspirin or paracetamol may be sufficient to treat the pain of the moderate attack but more severe attacks may require methadone, dextromoramide, pethidine or even morphine for relief. Especially in more prolonged attacks the patient's morale needs boosting at every opportunity, and suitable mood-elevating drugs may be necessary.

The administration of corticosteroids is still a matter of considerable controversy. In many patients, their administration results in a dramatic relief of symptoms and marked general improvement in the patient's condition. However, there is as yet no good evidence that hormonal therapy in addition to suppressing the toxic and inflammatory reactions does anything to eliminate the cause or in any way influence the natural history of the disease (Dressler, 1962). In one patient (Dressler, 1959b) flare-ups of pericarditis, pleurisy and pneumonitis were observed after 1 and 2 years, respectively, of continuous steroid therapy, on each occasion on attempting to withdraw the drug. North & Jamplis (1962) describe a 23-year-old housewife who developed a severe relapse while on 40 mg of prednisolone per day. One of our own patients, a woman of 31, also suffered a relapse while on the same dose. For this reason we

feel that, until further research establishes which cases are likely to benefit from steroid therapy, the view of the *British Medical Journal* (1965) that 'there need be no hesitation in giving these agents' is not justified. If steroids are used the initial dose should be high (40–60 mg of prednisolone per day) and reduction of the dose must be made gradually to avoid precipitating a relapse.

Patients with pericardial effusion may require diuretics and where myocarditis predominates digitalization may be necessary. The treatment of cardiac tamponade is immediate pericardiocentesis and aspiration of as much of the fluid as is possible, followed if necessary by surgical drainage of the pericardium if aspiration affords inadequate or too short-lived relief. We prefer the apical approach rather than the xiphisternal route as the former is less likely to result in damage to the heart or in confusion due to aspiration of blood from the right atrium rather than from the pericardial space.

Pericardiectomy is the only effective treatment once pericardial constriction has occurred. In patients with recurrent attacks of acute non-specific pericarditis sufficiently severe and protracted to result in chronic invalidism, pericardiectomy has brought complete relief to the majority (Zinsser *et al.*, 1959). More recently, Goldfarb *et al.* (1966) have described the persistence of pericardial pain after pericardiectomy. Such radical treatment should therefore be reserved for patients with pericardial constriction or recurrent large pericardial effusions and only undertaken as a last resort for the relief of symptoms.

Prognosis

The usual course of acute non-specific pericarditis is complete recovery from the initial attack in between 2 weeks and 3 months, the average duration being 6–8 weeks. However, 20% or more of patients suffer one or more relapses (Wood, 1956) and Swan (1960) described a patient with seventeen attacks in 16 years. Usually the patient finally recovers completely, but rarely the disease progresses to constrictive pericarditis (Krook, 1954 ; Rabiner *et al.*, 1954). Pericardial constriction may develop as quickly as 4 weeks after the onset of the acute attack (Caddell, Friedman & Johnson, 1960 ; Gibbons, Goldbloom & Dobell, 1965).

The retention of the term 'benign' for a condition which has been responsible for twelve reported deaths (Liu & Garcia, 1965) and which has been followed by constrictive pericarditis in approximately twenty-five patients (Krook, 1954 ; Gibbons *et al.*, 1965), is perhaps inappropriate. Of the twelve reported deaths, five were patients with

no associated heart disease who died of cardiac tamponade. Three of these patients had been given anticoagulant therapy. These three, and two other patients in the series who were also on anticoagulant therapy, all had sanguineous pericardial effusions. Six of the twelve patients had associated cardiac disease. The inference to be drawn from Liu & Garcia's (1965) review of fatal cases is that accurate diagnosis of the condition, prompt recognition and treatment of cardiac tamponade and the withholding of anticoagulant therapy from any patient in whom there is a suspicion of pericarditis would render a fatal outcome extremely unlikely in acute non-specific pericarditis, except where this condition is superimposed on pre-existing heart disease.

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