

Tuberculous Serositis Coexisting with Reversible High-Grade Atrioventricular Block

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We report two young male patients with documented tuberculous serositis that were complicated with high-degree atrioventricular block (AV block) during the course of the disease. In contrast to the previously reported irreversible nature of tuberculosis-related AV block, these conduction abnormalities in our cases resolved spontaneously under antituberculosis treatment. Such reversible tuberculosis-related AV block, to our knowledge, has never been reported before and could be important for physicians who treat patients with tuberculosis and newly-developed conduction block.

Key Words: Tuberculosis • Serositis • Atrioventricular block

Tuberculosis remains a major infectious disease nowadays. Each year, more than eight million new cases of tuberculosis are diagnosed and three million people die of this disease.¹ Cardiac involvement in tuberculosis, though relatively rare in the post-antituberculosis chemotherapy era, can be hemodynamically life-threatening if not identified or treated appropriately. Tuberculous pericarditis represents the most common form of cardiac tuberculosis, which occurs in 0.35% of cases of tuberculosis.² Tuberculous involvement of the cardiac conduction system is extremely rare, and most instances were attributed to direct destruction of conductive tissue, especially in cases of myocardial tuberculosis. In this report, we describe two cases of tuberculous serositis diagnosed at National Taiwan University Hospital in 2001, which were complicated by reversible high-grade heart block during the course of the disease.

CASE REPORT

Case 1

A 17-year-old man was diagnosed with pulmonary tuberculosis and tuberculous pleurisy with a presentation of fever, diaphoresis, and right pleuritic chest pain. Chest radiograph showed a massive right-sided pleural effusion; thoracentesis revealed an exudative effusion with predominantly lymphocytes. Sputum and pleural effusion cultures both yielded *Mycobacterium tuberculosis*. The patient received antituberculosis therapy consisting of isoniazid, rifampin, ethambutol, and pyrazinamide. Pyrazinamide was discontinued later due to elevated liver enzymes. The patient did well until six weeks after initiation of antituberculosis treatment, at which point he experienced marked fatigue. Physical examination disclosed a slow pulse rate (52 beats per minute) and periodic appearance of cannon a-waves in the jugular venous pulse. Oxygen saturation was 97 percent on room air. Electrocardiogram revealed third-degree AV block with a ventricular escape rate of 50 beats per minute (Figure 1, Panel A). Temporary pacing was instituted for symptomatic bradyarrhythmia. Serum levels of myocardial enzymes were not elevated during the serial follow-up laboratory studies. Transthoracic echocardiogram did not reveal any structural cardiac abnormality. The cardiac rhythm reverted to sinus with a

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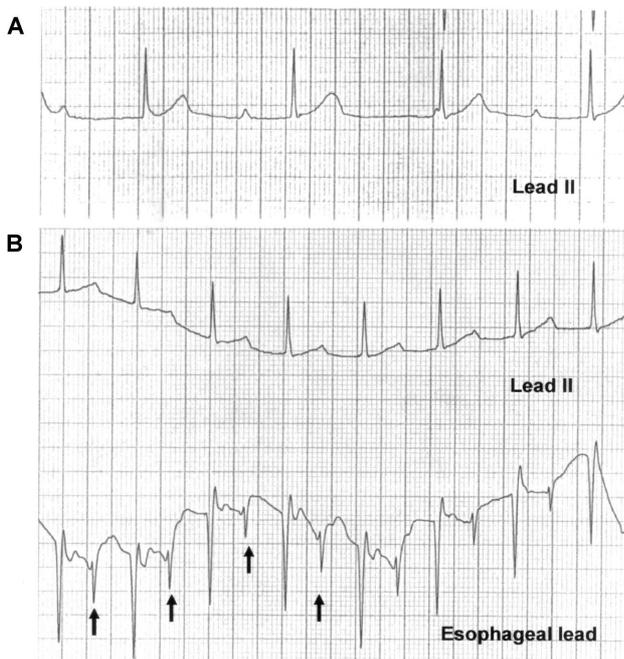


Figure 1. (A) ECG demonstrating complete heart block in a TB patient received six weeks of anti-tuberculous treatment. (B) ECG two days later in the same patient showing marked first degree AV block (PR = 425 ms). Top panel is lead II; lower panel is a simultaneous esophageal lead with atrial activity (arrows).

marked first-degree AV block (PR interval = 425 ms) two days later (Figure 1, Panel B). Blood biochemistry testing showed otherwise normal data except for slightly elevated liver enzymes. Endomyocardial biopsy was suggested, but the patient declined.

Case 2.

A 27-year-old man presented with a 10-month history of dry cough, night sweats, painless swelling of the cervical lymph nodes, progressive lower extremity edema and exertional dyspnea. Physical examination revealed frankly engorged neck veins with deep Y and X descents. Marked hepatosplenomegaly with abdominal shifting dullness and leg edema were also noted. Chest radiography revealed increased cardiac silhouette and massive bilateral pleural effusions. Transthoracic echocardiography disclosed a thickened pericardium, minimal pericardial effusion, and marked respiratory variation in mitral, tricuspid, pulmonary and hepatic flow, by which constrictive pericarditis was diagnosed. Diuretics and salt restriction were prescribed along with empirical four-drug combination antituberculosis therapy consisting of isoniazid, rifampin, ethambutol, and pyrazinamide. The patient was admitted

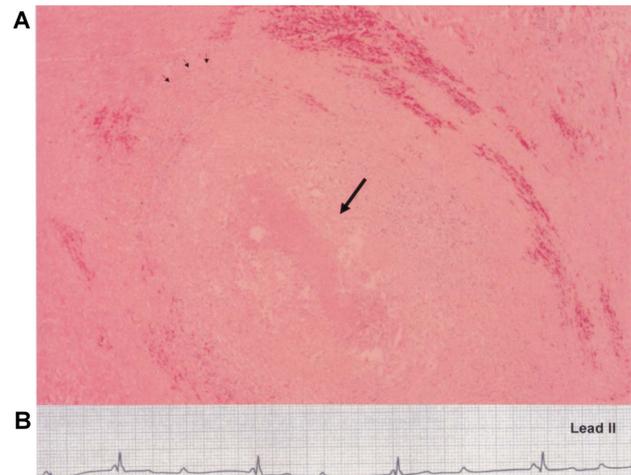


Figure 2. (A) Section of the resected peri-myocardium (100 X) showing tuberculous inflammation. Caseous necrosis can be seen in the central part of the figure (arrow). Fibrotic change of the peri-myocardium can also be found in the periphery (arrow heads). (B) ECG showing third-degree AV block in the patient with constrictive pericarditis due to tuberculosis. Normal AV conduction was restored one day after pericardiotomy.

due to intractable congestive symptoms. One day after admission, he was found unconscious on the floor, and pulseless electrical activity with complete AV block was noted on EKG (Figure 2B). He was successfully resuscitated but required extracorporeal membrane oxygenation (ECMO) because of profound shock refractory to medical treatment. Immediate blood testing did not reveal significant alkalosis, acidosis or alteration in the levels of electrolytes. Pericardiectomy was carried out two days later, at which point caseating necrosis and fibrotic changes in the peri-myocardium were noted (Figure 2A). Ziehl-Neelsen stain was negative, but a positive nucleic acid amplification test (Roche's COBAS AMPLICOR™ MTB Test) suggested the presence of *M. tuberculosis*. The patient was successfully weaned off of ECMO one day after cardiac decortication. Follow-up ECG showed restoration of normal AV conduction. There was no more AV block during the follow-up period of two months. Sputum and pericardial tissue culture yielded *M. tuberculosis* six weeks after the episode of cardiac event.

DISCUSSION

Myocardial tuberculosis is very rare, with an estimated incidence of 0.24-0.28% from two postmortem

studies prior to the introduction of antituberculosis treatment.^{3,4} Atrioventricular block as a complication of myocardial tuberculosis is even rarer.⁵⁻¹² However, most of these reported cases were irreversible and caused either by tuberculous inflammation with direct destruction of the AV node or inter-atrial/ventricular septal tuberculoma. We have presented in this report two cases with TB serositis and reversible AV block, a finding which, to our knowledge, has never been described.

The possibility that the AV blocks in these two cases were attributed to drug effect can be excluded, since none of the antituberculosis drugs prescribed in both cases has been reported to be associated with conduction disturbances. Metabolic factors are also unlikely to be the cause, because no derangement was detected in electrolyte and acid-base status in both cases.

We propose two possible mechanisms leading to high-grade AV block that can be reversed after appropriate medical treatment in our cases. In the first case, the transient and reversible complete AV block developed during effective antituberculosis treatment might be one of the manifestations of the paradoxical tuberculous responses, which were thought to be related to the recovery of the patient's delayed hypersensitivity response and increased inflammatory responsiveness to mycobacterial antigens released after antituberculosis therapy.^{13,14} The paradoxical response often subsides spontaneously while the patient is kept on antituberculosis treatment and this might explain the reversible nature of high-grade AV block in this patient. However, the hypothesis can only be approved if serial endomyocardial biopsy was done, which has been declined by the patients.

In the second case, pericardial and myocardial involvement by tuberculosis was evident from the pathology of resected peri-myocardium. Whether the AV node was directly involved by tuberculosis could not be confirmed from the limited surgical specimen. However, partial rather than global myocardial involvement by granulomatous inflammation might explain the reversible nature of high-degree AV block. The complete AV block could be the consequence of peri-nodal tissue inflammation rather than direct destruction of the AV node. Restoration of normal AV conduction after pericardiectomy also supports the likely reversible nature of the conduction disturbance.

Nonetheless, we could not exclude the possibility that the reversible high-grade AV block could have an-

other etiology, such as viral myocarditis or drug effect, and that there could be no causal relationship between the tuberculous infection and AV block. In the second case, constrictive pericarditis could result in increased right ventricular (RV) pressure and RV stretch. The high-grade AV block might be related to vagotonia as a consequence of RV stretch, which could be relieved after pericardiectomy. Moreover, it is our hypothesis that if the AV block is related to tuberculous infection, the best way to restore normal AV nodal conduction is to eradicate the infection with the use of antituberculosis therapy. However, it is also possible that the AV block could still be reversible even without any intervention.

In conclusion, high-grade AV block can develop in patients with tuberculous serositis and can lead to catastrophic consequences. With appropriate supportive care and anti-tuberculosis treatments, the conduction disturbances can recover spontaneously in a few days without the necessity of pacemaker implantation.

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結核性漿膜炎併發可逆性高度房室傳導阻滯

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我們報告兩位年輕男性罹患結核性漿膜炎，而併發高度房室傳導阻滯的個案。相對於過去大多數報告因結核病引起的心臟傳導異常，多為不可逆的破壞性病變，本報告的兩例個案在抗結核藥物治療下經一段時間的觀察後，自然恢復傳導功能，證實結核菌感染亦可併發可逆性心臟傳導阻滯，這個現象過去鮮有報導，對於處理結核病人併有新生傳導阻滯的醫師而言，該現象亦有其臨床的重要性。

關鍵詞：肺結核、漿膜炎、房室結傳導阻斷。