Extensive Involvement of the Myocardium and the Cardiac Conduction System in a Case of Wegener's Granulomatosis

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SUMMARY

A 61-year-old female who had shown Raynaud's phenomenon and articular swelling for 10 years, was admitted to hospital because of fever of unknown origin (FUO) and dry cough. She was diagnosed by skin biopsy to have a collagen disease or overlap syndrome. Anemia developed rapidly and FUO persisted, but blood culture was negative. Although indomethacin and prednisolone were administered for the progression of clinical signs and symptoms, severe dyspnea developed, resulting in bradycardia, followed by recurrent episodes of ventricular tachycardia. In spite of extensive treatment for her arrhythmia she died on the 9th hospital day. An autopsy revealed generalized Wegener's granulomatosis with extensive cardiac involvement. Necrotizing angitis and severe granulomatous inflammatory foci affected characteristically the common bundle of His and right bundle branch in addition to the ordinary myocardium. (Jpn Heart J 1999; 40: 509–515)

Key words: Wegener's granulomatosis, Ventricular tachycardia, Cardiac involvement, Conduction system

SINCE the initial description by Klinger in 1931[1] and confirmation by Wegener in 1936,[2] Wegener's granulomatosis is characterized by a necrotizing granulomatous vasculitis, mainly affecting the upper and lower respiratory tract and the kidney.[3] An often overlooked fact is that the heart is also involved in nearly 25% of the cases.[4] Histologic studies of the conduction system in this disease have only been reported in six cases.[5–7] Here we report a case of

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Received for publication June 10, 1999.

Accepted June 21, 1999.

Wegener's granulomatosis mainly involving the myocardium and the conduction system.

Case Report

A 61-year-old woman was admitted to hospital with the chief complaints of fever, dry cough and loss of body weight. For ten years she had experienced Raynaud's phenomenon and articular swelling. At first she was diagnosed with rheumatoid arthritis, but she did not receive further evaluation and treatment. From July, 1991 she suffered from slight fever and dry cough. Because antibiotics and sedatives were not effective, she was referred to our hospital. On admission she was alert, her blood pressure was 124/64 mmHg, pulse rate 90/min and regular. Her skin was dry and showed exanthema on the chest wall. Erythema and swelling of her hand joints were observed. Anemia was present with hemoglobin of 9.4 g/d*l*, a white blood cell count of 4,700/μl, proteinuria (1 +), a fibrinogen of 746 mg/d*l*, a gamma-globulin of 34.2%, cholinesterase of 81 IU/*l*,

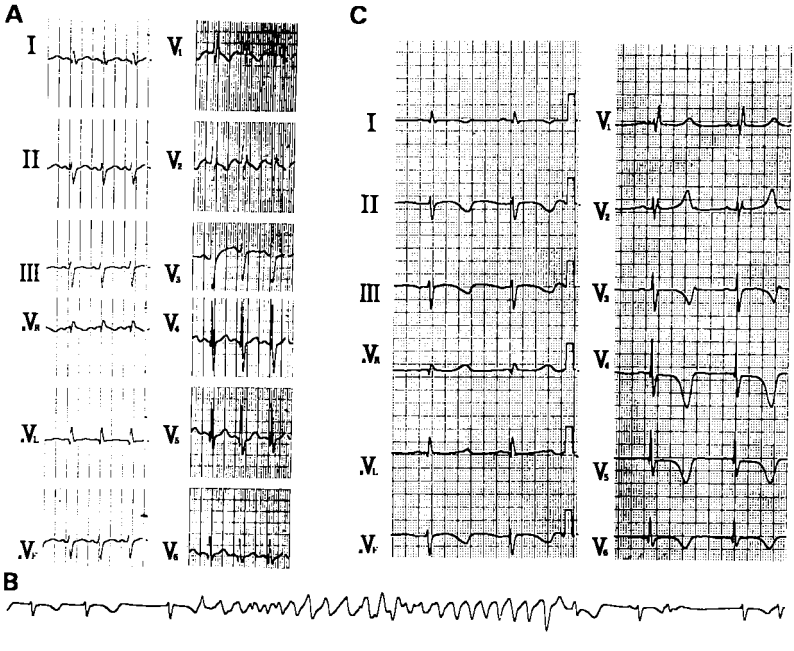

Figure 1. Electrocardiograms. **A:** Sinus tachycardia, complete right bundle branch block associated with left anterior hemiblock on admission (8/15/91). **B:** AV junctional rhythm (HR; 40 bpm), followed by QT prolongation and ventricular premature beat (R on T phenomenon) developed polymorphic ventricular tachycardia on 8th hospital day (at p.m. 7:00, 8/21/91). **C:** Sinus bradycardia with marked prolongation of QT interval (QTc = 0.64 sec) (at p.m. 9:10, 8/21/91).

CPK of 68 IU/*l*, a blood urea nitrogen of 9 mg/d*l*, a creatinine of 0.6 mg/d*l*, a serum iron of 4 μg/d*l*, serum potassium of 3.6 mEq/*l*, erythrocyte sedimentation rate of 145 mm/hr and CRP of 26.9 mg/d*l*. The electrocardiogram (ECG) showed sinus tachycardia with complete right bundle branch block and anterior hemiblock (Figure 1A). Chest x-rays showed a reticular pulmonary shadow in the bilateral lower lung fields with a normal size heart. An echocardiogram showed moderate hypokinesis of the interventricular septum, left ventricular ejection fraction of 48%, Doppler signal of mitral regurgitation (MR) and tricuspid regurgitation (TR) with moderate degree. The skin biopsy revealed findings compatible with dermatomyositis or overlap syndrome. Anemia developed so a blood transfusion was performed. Remittent fever was present despite a negative blood culture. Indomethacin was administered and the fever temporarily responded. On the 8th hospital day convulsion suddenly appeared but her brain CT scan and electroencephalogram were normal. Active stage of collagen disease was suspected and prednisolone (60 mg/day) administration started. However, dyspnea developed, the ECG showed ST depression, and sublingual nitroglycerin administration was ineffective. CPK was normal, her ECG showed bradycardia (junctional rhythm), developing into the recurrent appearance of R on T phenomenon followed by Torsades de Pointes type of polymorphic ventricular tachycardia (VT) (Figure 1B). Her VT did not respond to lidocaine, but was stopped through DC shock treatment. Afterwards the ECG showed sinus bradycardia with a marked prolongation of QT interval (QTc = 0.68 sec; serum K = 5.5 mEq/*l*) (Figure 1C), followed by repeated VT attacks. She died on the

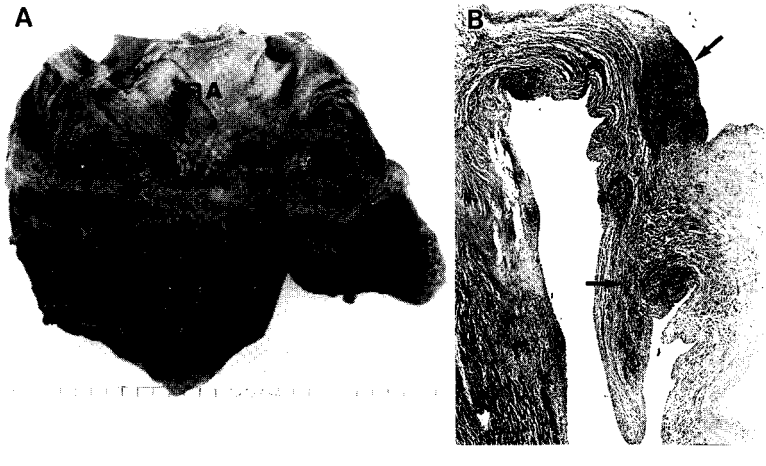

Figure 2. **A:** Multiple, miliary-sized white nodules (arrow) are visible on the endocardium of the right atrium (RA) and the tricuspid valve (TV). **B:** Granulomatous endocarditis (arrows) involving the tricuspid leaflet (H.E. × 10).

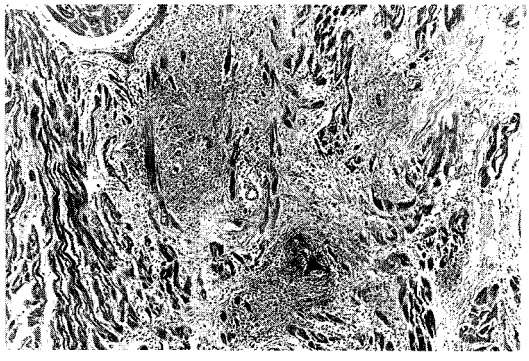

Figure 3. Photomicrograph of the myocardium, showing necrotizing arteritis and granulomatous myocarditis (H.E. × 25).

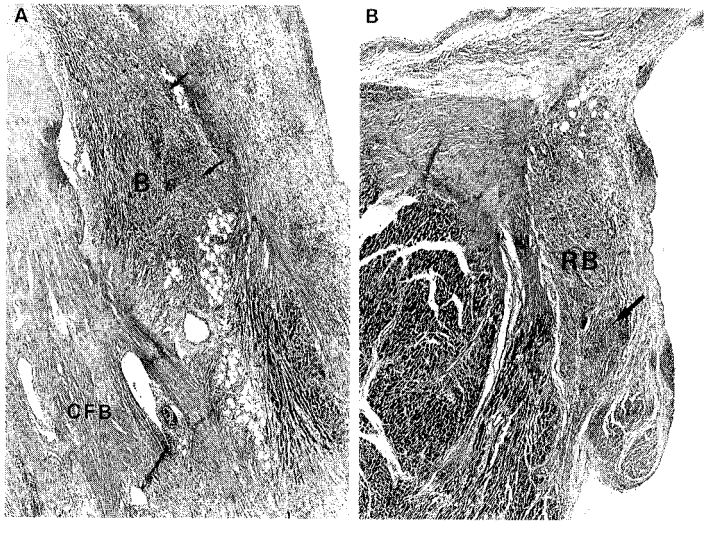

Figure 4. Photomicrographs of the conduction system. **A:** Granulomata (arrows) in the penetrating His (B) (H.E. × 10). **B:** Granulomatous changes (arrow) in the first portion of the right bundle branch (RB) (H.E. × 10) CFB = central fibrous body.

9th hospital day. Postmortem examination of the serum revealed an antineutrophile cytoplasmic antibody (ANCA) level, measured by flow cytometry, of 98 SLI units (moderately positive) and a perinuclear pattern ANCA was also demonstrated by an indirect fluorescent method, both of which were compatible with Wegener's granulomatosis.

An autopsy revealed typical, although limited, changes in Wegener's

granulomatosis, involving the lung, trachea and bronchi. In the kidney scattered foci of necrotizing arteritis of small arteries and arterioles, and segmental necrotizing glomerulitis were present. Similar changes in the arteries and arterioles were found in the spleen and uterus.

However, the most characteristic finding of this case was the lesions in the heart. Exudative and granulomatous endocarditis was also present, mainly in bilateral atria (Figure 2A) involving the tricuspid (Figure 2B) and mitral valves. Extensive necrotizing arteritis involving intramural arterioles and innumerable patchy, granulomatous inflammatory foci of the myocardium were found (Figure 3). Fibrinous pericarditis was also present. The conduction system using serial sections according to Lev's method as previously reported,[8] revealed small foci of inflammation in the sinus node and the atrioventricular (AV) node associated with AV nodal arteritis in its branches. Peculiar findings were severe granulomatous inflammatory changes with necrosis in the common bundle of His (Figure 4A) and right bundle branch (Figure 4B) as well as in the distal portion of the left bundle branch. The third portion of the right bundle branch showed chronic fibrotic changes. Advanced gastric carcinoma, Borrmann IV, of the lesser curvature with subserosal invasion without metastasis was also observed.

Discussion

Since the first description of Wegener's granulomatosis in 1931,[1] numerous case reports and reviews have documented that the target organs are the upper and lower respiratory tracts and the kidney. As early as 1936 Wegener[2] noted the potential involvement of the heart, and by 1958, Walton[9] documented 10 patients with Wegener's granulomatosis. His review of published reports at that time stated that some 11% of these patients had cardiac involvement with granulomata and approximately 28% had focal necrotizing arteritis of the heart. In 1980, Forstot, *et al.*[4] emphasized the variation in electrocardiographic and morphologic findings. They noted coronary arteritis and pericarditis in 50% of the reported cases of Wegener's granulomatosis, myocarditis in 25%, and myocardial infarction in 11%. Our case had serofibrinous pericarditis, myocarditis, and endocarditis with granulomata; in addition, extensive damage of the common bundle of His and right bundle branch occurred.

As to the involvement of the conduction system in Wegener's granulomatosis, James, *et al.*[5] in 1966, first reported the histologic findings of the conduction system in 3 cases of Wegener's granulomatosis among six cases of polyarteritis nodosa or its allied disease. They said that the sinus node was severely affected by granulomatous changes, associated with sinus node arteritis. The AV node also had similar changes, although the degree of the lesion was less

in the AV node. In this report they never differentiated Wegener's granulomatosis from periarteritis nodosa.

In 1968 Longauer[6] reported the case of a 47-year-old female with advanced AV block associated with this disease. The patient showed fibrosis, hyalinization, necrosis, and granulomatous tissue in the conduction system.

In 1984 Allen, *et al.*[7] reported two women, aged 53 and 67, who died of renal failure due to severe necrotizing granulomatosis involving the kidneys, lungs, spleen, heart, systemic vessels, and skin; abnormal P waves were found in the ECG of one, attributable to atrial involvement. Histology of the conduction system was studied by serial section. The sinus node of the first case revealed loss of conducting myofibers and excess fibrous tissue, but no recent or active damage. There was severe inflammation in the AV node and the penetrating His bundle. In the second case, despite the loss of myofibers in the sinus node and an excess of fat cells in the penetrating His, the inflammatory changes were not present in the conduction system.

Contrary to the findings of James, *et al.*[5] our case presented remarkable changes of the conduction system such as granulomatous inflammation located in the common bundle of His and the first and second portion of the right bundle branch as well as the distal part of the left bundle branch. Conduction system changes and extensive, active granulomatous, necrotizing myocarditis, may induce terminal refractory ventricular tachyarrhythmias. The inflammatory changes of the tricuspid valve and the mitral valve were also remarkable, which may explain the existence of MR and TR signals by color Doppler imaging. Godman, *et al.*[10] reported the changes of the mitral valve in Wegener's granulomatosis, but no report on the changes of the tricuspid valve like our case was done.

In summary, this case presents the effects of Wegener's granulomatosis involving the heart and the conduction system (pancarditis).

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