Virchows Archiv A Pathol Anat (1992) 420:109–112

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Non-arthritic rheumatoid valvulitis with coronary arteritis causing myocardial infarction

Miri Fujita[1], Masakazu Abe[3], Tomoo Itoh[1], Katsuharu Saitoh[2], Munechika Noguchi[4], Kimiaki Sano[3], Yasunori Fujioka[1], and Kazuo Nagashima[1]

Departments of [1] Pathology and [2] Cardiovascular Medicine, Hokkaido University School of Medicine, Sapporo, Japan
Departments of [3] Internal Medicine and [4] Cardiovascular Medicine, Aiiku Hospital, Sapporo, Japan

Received June 11, 1991 / Received after revision August 24, 1991 / Accepted September 6, 1991

Summary. Rheumatoid valvulitis occurring in an individual without arthritis has rarely been reported. A 62-year-old woman died after repeated myocardial infarction, with no articular symptoms but with a fever of unknown origin and a positive rheumatoid factor. Autopsy examination revealed granulomatous inflammatory lesions with rheumatoid nodules present in the aortic valve and the base of the left coronary artery. Widespread myocardial infarction was found in the septal and anterolateral walls of the left ventrilce.

Key words: Aortic valvulitis – Coronary arteritis – Non-arthritis – Rheumatoid granuloma – Immunofluorescence study

Introduction

Rheumatoid arthritis (RA) is an autoimmune systemic chronic inflammatory disorder. It is usually a disease of the joints and articular manifestations develop in advance of other symptoms. On rare occasions, however, extra-articular involvement precedes joint symptoms in the lungs (Spencer 1985; Stanford 1988), skin (Lowney and Simons 1963) and eyes (Kleiner et al. 1984). Rheumatoid heart disease without articular manifestations is extremely rare; only three cases of aortic and mitral valvulitis have been reported previously (Legier 1966; Good et al. 1970). Here we present an autopsy case of a patient with chronic granulomatous valvulitis who had repeated attacks of myocardial infarction with fever of unknown origin and a positive rheumatoid factor, but who lacked articular symptoms. The valvulitis which involved the coronary arteries was verified histologically as rheumatoid disease because of the presence of rheumatoid nodules. The deposition of fibrin and infiltration of mononuclear cells with cytoplasmic IgG were demonstrated immunohistochemically.

Case report

A 62-year-old woman visited a physician on 15 May 1990 because of a dry cough and night sweats of 2 weeks' duration. The patient was hospitalized in Aiiku Hospital, Sapporo on 10 June with continuous uncontrollable fever of 38° C. Her history was significant in that she had undergone an upper lobectomy of the right lung for pulmonary tuberculosis 30 years before. She had no history of rheumatic fever, joint pain or swelling, chest pain, hypertension, or syphilis. Her family history was unremarkable.

At the time of hospitalization, her temperature was 38.4° C. She had a systolic ejection murmur of 3/6 (Levine), which was heard best along the left sternal border at the fourth intercostal space. Moist rales were heard in the lower lung field on the left side. Her peripheral joints were normal. Chest radiographs showed cardiomegaly (cardiothoracic ratio 59%) with prominence of the left ventricle, as well as pulmonary congestion with a small pleural effusion. An ECG revealed a first-degree atrio-ventricular block and an incomplete right bundle branch block. No remarkable changes were found in the ST segment and T wave, and no abnormal Q wave was found.

The following results of laboratory studies were obtained: blood sedimentation rate, 135 mm/h; Mantoux test, 10 × 8 mm; C-reactive protein, 9.5 (5+); antistreptolysin-O, 1:80; rheumatoid factor, 2+; RA haemagglutination, 1:320 (normal less than 1:40). LE cell and anti-nuclear antibodies were negative. Her white blood cell count was 8400/mm^3, with differential counts of 59% neutrophils, 39% lymphocytes and 2% monocytes. The red blood cell and platelet counts were within normal ranges. The IgG and IgM were slightly increased with a slight decrease in complement. Repeated blood cultures yielded no growth. Examinations by fibrescope, CT scan and echography on abdominal organs and the gastro-intestinal tract yielded negative results. Aortography was unremarkable.

On 7 July, she had sudden onset of severe and prolonged chest pain, and ECG and laboratory data indicated acute myocardial infarction of the anterior wall of the left ventricle. Echocardiographic findings at that time showed aortic regurgitation, thickening of the aortic valve, a small pericardial effusion, and akinetic wall around the apex. The fever continued despite treatment with several antibiotics and anti-tuberculous drugs. On 15 September, an oppressive sensation in the chest developed, accompanied by ECG changes and abnormal laboratory values, both suggestive of acute myocardial infarction. She died during the following night.

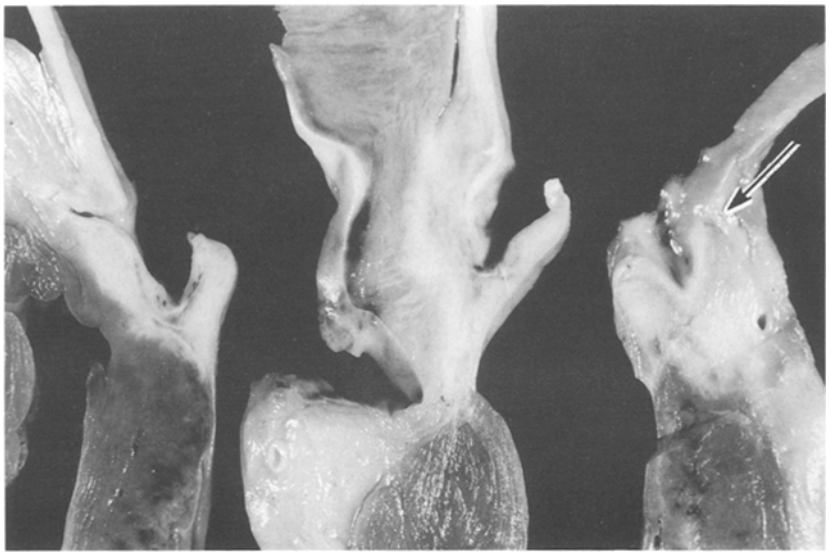

Fig. 1. Macroscopic appearance of the aortic valve on cut surface, showing thickened and shortened cusps and narrowed, shallow Valsalva's sinuses caused by fibrous inflammatory infiltrates. Extension of the lesions into adventitial tissue and myocardium can be seen. The ostium of the left coronary artery (indicated by *arrow*) is almost completely occluded, but its distal part is patent. The right coronary artery was patent (the figure shows a tangential section through the area slightly away from the centre of the lumen). *Left:* Right aortic cusp with right coronary artery. *Centre:* Non-coronary aortic cusp. *Right:* Left aortic cusp with left coronary artery

Pathological findings

Autopsy was performed about 3 h after her death. Significant findings were limited to the heart. On gross examination, there was 100 ml of clear pericardial effusion, but no features of pericarditis were noted. The heart was enlarged (460 g), with hypertrohy and dilatation of the left side. The aortic valve was thickened and shortened, with yellow-tan, rubbery nodules. There were no commissural adhesions, no cuspid calcification and no verrucous vegetations. The base of the aortic valve and the posterior walls of Valsalva's sinuses were also thickened (Fig. 1). The left main coronary artery showed a marked stenosis starting from the ostium and approximately 1 cm in length, but was patent distal to this portion. There was no abnormality in the right coronary artery or in the aortic arch above the valve. No atherosclerotic changes were observed in the three coronary vessels and no significant abnormalities in the mitral, tricuspid or pulmonary valves. On cross-sections of the heart myocardial fibrosis mixed with and surrounded by acute ischaemic changes were found in the anteroseptal to lateral wall of the left ventricle (Fig. 2). The scar extended continuously to the apex.

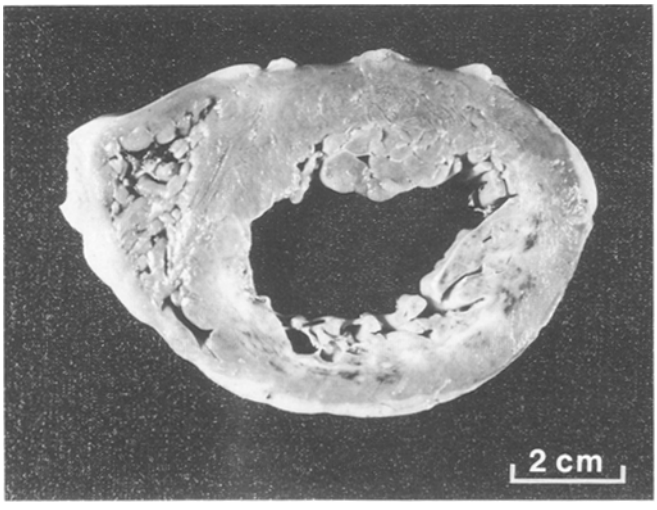

Fig. 2. Horizontal slice through both ventricles. Patchy and irregularly fibrosed areas superimposed on haemorrhagic acute infarction are seen in the anteroseptal and lateral walls of the left ventricle

Histologically, there were marked inflammatory changes in the aortic valve. The inflammation consisted of infiltration by lymphocytes, plasma cells, and histiocytes and extensive fibrosis. Multinucleated giant cells and polymorphonuclear leucocytes were also encountered. In the ostium of the left coronary artery there were granulomas consisting of several areas of fibrinoid necrosis; in addition, regions of collagenous fibrosis were surrounded by palisaded histiocytes with a peripheral zone of lymphocytes and plasma cells that showed the typical features of rheumatoid nodules (Fig. 3). The rheumatoid nodules were restricted to the aortic valve and its surroundings, but the granulomatous inflammation involved a part of the bundle of His. In the pericardium, a massive severe lymphocytic infiltrate formed lymphoid follicles, but no granulomatous lesions were noted. No micro-organisms were identified with special stains.

We applied immunofluorescence studies to paraffin-embedded tissue from the inflamed regions, and evaluated the results by comparing the positive control of paraffin-embedded specimens established in frozen-section studies. Deposition of fibrin in the necrotic areas was readily demonstrated (Fig. 4a) and infiltrating cells were shown to contain mostly IgG in their cytoplasm (Fig. 4b). A few IgA-positive cells were also found, but IgM-positive cells were very rare. Deposition of complements (Clq, C3, and C4) was not detected.

Discussion

Rheumatoid disease affecting the heart of patients without articular symptoms is very rare; only three cases have been reported. Legier (1966) described an autopsy case of a 69-year-old woman who had rheumatoid aortic valvular disease without joint involvement, which terminated in haemorrhagic gastroenteropathy. Good et al. (1970) reported on two cases of cardiac rheumatoid granulomas without arthritis; one of these was an autopsy case of a 46-year-old man who had mitral and aortic valvulitis and who died of heart failure and pneumonia, and the other was a case of a surgically resected mitral valvulitis in a 37-year-old labourer. These findings were verified histologically by the presence of typical rheumatoid nodules in the affected regions. However, none of the patients was suspected of having rheumatoid disease before autopsy or surgical examination.

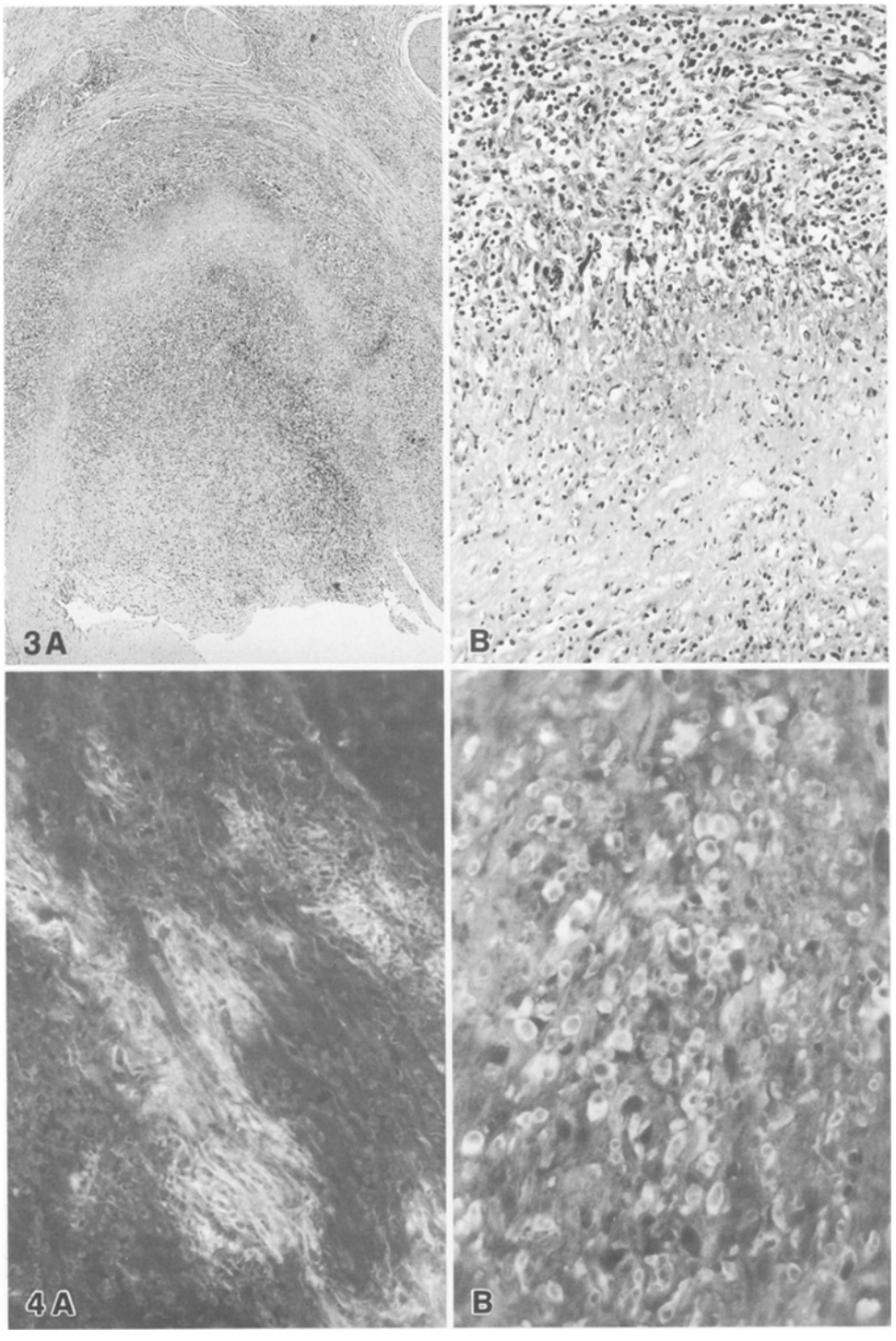

Fig. 3A, B. Microscopic features of aortic valvulitis and coronary arteritis.
A Left main coronary artery showing marked intimal thickening due to chronic inflammation and rheumatoid arteritis. H & E, ×10.
B Small fibrosed focus with "palisaded" histiocytic cells and a few multinucleated giant cells in the aortic valve

Fig. 4A, B. Immunofluorescence findings on paraffin sections of the aortic valve.
A Plentiful fibrin deposits are seen in the necrotic foci of the aortic valve. No deposition of immunoglobulins or complements was detected. Fluorescein isothiocyanate (FITC), ×100.
B Plasma cells in the inflammatory lesions are shown to contain IgG in their cytoplasm. FITC, ×400

Coronary arteritis causing myocardial infarction is also rare in patients with RA. We found 12 cases of the disease in published reports (Gravallese et al. 1989; Virmani et al. 1991). Because it is a life-threatening condition, major epicardial coronary arteritis is one of the most important lesions requiring clinicopathological attention. However, there has been no report of coronary arteritis resulting in myocardial infarction in patients with rheumatoid disease without articular manifestations. In rheumatoid disease occurring initially in the lungs, subcutaneous tissues, or eyes, some patients developed articular symptoms later, confirming the pathological diagnosis of non-arthritic rheumatoid disease (Lowney and Simons 1963; Kleiner et al. 1984; Spencer 1985; Stanford 1988). In our case, however, rheumatoid lesions affected the heart and there was no time for the patient to develop signs of rheumatoid origin in the joints. In these circumstances, diagnosing the rheumatoid disease would have been very difficult without the presence of specific rheumatoid granulomata in the heart.

Diseases to be considered in the differential diagnosis in this case are rheumatic fever, infectious endocarditis, ankylosing spondylitis, Takayasu's disease, polyarteritis nodosa, giant cell arteritis, and syphilitic aortitis. However, the presence of rheumatoid nodules in the lesions together with positive serum rheumatoid factor was enough to rule out these diseases (McAllister and Ferrans 1983; Tejada and Waller 1988; Gallagher 1989; Lie et al. 1990; Virmani et al. 1991).

The pathogenesis of rheumatoid disease has not been clarified. There are some reports on the immunofluorescence and immunohistochemical findings in the rheumatoid nodules (Fukase et al. 1980; Rasker and Kuipers 1983; Aherne et al. 1985). It is controversial whether immune complexes of rheumatoid factor (IgM)-IgG are deposited in the rheumatoid nodules with activated complement. Immune complexes are not always deposited in the rheumatoid lesions, but marked fibrin deposits are found consistently, as was shown in our case. A low or variable incidence of deposition of immune complexes and vasculitis is observed in relation to rheumatoid nodules in various stages. The results of immunofluorescence studies on paraffin sections in the present case were similar to those reported in patients with classical or definite RA examined with immunofluorescence on alcohol-fixed, paraffin-embedded specimens (Fukase et al. 1980) with immunofluorescence on frozen-sections (Rasker and Kuipers 1983) and with paraffin immunohistochemical methods (Aherne et al. 1985).

In conclusion, rheumatoid disease in the heart can precede or be accompanied by arthritis. In the absence of obvious arthritis, if there is a positive rheumatoid factor, rheumatoid disease should be considered as part of the differential diagnosis of acquired valvular heart lesions. Emergency operation and histological examination of the excised lesion are required in these rare cases. Immunofluorescence techniques applied to paraffin-embedded sections were shown to be useful in revealing fibrin deposits in the necrotic rheumatoid granuloma, and cytoplasmic immunoglobulins were produced locally by plasma cells around the granuloma, despite the absence of immune complexes.

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