worms and that she appeared to want to pass a stool all the time. She is said to have passed several coils of worms on the morning of the second day, and by noon appeared to be somewhat listless and cold. She was admitted to hospital for observation and was given a rectal washout and glucose by mouth. She was discharged the same evening and was quite comfortable when seen later that night. She passed a large coil of worms next morning as well.

It was subsequently disclosed that the child had been given a dose of ½-oz. (15 g.) of piperazine citrate two days earlier, but had not passed worms. The parents had not disclosed this to us as they were anxious to have her treated again because she was in the habit of eating plaster off the wall, which they attributed to worm infection. The symptoms that developed were probably caused by a sudden release of intra-abdominal pressure after evacuation of a large number of worms. The distension that followed was probably due to the loss of tone in a gut that had been chronically distended by large masses of worms. We had earlier had this eventuality in mind in not treating under field conditions another 2½-year-old child with an egg count of 199,000, but did not expect it in this particular instance. The possibility of this eventuality should be borne in mind when any child passes large numbers of worms after anthelmintic treatment. The dose could not have been too high, for a younger sister, 1½ years old, had the same dose and was unaffected. The child has since had an improved appetite and her general health is reported to be much better.

We had two sisters, aged 8 and 2½ years, who developed wheezing 36 hours after receiving bephenium hydroxynaphthoate. They had 1.25 g. twice on the same day and had passed 25 and 30 worms respectively. They had no previous history of asthma. The elder girl showed a fair amount of distress when seen by us 48 hours after treatment. They both responded well to an injection of aminophylline, were observed for a period of six hours, and subsequently were quite well. Several doctors in charge of out-patient dispensaries have informed us that wheezing and transient fever are often seen in children treated with piperazine citrate for ascariasis. In our experience these were the only allergic manifestations in over 400 children treated with varying doses of bephenium hydroxynaphthoate.

Vague abdominal pain was sometimes complained of by a few children, but in none was it severe enough to cause anxiety.

Summary

Different preparations of bephenium hydroxynaphthoate ("alcopar") in varying doses were given to groups of children, to determine the minimum effective dose for treating ascariasis.

1.25 g. was found to be the minimum dose with optimum results.

The best preparation was a freshly prepared suspension in lemon-flavoured syrup (3.5%).

Vomiting was the only disagreeable side-effect directly attributable to the drug. It was significantly more in children under 4 years of age.

The small dose recommended for treatment of ascariasis could be safely given to any age-group without causing anxiety.

Our thanks are due to Dr. P. G. Somasundaram, who did the statistical analysis of our results, and to Dr. D. B. Gunasekara, who made many valuable suggestions in the course of our work.

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AORTIC INCOMPETENCE IN ANKYLOSING SPONDYLITIS

BY

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Only recently has it been recognized that patients suffering from ankylosing spondylitis may develop aortic incompetence due to a type of aortitis and aortic endocarditis that has distinctive pathological features. The earliest description of this lesion was given by Mallory *et al.* (1936), but its unique nature and its relationship to joint disease were first recognized by Bauer *et al.* (1951). These workers (Clark *et al.*, 1957) later reported on 22 cases collected over a period of 20 years. Further examples have been recorded by Baker *et al.* (1955), MacMahon *et al.* (1955), Schilder *et al.* (1956), and Toone *et al.* (1959). Ansell *et al.* (1958), giving the first description of the condition in this country, described two cases, with necropsy details of one.

The purpose of this communication is to record the clinical and pathological features of a further case.

Case Report

In 1935 the patient, then a man of 27 with no history of significant previous illness, was passed fit for service in the regular Army. In 1942, at the age of 34, he complained of pain in the back while on a battle course, but continued on full active service as an officer. Three years later he developed painful swelling of the right knee-joint accompanied by pyrexia, followed by pain in other joints and in the back. Radiographs of the spine revealed moderately advanced ankylosing spondylitis.

During the next eight years he continued to serve in the Army, while the joint disease pursued an intermittent progressive course. He received various forms of treatment, including radiotherapy to the spine. In 1949 he had an attack of iritis. In the same year, for the first time in many medical examinations, an apical systolic murmur was noted. This was considered by an experienced physician to be of no pathological significance, and the heart appeared normal on a radiograph of the chest.

In 1954 an exacerbation of spondylitis, with pain in the back, knees, and left shoulder, and with considerable loss of weight, led to his admission to the Queen Alexandra Military Hospital. He was found to have an aortic diastolic murmur, with left ventricular enlargement, collapsing pulse, and high pulse-pressure. There was no evidence of syphilis, and Dr. Evan Bedford thought that the aortic lesion was an example of the aortitis of ankylosing spondylitis.

In 1955 another exacerbation of joint pain and swelling led to his readmission. He now had diminished exercise tolerance and intermittent oedema of the ankles. There was free aortic regurgitation with blowing to-and-fro murmurs in the aortic area, and in addition a low-pitched mitral diastolic murmur. This was thought to be an Austin Flint murmur, as the left auricle was not enlarged.

Thereafter his effort dyspnoea increased rapidly, and in April, 1956, he developed congestive heart failure. The

cardiac murmurs were unchanged, but there were now peripheral circulatory signs of severe aortic incompetence, gross cardiac enlargement, triple rhythm, and intermittent flutter-fibrillation. The heart failure was controlled by treatment and he was invalided from the Army.

He then came under the care of Dr. C. J. Fuller, of the Royal Devon and Exeter Hospital. He complained of stiffness of the back, hips, and shoulders and pain in the right knee. The vertebral column was quite immobile, though with little deformity; there was slight limitation of movement of both hip-joints but full movement of the shoulders; the right knee was swollen, with severe limitation of movement. There was no abnormality of the joints of the hands or feet.

The radiographic features were characteristic of advanced ankylosing spondylitis (Middlemiss, 1956). The summarized findings, as reported by Dr. J. H. Middlemiss, were as follows. The vertebral column throughout its length presented the picture of a typical "bamboo spine" with complete bony ankylosis of the diarthrodial joints and complete bony ossification of the lateral ligaments and the anterior longitudinal ligament. Many of the costo-vertebral joints were ankylosed. In the pelvis, both sacro-iliac joints were completely fused, the symphysis pubis was fused and ossified, and there were typical advanced changes in the ischial tuberosities and the outer aspects of the iliac bones. The hip-joints, the right knee-joint, and the right acromio-clavicular joint showed the non-specific changes of a chronic inflammatory arthritis.

The heart was greatly enlarged, with a forceful left ventricular impulse at the apex. The pulse was regular and collapsing, the blood-pressure 130/30. There were loud aortic systolic and diastolic murmurs, with a palpable aortic systolic thrill. At the apex there was a systolic murmur well conducted into the axilla, and a rumbling diastolic murmur.

He suffered from disabling pain in the affected joints, but there was no change in his cardiac condition until March, 1957, when he suddenly deteriorated with severe dyspnoea and haemoptyses. He was admitted to hospital in severe congestive heart failure, with signs suggesting infarction of the right lower lobe. The cardiac signs were unchanged and the rhythm remained regular. There was no evidence of peripheral venous thrombosis. In spite of vigorous treatment the heart failure increased and he died four days later.

Necropsy Findings

The relevant findings at necropsy were as follows. "There was a slight excess of clear fluid in the pericardial sac. The heart was greatly enlarged (820 g.). On the surface of the heart, near the base of the ventricles, were several blotchy sub-epicardial haemorrhages. Right auricle: moderately enlarged. A small amount of adherent clot was present in the auricular appendage. Tricuspid valve: cusp not thickened; valve dilated and admitting more than four fingers. Pulmonary orifice: moderately dilated. Right ventricle: considerably dilated and muscle slightly thickened. Mitral valve: admitted four fingers and was dilated; both cusps showed chronic thickening, but there was no evidence of stenosis or any indication of either present or old infective endocarditis. Aortic valve: the aortic cusps were thickened and slightly fused. The aortic ring was somewhat enlarged. Most of the thickening noted was behind the cusps on the aortic wall. From the base of the aortic valve for a distance of 2.5 cm. the surface of the aorta was corrugated and showed a raised, smooth, pearly-grey surface. Similar pearly areas were present on the anterior cusp of the mitral valve and on the adjacent aortic cusp. The orifices of both coronary arteries were distorted, but the arteries themselves were free from disease. There was very little aortic atheroma. The condition suggested chronic mitral and aortic endocarditis with incompetence of both valves. The left ventricle was grossly enlarged and the muscle moderately thickened.

"Microscopical examination of the aorta and thickened aortic cusps showed that in the affected area there were thickening and hyalinization of the intima and some fibroblastic proliferation in its deeper part. Many large collections of lymphocytes were present in the adventitia, sufficient in places to give an appearance of lymphadenoid deposits. These collections were sometimes perivascular and sometimes not."

In the lower lobe of the right lung there was a firm haemorrhagic infarct measuring about 4 × 3 cm., and one or two smaller more recent infarcts. The abdominal organs revealed the changes of long-standing chronic venous congestion. The joints were not examined at necropsy.

Comment

This patient had never had acute rheumatism, and there was no history or clinical or pathological evidence of syphilis. He first had symptoms of ankylosing spondylitis at the age of 34, and the diagnosis was made three years later. His heart was thought to be normal until, at the age of 46, in the twelfth year of the disease, aortic incompetence was discovered during an exacerbation of the spondylitis. Effort symptoms developed within two years, and a few months later congestive heart failure supervened. Death occurred from congestive heart failure at the age of 49, little more than three years after the aortic lesion was discovered. The ankylosing spondylitis, which was of at least 16 years' duration, remained active until his death. During its course he had suffered from severe involvement of large peripheral joints which frequently overshadowed the spinal symptoms, and he had one attack of iritis.

Clinical Features

Nearly 40 cases have now been reported of this type of heart disease, of which the present case is a typical example. The clinical features, based on these published accounts, may be summarized as follows.

All the patients have been male. The age of onset of the joint disease, though often not definitely known, has varied from 9 to 51 years, being commonly in the third and fourth decades. The time of onset of the cardiac lesion is also often not precisely known, but it varies from the third to the thirtieth year of the disease, usually being between the tenth and fifteenth years.

Aortic incompetence is thought to appear during exacerbations of the arthritis, sometimes accompanied by pericarditis, and may progress rapidly during subsequent exacerbations. Gleckler (1954) has given an account of a case of acute carditis occurring during an exacerbation of long-standing spondylitis, and it may well be that all cases begin with an acute aortitis and endocarditis which usually escapes recognition. Clinically detectable involvement of the mitral valve rarely occurs, though, as in any severe aortic incompetence, Austin Flint murmurs are a fairly frequent finding.

The aortic lesion has in some cases led to the patient's death within one or two years, but in other instances patients have remained relatively well for 15 years or more (Baker *et al.*, 1955). In general it is progressive, and causes increasing disability within a few years. Angina pectoris, due to deformity of the coronary ostia, is a not uncommon feature, and once it occurs the expectation of life is short. The onset of congestive heart failure also bears a bad prognosis.

In the great majority of cases the ankylosing spondylitis has been accompanied by arthritis of peripheral joints. Many have suffered from attacks of

iritis as an additional complication of their joint disease. Electrocardiographic changes are very common at all stages of the cardiac affection, notably conduction defects varying from prolongation of the P–R interval to complete left bundle-branch block. Auricular fibrillation is a frequent occurrence. The radiological features are those of aortic incompetence in general, but it is most unusual for the aorta to be significantly dilated.

The incidence of this cardiac lesion in cases of spondylitis cannot be assessed with any accuracy, for the clinical diagnosis can never be certain, but it is certainly low. It is probably in the region of 2%. Schilder *et al.* (1956) found five cases in a survey of 100 males suffering from aortic incompetence of varied aetiology.

Pathological Features

Detailed descriptions of the pathological findings in 16 cases have been reported. The most striking macroscopic feature is a curious thickening of the aortic intima and endocardium, usually smooth, glossy, and pearly grey, but in early more active lesions pinker and more granular. It occurs characteristically at the root of the aorta, spreading fanwise upwards from the commissures of the aortic valve (rarely extending more than a few centimetres into the ascending aorta) and downwards over the aortic cusps. Sometimes it extends into the left ventricular endocardium, occasionally reaching the anterior leaflet of the mitral valve. Thickening, rigidity, and distortion of the aortic valve cusps occur, with rolling of their edges but rarely any adherence between them in the commissures. Sometimes there is some dilatation of the aortic ring but usually little separation of the cusps such as occurs in syphilitic aortitis, the regurgitation being due rather to distortion and rigidity of the cusps. In a few cases, where the characteristic endocardial changes have extended into the anterior leaflet of the mitral valve, this has been somewhat thickened, but the mitral valve is not otherwise affected.

The histological features of the aorta resemble those of syphilis. Thickening and hyalinization of the intima occur, with foci of inflammatory cells. In the media focal necrosis, disintegration of the elastica, and fibrosis are present. The adventitia shows fibro-muscular thickening and endarteritis obliterans of the vasa vasorum, with perivascular inflammatory infiltration. In the myocardium, foci of necrosis, interstitial fibrosis, and sometimes endarteritis are found.

Discussion

It is clear from the pathological evidence that the lesion described here is a distinctive type of aortitis and endocarditis which occurs in cases of ankylosing spondylitis. A unique relationship to this disease is, however, not definitely established.

In this country anklyosing spondylitis is regarded as a disease *sui generis,* whereas in the United States it is generally thought to be a variant of rheumatoid arthritis. In American publications it is sometimes accorded separate recognition as "rheumatoid spondylitis," but often no distinction whatever is made. In all the reported cases of this cardiac lesion in which adequate information is given the joint disease has been what, in this country, would be called ankylosing spondylitis. There are, however, a few possible exceptions.

Clark *et al.* (1957) record that "by the usual criteria all but two [of their 22 cases] might be said to have rheumatoid spondylitis," but they give no details of these. Pirani and Bennett (1951) describe a very similar lesion in a case of juvenile rheumatoid arthritis; Levin *et al.* (1955) report "inflammatory lesions of the ascending aorta" in four cases of rheumatoid arthritis (without spondylitis), but these may be a different entity, similar to that described by Cruickshank (1958).

Cruickshank (1958) discusses the cardiac complications of rheumatoid arthritis and their relation to this spondylitic type of lesion. He considers them to be different conditions and calls for the recording of all such cases; "for if the occurrence of distinct lesions in rheumatoid arthritis and ankylosing spondylitis can be conclusively established, this will constitute still further evidence for regarding these conditions as separate entities rather than as varieties of the one disease."

Apart from these few possible exceptions the lesion described here has occurred exclusively in ankylosing spondylitis. The existing evidence suggests that it should be regarded as a visceral complication of this disease.

A high incidence of electrocardiographic and clinical cardiac abnormalities was found in ankylosing spondylitis by Bernstein and Broch (1949) and by Blumberg and Ragan (1956). The former authors, on inadequate grounds, ascribed these to coincident rheumatic heart disease. It seems more likely that there exists a distinct "spondylitic" type of disease of the heart and aorta which in its gross form as described here is rare, but which may occur in lesser degrees more frequently than has been recognized.

Summary

An account is given of the clinical and pathological features of a case in which ankylosing spondylitis was complicated by a distinctive type of aortitis and endocarditis of the aortic and mitral valves. The literature concerning this cardiac lesion is reviewed and its characteristic clinical and pathological features are summarized. The relationship of this lesion to ankylosing spondylitis, and to rheumatoid arthritis and rheumatoid heart disease, is briefly discussed. The existing evidence indicates that it is a visceral manifestation of ankylosing spondylitis.

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