Polyarteritis nodosa in the adult

Report of a case with repeated myocardial infarction and a review of cardiac involvement

J. Z. PRZYBOJEWSKI

Summary

A young Coloured man with a history of acute transmural anteroseptal and anterolateral myocardial infarction presented with angina pectoris. Skeletal muscle biopsy showed unequivocal evidence of polyarteritis nodosa. Complete cardiac catheterization, left ventricular cine angiography, and selective coronary arteriography demonstrated a large aneurysm involving the apex and the left ventricular free wall. Diffuse aneurysmal dilatation of the right coronary artery was noted, as well as very severe obstructive lesions of the proximal left anterior descending and left circumflex coronary arteries. Five days after cardiac catheterization the patient suffered an acute transmural inferior myocardial infarction, complicated by acute pericarditis and complete heart block, which necessitated insertion of a pacemaker. This was soon followed by acute perforation of a peptic ulcer (documented at laparotomy), after which the patient died.

As far as the author can ascertain, this is the first adult with polyarteritis nodosa (PAN) who underwent cardiac catheterization and selective coronary arteriography. The literature on cardiac involvement in the adult with PAN is reviewed.

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Clinical presentation

A 29-year-old Coloured man presented with a 2-month history of frequent episodes of stabbing pain in the left chest, unrelated to effort and respiration. There was no history of cough or haemoptysis, and he was not dyspnoeic but had dyspepsia. A barium meal revealed Ménétrier's disease, but failed to identify any other lesion. A resting ECG taken 2 months before his admission to the Intensive Coronary Care Unit of Tygerberg Hospital revealed evidence of an old transmural anteroseptal and anterolateral myocardial infarction. There were also nonspecific ST-T-wave changes in the inferior leads (Fig. 1).

On examination he was found to be in good general condition, with a normal radial pulse, all peripheral pulses easily palpable and equal, and no evidence of radiofemoral delay. The jugular venous pressure was not elevated and the blood pressure was 130/80 mmHg. There was no ventricular enlargement. The apex beat was normal, as were the cardiac sounds, with no murmurs audible. Examination of the remaining systems revealed no abnormality.

Cardiac Clinic, Tygerberg Hospital, and Department of Internal Medicine, University of Stellenbosch, Parowvallei, CP
J. Z. PRZYBOJEWSKI, M.B. CH.B., F.C.P.(S.A.)

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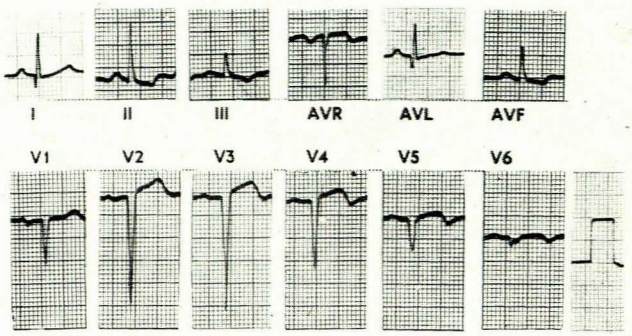

Fig. 1. Resting ECG showing evidence of an old transmural anteroseptal and anterolateral myocardial infarction.

The resting ECG was unchanged from that taken 2 months previously (Fig. 1). The chest radiograph indicated borderline left ventricular cardiomegaly with a suggestion of left ventricular aneurysm formation. The lung fields appeared normal.

Side-room investigations showed a normal urine, a haemoglobin concentration of 8 g/dl, a haematocrit of 27% and an ESR of 37 mm/h. The white blood cell count was elevated at 11 300/μl with a slight polymorphonucleocytosis and no eosinophilia. Renal and liver function was normal. Tests for rheumatoid factor, antinuclear factor, and lupus erythematosus cells were all negative. Serological tests (Wassermann reaction, VDRL and rapid plasma reagin) were also negative. A fasting lipogram and a glucose tolerance test were both normal. Acute myocardial infarction and pulmonary embolism were excluded by relevant investigations.

In view of the ECG evidence of previous myocardial infarction, it was decided to perform cardiac catheterization and

TABLE I. INTRACARDIAC PRESSURES

Catheter position	Pressure (mmHg)	Comment
Right atrium	**'a' wave 5, 'v' wave 3, mean 4**	**Normal pressures**
Right ventricle	**21/0-4**	**Normal**
Main pulmonary artery	**21/6, mean 10**	**Normal**
Ascending aorta	**108/74, mean 89**	**Normal pressures**
Left ventricle	**111/0-4**	**Normal**
dp/dt (mm/s)	**1377**	
Pulmonary capillary wedge	**'a' wave 4, 'v' wave 5, mean 4**	**Normal pressures, no mitral stenosis**

selective coronary arteriography in order to make a definitive diagnosis.

Cardiac catheterization was performed using the standard percutaneous Seldinger technique via the right femoral artery and vein. A 7F pigtail and Goodale-Lubin catheter was used to measure intracardiac pressures on the left and right sides, as well as oxygen saturations in the central aorta and main pulmonary artery (Tables I and II). Intracardiac pressures were within normal limits, but the cardiac output was somewhat reduced and the pulmonary vascular resistance raised.

Left ventricular cine angiography (right anterior oblique view) demonstrated a large aneurysm involving the left ventricular apex and free wall (Fig. 2) but no evidence of mitral insufficiency. Aortic cine angiography (left anterior oblique view) showed a normal aortic valve and arch.

Selective coronary arteriography using 7F 5 cm Judkins catheters showed a dominant right coronary artery which was diffusely aneurysmal but without any obstructive lesions (Fig. 3). The left coronary displayed an obstructive lesion in the left circumflex branch and a similar lesion in the left anterior descending artery just distal to its first diagonal branch (Fig. 4). The procedure was completed without complication.

TABLE II. HAEMODYNAMIC CALCULATIONS

Parameters	Results
Oxygen consumption (ml/min)	**180**
Arteriovenous O_2 difference (vol %)	**5,3**
Cardiac output (Fick) (l/min)	**3,4**
Cardiac index (Fick) (l/min/m²)	**1,9**
Pulmonary vascular resistance (U)	**2,6**
Index (U/m²)	**3,1**
Systemic vascular resistance (U)	**26,1**
Index (U/m²)	**44,7**
Resistance ratio (pulmonary/systemic) (%)	**10**
Stroke volume (ml/beat)	**39**

As the cause of the coronary artery lesions was thought to be some form of coronary arteritis, most likely from a collagen

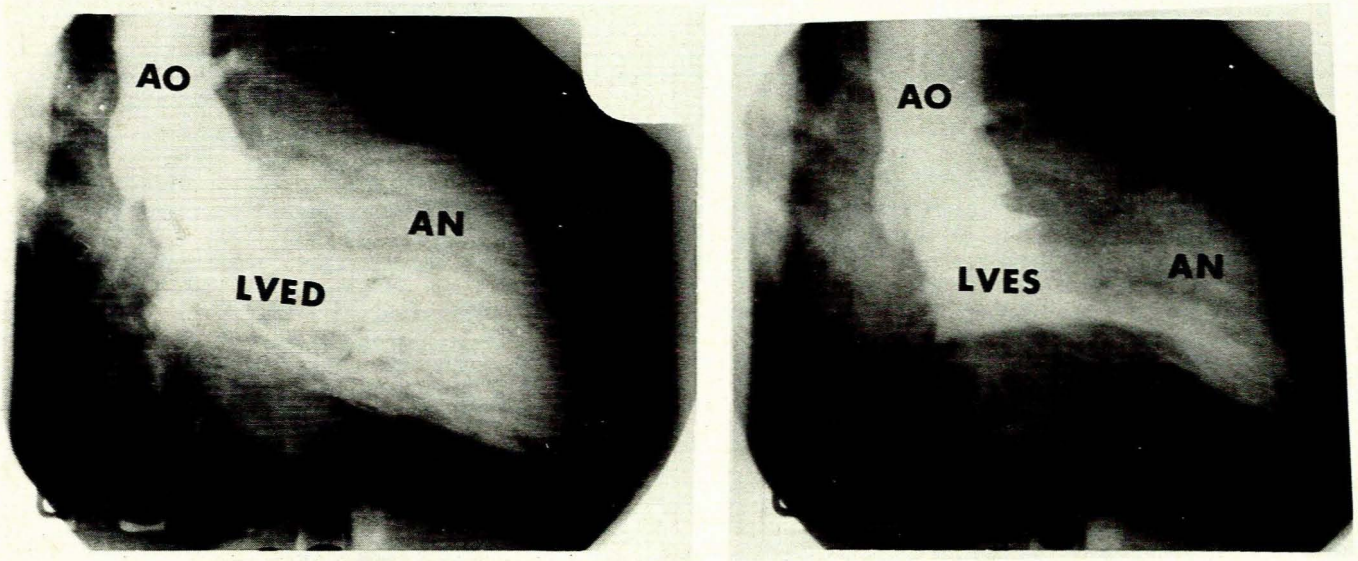

Fig. 2. Left ventricular cine angiograms (right anterior oblique projection) showing a large aneurysm involving the left ventricular apex and anterolateral segment (AN = aneurysm; AO = ascending aorta; LVED = left ventricle in end-diastole; LVES = left ventricle in end-systole).

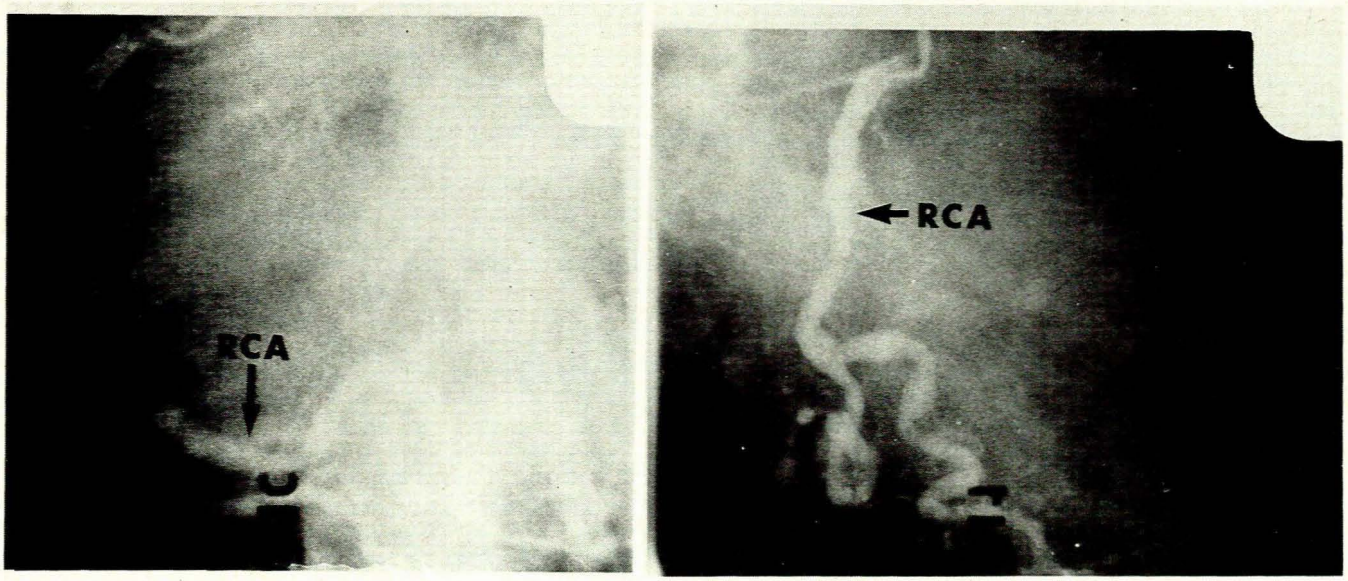

Fig. 3. Selective coronary arteriograms of the right coronary artery (RCA) in (*left*) the left anterior oblique and (*right*) the right anterior oblique projections. Diffuse aneurysmal dilatation of the RCA is seen.

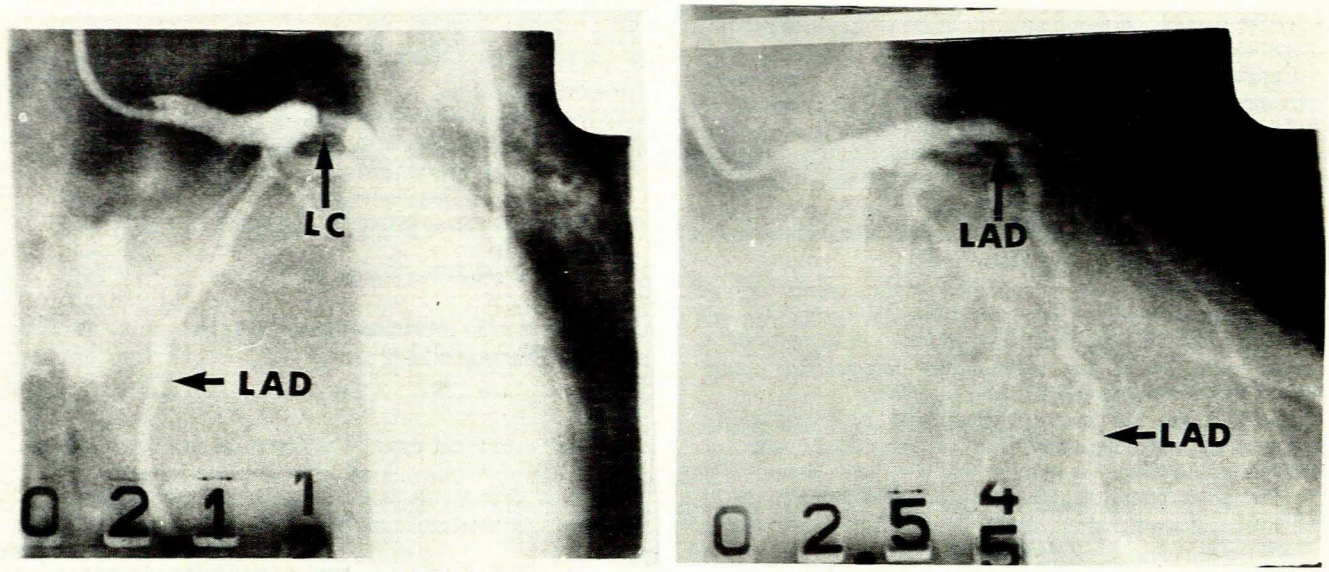

Fig. 4. Selective coronary arteriograms of the left coronary artery in (*left*) the left anterior oblique and (*right*) the right anterior oblique views. Subtotal (90%) obstructive lesions (*arrowed*) of the proximal portions of the left anterior descending (LAD) branch and the left circumflex (LC) artery are seen. The distal parts of these vessels appear normal.

disease or tuberculosis, the patient was given full antituberculosis therapy as well as high doses of oral steroids.

A muscle specimen from the thigh was then obtained in the hope of establishing a possible diagnosis of polyarteritis nodosa; it showed the features of 'fibrinoid necrosis' (hyaline necrosis) affecting connective tissue as well as blood vessels in the muscle epimysium and adjacent fascia (Fig. 5). One of the large vessels was thrombosed. The inflammatory process also extended into the muscle to involve the intrafascicular arterioles with possible resultant myopathic changes which included focal muscle cell necrosis. The inflammatory infiltrate consisted mainly of lymphocytes, but many polymorphs were also evident. These features are characteristic of a collagen vascular disease, the most likely being polyarteritis nodosa (PAN).

Some 5 days after the cardiac catheterization the patient complained of severe precordial pain. A resting ECG (Fig. 6) showed the presence of an acute transmural inferior myocardial infarction; this was corroborated by serial serum enzyme studies. Soon afterwards the patient went into third-degree atrioventricular heart block which necessitated the insertion of a temporary transvenous pacemaker. The following day he complained of severe epigastric pain unrelieved by antacids and antispasmodics. At the same time a loud pericardial friction rub was detected and the steroid therapy was discontinued. Because the abdominal symptoms worsened and melaena appeared, the patient was subjected to laparotomy, at which a perforated peptic ulcer was repaired. On the 2nd postoperative day the patient suddenly collapsed and could not be resuscitated. Permission to conduct a postmortem examination was refused.

Discussion

Kussmaul and Maier first introduced the term 'periarteritis nodosa' in 1866. The vascular lesions are basically characterized by an inflammatory reaction and fibrinoid necrosis. The term 'necrotizing angiitis'[1] has been considered more appropriate in describing the pathological lesion, in that the aetiological causes are more diffuse and because both venous and arterial vessels of any size, anywhere in the body, may be involved. Initially, it was believed that there was a predilection for involvement at sites of branching of medium-size arteries in splanchnic areas, with formation of small aneurysms in these regions. Apart from periarteritis nodosa, the other distinct types of 'necrotizing angiitis' are hypersensitivity angiitis, rheumatic arteritis, allergic granulomatous angiitis and temporal arteritis. Conditions such as scleroderma and disseminated lupus erythematosus demonstrate fibrinoid necrosis in vessel walls and elsewhere, but there is usually little or no inflammatory reaction related to these vessel walls.

PAN often involves the heart and the manifestation of congestive cardiac failure is considered to be the second most frequent cause of death.[2] Holsinger *et al.*,[3] in a review of 66 autopsy cases, documented myocardial infarction in 62%, coronary arteritis in 62%, and arrhythmias in 9%.

Pathology

Coronary artery involvement

It is generally accepted that the coronary vessels are second only to renal vessel involvement in PAN.[4] Thrombosis, aneurysms, and arteritis of the coronary vessels are complications of the disease. Coronary artery aneurysms were among the features initially documented.[5] In the 66 patients documented by Holsinger *et al.*[3] coronary arteritis was noted in 41 cases (62%). Approximately 60% had involvement of the large coronary arteries, i.e. the right coronary, left anterior descending and left circumflex coronary arteries, and both acute and chronic forms of arteritis were represented. The small intramural (intramyocardial) coronary arteries, as well as small arterioles in the adventitia of the large coronary arteries, were affected in some 40% of cases.

Griffith and Vural[6] analysed 17 cases of proven PAN at autopsy. Of these, 7 cases showed involvement of the heart. In 5 cases there were lesions in the large coronary vessels, and in 2 involvement of the intramyocardial coronary arteries. Some showed fibrosis and round-cell infiltration around the coronary vessels.

The present author could not find any cases of PAN in adults with antemortem selective coronary arteriography, although this investigation has been reported frequently in patients with infantile PAN in whom coronary artery aneurysms were detected,[7,8] as well as the mucocutaneous lymph node syndrome,[9] otherwise termed Kawasaki disease.[10,11] Coronary aneurysms in adults with PAN are therefore usually first documented at autopsy. Diaz-Rivera and Müller[12] reported on a

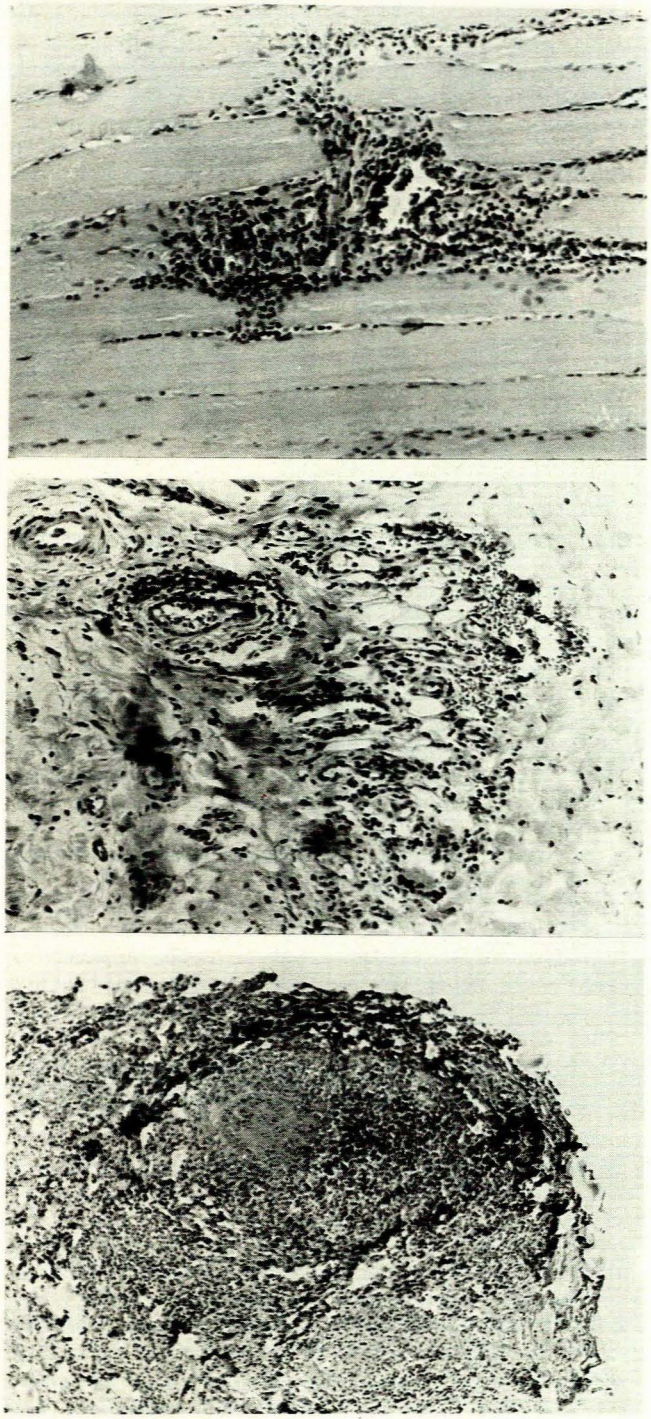

Fig. 5. Skeletal muscle specimen showing features of 'fibrinoid (hyaline) necrosis', an inflammatory infiltrate of lymphocytes and polymorphs, and a large thrombosed vessel, in keeping with PAN.

death from a haemopericardium secondary to rupture of a coronary artery aneurysm. On account of this report, Leonhardt *et al.*[13] considered it too dangerous to undertake coronary arteriography in their patient with PAN. In the present case this investigation was undertaken without any complication and defined the presence of diffuse aneurysmal dilatation of the right coronary artery, as well as very severe obstructive lesions of the proximal left anterior descending branch of the left coronary artery and left circumflex coronary artery.

The adult form of PAN is also similar to the childhood form in that the epicardial and/or intramural coronary arteries are

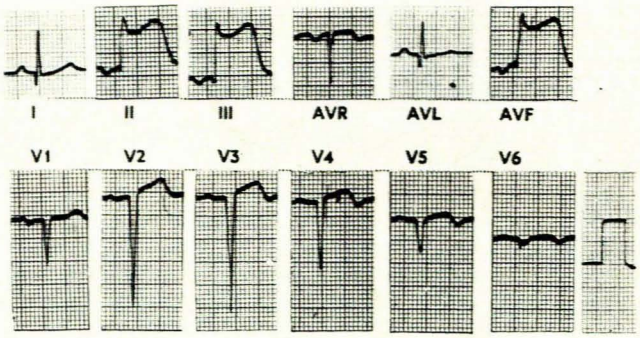

Fig. 6. Resting ECG illustrating an acute transmural inferior myocardial infarction, as well as an old transmural anteroseptal and anterolateral myocardial infarction.

involved, as well as many other arteries; however, in the infantile form of PAN there is a predilection for the coronary arteries alone and it tends to be more fulminating.

Myocardial involvement

Of 66 autopsy cases described by Holsinger *et al.*[3] 41 were found to have myocardial infarctions. Most had histological evidence of coronary arteritis, and some had clear-cut coronary artery occlusion related to the site of myocardial infarction. However, it is interesting to note that 5 of the 41 cases had no evidence of coexistent coronary arteritis, although there was demonstrable minimal coronary atherosclerosis thought to be insufficient to cause haemodynamic abnormality. In these latter there were small, scattered areas of infarction usually not detectable on macroscopic examination, and the authors suggested that small-vessel coronary arteritis was responsible. Severe coronary atherosclerosis was noted in only 4 of the 41 cases of myocardial infarction.

Holland[14] described an interesting case of a 46-year-old woman who suffered a silent acute anterior myocardial infarction complicated by severe left ventricular failure. This patient also had severe peripheral gangrene and was initially misdiagnosed as having systemic lupus erythematosus.

Griffith and Vural,[6] in their series of 17 postmortem studies, found 3 examples of anterior myocardial infarction and 3 others of diffuse myocardial fibrosis, usually related to epicardial coronary artery involvement.

Nachman[15] described a 34-year-old man with a silent anterolateral myocardial infarction after steroid therapy, and postulated rapid and extensive healing of coronary arteritis which had progressed to reparative fibrosis and obliteration of the coronary arterial lumen and subsequent infarction. Two similar cases were reported by Baggenstoss *et al.*[16]

In the present case the lesions in the left coronary artery, demonstrated angiographically, could be related to the initial pre-admission ECG showing transmural anteroseptal and anterolateral myocardial infarction, which was in turn delineated by left ventricular cine angiography. The preterminal acute transmural inferior myocardial infarction seen on the ECG was not surprising considering the angiographic finding of a diffusely aneurysmal right coronary artery. Although no postmortem examination was allowed, it can be safely assumed that there was extensive underlying coronary arteritis secondary to PAN, as established by the muscle biopsy.

Holsinger *et al.*[3] noted myocardial hypertrophy in 64% of their autopsy series. The great majority of these patients had had previous clinical systemic hypertension which probably accounted for the myocardial findings. Other workers[6] showed that hypertension was always associated with glomerulonephritis, which was in turn associated with left ventricular

hypertrophy. Myocarditis was documented in 2 of the 66 autopsy cases of Holsinger *et al.*[3] These workers thought that this was of minimal clinical importance, since areas affected by this inflammation were sparse.

Acute pericarditis

In the series of Holsinger *et al.*[3] 33% of the patients had acute fibrinous pericarditis. Uraemia was thought to be the cause in nearly half of these cases; only 1 of the 10 patients who were not uraemic did not have an acute myocardial infarction. Only one of the myocardial infarctions was large and transmural. Three of the 6 patients with pericardial friction rubs had uraemia, but only 2 of these had acute fibrinous pericarditis at autopsy. None of the patients had any evidence of pericardial effusion. In our case the pericardial friction rub appeared fairly acutely after the transmural inferior myocardial infarction, and was thus probably secondary to this since the patient was not uraemic.

Griffith and Vural[6] described 7 patients with cardiac involvement by PAN. Three of these patients had clear yellow pericardial fluid, while a further 2 had definite extensive fibrinous pericarditis. In none of these patients could a pericardial friction rub be heard.

James and Birk[17] autopsied 6 adults with PAN. All had an abnormal pericardium, in 1 case frankly fibrotic and in the remaining 5 showing both fibrinous pericarditis and pericardial fibrosis.

It is generally accepted that the presence of acute pericarditis, as manifested by a clinical pericardial friction rub and pericardial pain, indicates acute cardiac involvement by PAN and heralds a uniformly fatal outcome. Uraemic pericarditis, likewise, is usually a preterminal event.

Conduction system involvement

James and Birk[17] were the first to recognize and describe the importance of involvement of the cardiac conduction system in PAN. Two of their patients, aged 57 years and 73 years, suffered from classic PAN. The remaining 4 patients, aged 47-65 years, had other forms of 'necrotizing angiitis'; 3 had Wegener's granulomatosis and the 4th had hypersensitivity angiitis.[1,2,18] All of the patients had supraventricular arrhythmias, especially atrial flutter, shortly before death. Extensive histological examination of the conduction tissue showed that the sinus node was most severely affected by inflammatory, ischaemic and fibrotic changes. Pericarditis was observed in all 6 hearts and the authors postulated that the inflammatory changes in the sinus node were due to extension, as this structure is usually located less than 1 mm below the epicardial surface. Another reason quoted was the fact that the sinus node is a periarterial structure, arranged immediately around a central artery.[19] The atrioventricular node was also involved in all cases, but to a lesser degree, owing to the fact that the artery to this structure is not periarterial. Pathological changes in the His bundle were similar in extent and form to those of the atrioventricular node. In 2 cases the right coronary artery was totally occluded proximal to the origins of the nodal arteries, one by old atheroma and the other by a recent thrombosis.

Thiene *et al.*[20] described 2 adults, aged 28 years and 39 years, with classic PAN but no involvement of the large coronary arteries or myocardial infarction. In 1 case diffuse arteritis of the artery to the sino-atrial node was complicated by fairly acute thrombosis causing extensive infarction of the node. In the other case there were features of an acute necrotizing angiitis of the artery to the sino-atrial node accompanied by fibrinoid necrosis, inflammatory infiltration and aneurysmal dilatation of the arterial wall. Neither of these 2 patients had involvement of the atrioventricular node or His bundle, and they did not present with documented arrhythmias or an ECG suggesting possible conduction system lesions. These authors thus showed that the pathogenetic mechanisms affecting the conduction tissue in classic PAN may be secondary to inflammatory or ischaemic factors and obstruction of the nodal nutrient arteries, or due to spread of the inflammatory reaction to the periarterial tissue.

In our patient the only suggestion of conduction system involvement documented was the onset of complete heartblock (third-degree atrioventricular block) soon after his preterminal infarction. The most likely cause was a proximal right coronary artery obstruction rather than an isolated occlusion of the atrioventricular nodal artery, since temporary complete heart block is such a common complication of acute inferior myocardial infarction. There were certainly no arrhythmias noted on continual ECG monitoring and the ECG failed to demonstrate any lesser degree of atrioventricular block.

Clinical features

Hypertension

The development and pathophysiology of hypertension in PAN has been most controversial. Rose and Spencer[21] carried out a retrospective study of 111 proven cases of PAN of whom only 86 had blood pressure readings recorded. In the 48 patients with normal blood pressure there was frequent evidence of recent renal involvement, but healed lesions were rare. Seventeen other patients developed hypertension during the course of the disease but the great majority of these showed evidence of healed renal lesions. Of a further 21 patients in whom hypertension was present, all but 2 had readings taken months or years after the disease onset and the autopsy features were those of healed renal PAN. These authors concluded that the development of hypertension in this disease is directly associated with the healing process in the kidneys.

Griffiths and Vural[6] found hypertension in 13 of their 17 cases, all with renal changes characteristic of PAN. A further patient with renal PAN did not have hypertension but numerous infarcts of the kidney were seen. These authors also noted that although hypertension is one of the most frequent signs of PAN it often develops late in the disease, so that the absence of hypertension should not exclude the possible diagnosis of PAN. Other authors[22] clearly documented that hypertension in this disease is consequent upon involvement of the renal vessels with resulting secondary ischaemia.

Hypertension was the most frequent (67%) clinical feature related to the heart in the series of 66 cases of PAN analysed by Holsinger *et al.*[3] In the great majority of patients the hypertension was known to be present during the course of the disease or coincidentally at the time of clinical onset. However, in a few cases this physical sign antedated the beginning of the PAN, sometimes by many years. The onset of hypertension often precipitated congestive cardiac failure. Thus, hypertension alone was seen in 32% of the patients who developed congestive cardiac failure, whereas the combination of hypertension and myocardial infarction was seen in 43% of cases complicated by congestive heart failure.

Both young adults with PAN described by Thiene *et al.*[20] had evidence of severe hypertension associated with amaurosis and pulmonary oedema. Postmortem examination revealed extensive involvement of the renal vessels by classic PAN.

Frohnert and Sheps,[23] in their review of 130 cases of histologically proven PAN at the Mayo Clinic, noted a 35% incidence of hypertension in untreated patients and a 21% incidence in patients pretreated with steroids. Hypertension was noted in the only patient with myocardial infarction, as well as in the 2 patients with pericarditis.

Dines[24] reported on a 32-year-old patient with multisystem involvement by PAN who developed malignant hypertension and in whom a pericardial friction rub was directly related to uraemia.

Our patient failed to show any evidence of renal involvement and hypertension despite obvious extensive cardiac disease secondary to PAN. However, he almost certainly would have shown signs of this postmortem. It is likely that, if he had lived for a few more years, he would have presented with hypertension.

Congestive cardiac failure

Griffith and Vural[6] found that congestive cardiac failure was the prime cause of death, accounting for 6 patients of their 17 adult cases of PAN. Dyspnoea was the most common symptom (47%), and the left ventricle was enlarged in 52%.

Of Holsinger *et al.*'s[3] 66 patients, 62% complained of dyspnoea and 57% had obvious clinical congestive heart failure. These authors found that this presentation was the most outstanding clinical cardiac manifestation of PAN. They also showed that congestive cardiac failure was the cause of death in no fewer than 44% of the patients. It was quite obvious from their study that the two commonest precipitating factors of congestive heart failure were acute myocardial infarction and hypertension.

James and Birk[17] noted the presence of congestive cardiac failure in 4 of their 6 documented cases. The coexistence of supraventricular arrhythmias in these patients made the cardiac failure more resistant to conventional therapeutic measures.

Of the 130 patients reviewed by Frohnert and Sheps,[23] 8 had frank clinical congestive cardiac failure. The cause of delayed death was often a combination of acute myocardial infarction, renal failure and congestive cardiac failure.

Holland[14] described the case of a middle-aged woman who went into severe left ventricular cardiac failure secondary to a silent myocardial infarction. She also developed peripheral gangrene with extension of her myocardial infarction on ECG, but her cardiac failure appeared to be adequately controlled on medical therapy.

Thiene *et al.*[20] noted 2 adults with involvement of the cardiac conduction tissue by PAN, in whom congestive cardiac failure was prominent. Both had severe concomitant hypertension, thought to be an important aggravating characteristic.

Although our patient had extensive myocardial damage secondary to repeated myocardial infarctions, there was never any clinical evidence of congestive cardiac failure. Undoubtedly, if he had developed hypertension, he would have rapidly gone into left heart failure, a feature which has been verified by so many authors.

Angina pectoris

This symptom is most uncommon in PAN. Only 2 of the 17 patients reported by Griffith and Vural[6] complained of this: 1 of them had small coronary vessel involvement at autopsy. 'Thoracic pain', in some probably angina pectoris, was encountered in 26% of cases in the series published by Holsinger *et al.*[3] Frohnert and Sheps,[23] in their review of 130 cases, only mentioned 2 patients with angina.

Our patient had a fairly short history of pre-infarctional, as well as post-infarctional angina pectoris. This symptom could be readily explained on the basis of coronary artery disease when the selective coronary arteriography was evaluated. It is also interesting that this patient did not have any significant coronary collateralization on angiography, which suggests that ischaemia was probably not of haemodynamic significance for a long period; this would also explain his relatively short history of angina pectoris.

Cardiac murmurs

There has been much discussion in the literature of the relationship between rheumatic fever and classic PAN. Rose and Spencer[21] thought that the two were definitely associated. However, Owano and Sueper [25] recognized PAN as a syndrome and Zeek[1,18] categorized it under the the term 'necrotizing vasculitis', rheumatic fever being placed in a separate category of 'allergic' disorders. If these factors are accepted, then the cardiac murmurs of 'classic' PAN will not be confused with those occurring in acute rheumatic fever or as a result of chronic rheumatic valvular heart disease.

Griffith and Vural[6] noted apical systolic murmurs in 3 out of 17 cases, but it is not clear whether these patients had a functional systolic murmur secondary to severe congestive cardiac failure, pyrexia, or anaemia or whether there was actual organic involvement of the mitral valve.

Holsinger *et al.*[3] noted systolic murmurs in 24 of their 66 patients; 16 had apical murmurs, whereas 8 had both apical and basal murmurs. There is no further information as to the possible cause.

Leonhardt *et al.*[13] described a young man with classic PAN and moderate mitral stenosis, thought to be rheumatic in origin and purely coincidental to the PAN.

Pericardial friction rub

The incidence of this physical sign in classic adult PAN varies quite considerably in the literature. Griffith and Vural[6] found no instance of pericardial friction rub in their 17 cases, although 2 of these had extensive fibrinous pericarditis at autopsy. Holsinger *et al.*,[3] in their series of 66 cases, documented 6 patients with pericardial friction rubs, half of whom were grossly uraemic. Dines[24] described a further patient who developed a pericardial rub with the onset of uraemia secondary to renal involvement by PAN. In the 6 cases reported by James and Birk,[17] all showed evidence of pericarditis at autopsy but none had a pericardial friction rub antemortem. The appearance of a friction rub in our patient followed his acute transmural inferior myocardial infarction and was probably a complication of this, since he was not uraemic.

Electrocardiographic features

Arrhythmias

Supraventricular arrhythmias are by far the most common in PAN. Griffith and Vural[6] found an 18% incidence of atrial fibrillation in their series of 17 cases. Temporary sinus tachycardia was noted in 7 patients. Holsinger *et al.*[3] documented some rhythm abnormality in 10% of their subjects; 1 had paroxysmal atrial tachycardia, 1 had atrial flutter with 2:1 block, and a further 4 had atrial fibrillation. Sinus tachycardia was the second most common clinical abnormality (66%) and was frequently out of proportion to the patient's pyrexia. James and Birk[17] documented autopsies on 6 patients with arrhythmias of recent onset; one of the patients had intermittent atrial tachycardia, atrial flutter and atrial fibrillation. All the others, except one, had atrial flutter as well as additional supraventricular arrhythmias. In these 6 patients the arrhythmias were transient, lasting between a few days and weeks before reverting to sinus rhythm. However, therapy of these rhythm disturbances proved most difficult as they did not respond to conventional treatment. Laitinen *et al.*[26] noted the appearance of ventricular ectopic beats and a variety of arrhythmias in their 7 cases of PAN.

Left ventricular hypertrophy

There was a good correlation between left ventricular hypertrophy found at autopsy and on ECG.[6] Some 50% of patients with pathological left ventricular hypertrophy were noted to have significant left axis deviation on ECG. A few patients with right axis deviation were known to have additional pulmonary involvement by PAN.

ST- T-segment changes

These were the most commonly encountered abnormalities, occurring in up to 42% of subjects.[26] Very often the features were nonspecific, but distinction from ischaemic heart disease would usually prove most difficult. Typical ECG changes were sometimes found in subjects who had clinical acute pericarditis. Evidence of non-transmural myocardial infarction (acute and old) was occasionally seen in those patients in whom this complication was documented at autopsy. Secondary ST- T-wave abnormalities were also seen in subjects with a left axis deviation and left ventricular hypertrophy by voltage criteria.

Differential diagnosis

The most important diseases which have to be considered in differential diagnosis are the numerous collagen and auto-immune disorders, chiefly systemic lupus erythematosus, scleroderma, dermatomyositis and rheumatoid arthritis. The relationship between adult PAN and rheumatic fever has been alluded to earlier in this article. The clinical features of these various diseases can be very similar. Ultimately, biopsy specimens from various sites, for example skeletal muscle and testes, will give the correct diagnosis.[1,18,27] However, there will still be instances where a definitive pathological diagnosis cannot be made,[25] especially as there appears to be much overlap among these various disorders characterized essentially by 'necrotizing angiitis'.

Treatment and prognosis

It is generally accepted that PAN is a relentlessly progressive disease characterized by very few remissions. The two most important determinants of prognosis appear to be hypertension and renal disease.[21,23] Steroid therapy has been the mainstay of treatment and an expected 5-year survival rate of 48% has been documented.[23] However, several authors have emphasized the dangers of steroid therapy in hastening the onset of renal infarction and secondary hypertension, thought to be due to the reparative fibrosis of the vascular lesions.[15,16] Nachman[15] reported on a patient with adult PAN who developed a silent myocardial infarction shortly after starting corticosteroid therapy. Nevertheless, it has been frequently stressed that early recognition and prompt and energetic therapy with steroids are of the utmost value in making the prognosis less gloomy. Leonhardt *et al.*[13] clearly documented a significant functional improvement in the cardiovascular status of a patient who received long-term corticosteroid therapy, and who was still alive approximately 11 years after the presumed onset of the disease.

The use of long-term anticoagulant therapy in this disease has been most controversial. It has been considered to be highly risky in patients with micro-aneurysms and perivascular haematomas.[13] Nevertheless, Dines[24] reported the successful long-term use of anticoagulants in combination with long-term corticosteroid therapy over a period of $2^1/_2$ years. He found that the anticoagulants permitted reduction of steroid dosage and maintained the patient's blood pressure at normal levels with antihypertensive drugs. The rationale for using a combination of anticoagulants and corticosteroid therapy is that PAN essentially causes a diffuse vasculitis with diminution of internal luminal diameter, and subsequent extensive thrombosis. The corticosteroids were prescribed to combat the former situation, and the anticoagulants were presumed to be effective in controlling the latter.

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