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CASE REPORT

Ventricular tachycardia in a disseminated MDR-TB patient: a case report and brief review of literature

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Abstract **Although significant breakthroughs have been achieved in tuberculosis management, we still encounter numerous difficulties in diagnosis and treatment of the disease. Additionally, a new challenge, multidrug-resistant tuberculosis (MDR-TB) with unspecific clinical presentation, often results in delayed diagnosis. In this paper, we reported a case of disseminated tuberculosis with rare presentation of ventricular fibrillation, which proved resistant to both isoniazid and rifampicin. A review of literature showed that ventricular fibrillation or tachycardia in tuberculosis patients with pericarditis or myocarditis has been sporadically reported in the past, but none has been conducted involving patients with MDR-TB infections.**

Keywords tuberculosis; MDR-TB; ventricular tachycardia

Introduction

Ventricular tachycardia or fibrillation in tuberculosis patients has been intermittently reported, but not in severe disseminated multi-drug resistant tuberculosis (MDR-TB) patients who responded well to reserve anti-tubercular drugs. We revealed a case of severe disseminated MDR-TB with a rare presentation of ventricular fibrillation. *Mycobacterium tuberculosis* had infected almost every organ of the body, including the brain, lung, heart, liver, spleen, bone and joint. After treatment with electrical defibrillation, anti-arrhythmia agents, and a 5-drug anti-tuberculosis regimen, the female patient achieved a stable condition.

Case presentation

On June 19, 2012, a 22-year-old, previously well female college student was transferred to our hospital with a history of arthralgia for 1.5 years. She also suffered from fever (T_{max} 41 °C), cough, and progressive dyspnea for 1.5 months. Rheumatoid arthritis was suspected 1.5 years previously when she consulted a doctor regarding pain in her distal interphalangeal joints, which was later excluded due to negative results for related factors, including rheumatoid factor, anti-citrullinated peptide, anti-keratin antibodies and anti-perinuclear factor. Six months before admission, her right ankle became swollen with severe pain, and the swelling portion burst spontaneously with dark bloody secretion after 2 months of treatment with traditional Chinese medicine. Unfortunately, the thick, bloody secretion garnered little attention from the doctor, and it was not tested for TB and other pathogens. Enhanced computed tomography (CT) revealed several small nodules in the right lung and enlarged mediastinal lymph nodes, as well as enlarged liver and spleen accompanied by well-defined ovoid low-density lesions (Fig. 1). However, she opted out of further examination, and definite diagnosis was not made at that time.

Roughly one month before admission to our hospital, the patient began to suffer from fever, cough with yellow sputum, and shortness of breath on exertion, which were treated as symptoms of common cold. During treatment, her condition suddenly deteriorated, with the patient experiencing palpitation and orthopnea. Then, she was hospitalized in a tertiary hospital in Beijing for acute left heart failure. CT scan indicated multiple nodules in both lungs with pleural effusion accompanied by brain abscess and bony destruction of right ankle (Fig. 2A to 2C).

Diagnosis of infectious endocarditis was presumed. However, her condition deteriorated despite treatment with

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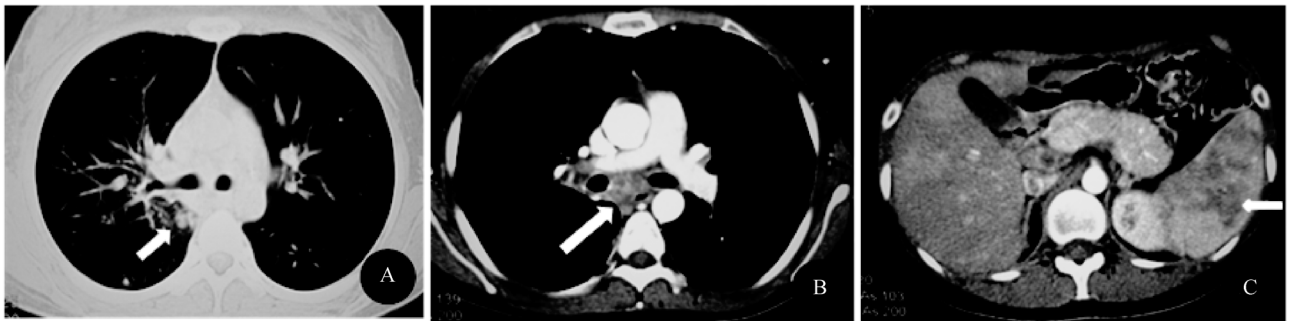

Fig. 1 Enhanced CT scan showing a few small nodules in the right lung (A, arrow), enlarged mediastinal lymph nodes (B, arrow), and enlarged liver and spleen accompanied by well-defined ovoid low-density lesions (C, arrow).

potent, broad-spectrum antibiotics and cardiovascular drugs. Particularly, her heart function noticeably declined, with the left ventricular ejection fraction decreasing from 59% to 22%. She even had two episodes of ventricular fibrillation (May 19, 2012) and recurrent ventricular tachycardia (electrocardiogram in Fig. 2E and supplementary Fig. 1). Echocardiography showed decreased motion of both ventricles without any vegetation, and repeated blood culture showed negative results. Therefore, infectious endocarditis was excluded from consideration.

On June 18, 2012, the patient was transferred to our hospital. At admission, her blood pressure was 86/40 mmHg, with heart rate of 150 to 160/min and with fever at 39 °C. Systolic murmurs in the mitral valve were observed, and the tricuspid valve and decreased breath sounds in the right lung could be noted. In addition, her liver and spleen were evidently enlarged, but no edema was seen in her lower extremities. A review of her history did not reveal the use of corticosteroids and other immunomodulators. Both her parents were healthy, and no previous or current history of tuberculosis was noted in her close contacts. Chest CT scan showed multiple nodules in both lungs (Fig. 2D). Hematological analysis revealed mild anemia and normal white blood cell count. Biochemical investigation yielded the following results: elevated alkaline phosphatase (ALP); lactate dehydrogenase (LDH) with decreased albumin; and troponin C (CTnI) levels in 48 h of serial monitoring during the worst condition of her heart function (ranging from 0.00 ng/ml to 0.04 ng/ml), which were within the normal range. The patient tested negative for HIV antibody. Pathogenic examination found acid-fast bacilli and positive TB-PCR in the sputum specimens collected on three days (June 19, 22, 23) (Fig. 3A). Pulmonary tuberculosis was suspected, and combined anti-tuberculosis therapy (isoniazid, rifampicin, ethambutol, and pyrazinamide) was provided. After four weeks of treatment, she still suffered from high fever and paroxysmal ventricular tachycardia. During hospitalization, she was afflicted with seizures, gastrointestinal bleeding, recurrent heart failure, and tachycardia. On July 20, sputum and bone marrow cultured positive for *M. tuberculosis* (Fig. 3B, 3C).

Gene mutations of *rpoB* and *katG* codon 315 were detected by new GenoType MTBDRplus assay [1] (Hain Lifescience GmbH, Nehren, Germany), which were responsible for rifampin and isoniazid resistance, respectively. Disseminated MDR-TB was subsequently diagnosed, and treatment was changed to reserve anti-tuberculosis drugs (amikacin, protionamide, pyrazinamide, ethambutol, and moxifloxacin), which yielded a satisfactory result. By August 3, 2012, ventricular tachycardia disappeared, the patient's temperature returned to normal, and she was discharged in a stable condition on the 5-drug anti-tubercular regimen. Two months later, the enlargement of the liver and spleen was slightly reduced, and echocardiography showed fibrosis changes in the left ventricular wall (Fig. 4). Her heart condition evidently improved, with the left ventricular ejection fraction normalizing to 66%.

Discussion

Since streptomycin, the first anti-tuberculosis drug, was introduced into clinical practice by Waksman 60 years ago, great breakthroughs have been achieved in tuberculosis management. Nearly 6 million people's lives have been saved over the past 15 years. However, the disease has not been completely conquered: tuberculosis continues to infect and even kill millions of people every year in the new century [2]. Due to inadequate treatment, a new challenge to the management of the disease is posed by multidrug-resistant tuberculosis.

Given the lack of effective and rapid laboratory diagnostic capacity for tuberculosis, especially for MDR-TB, most patients have been severely sick and already infected many others by the time they were treated [2]. MDR-TB is a serious challenge worldwide, especially in low-income countries [3]. A national survey in China revealed that 5.7% new cases and 25.6% previously treated cases were MDR-TB [3]. Due to its unspecific clinical presentation, disseminated tuberculosis exerts more difficulty in differential diagnosis. About 33% to 88% cases of all disseminated tuberculosis found at autopsy

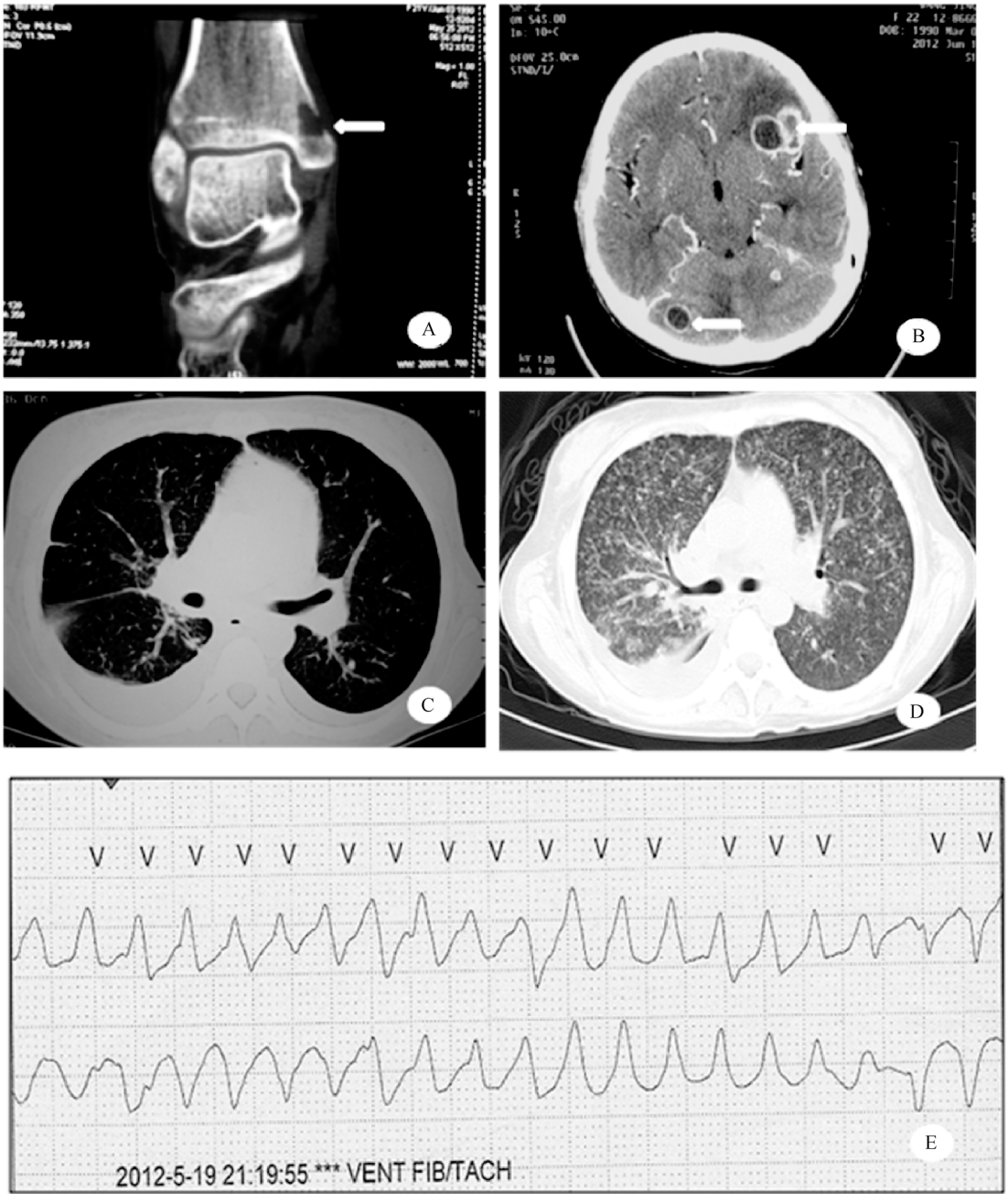

Fig. 2 (A) Computed tomography showed bone destruction in the right ankle (arrow). (B) Enhanced computed tomography of the brain revealed multiple lesions with ring-like enhancement in the edge (arrows). (C) Chest computed tomography showed disseminated nodules in both lungs with pleural effusion. (D) Disseminated tubercules could be seen in both lungs. (E) Electrocardiogram recorded from the patient when she complained of palpitation. Ventricular fibrillation featured by the disappearance of QRS wave, which was replaced by f wave.

were missed or misdiagnosed ante-mortem [4]. The most frequently seen symptoms include fever, cough, back or joint pain, dyspnea, and malaise, whereas ventricular tachycardia or fibrillation was only intermittently described by case reports [4].

We performed a literature retrieval of disseminated tuberculosis complicating ventricular arrhythmia. Overall, 7 cases have been described in both English and Chinese literature, including 5 men and 2 women with ages ranging from 19 to 64 years [6–12]. Ventricular tachycardia happened to all of them, and ventricular fibrillation supervened in 3 patients. Of the 7 cases, tubercular pericarditis was observed in only 2, and 5 patients were confirmed to have myocardial tuberculosis. Histologically, tuberculoma was seen in three

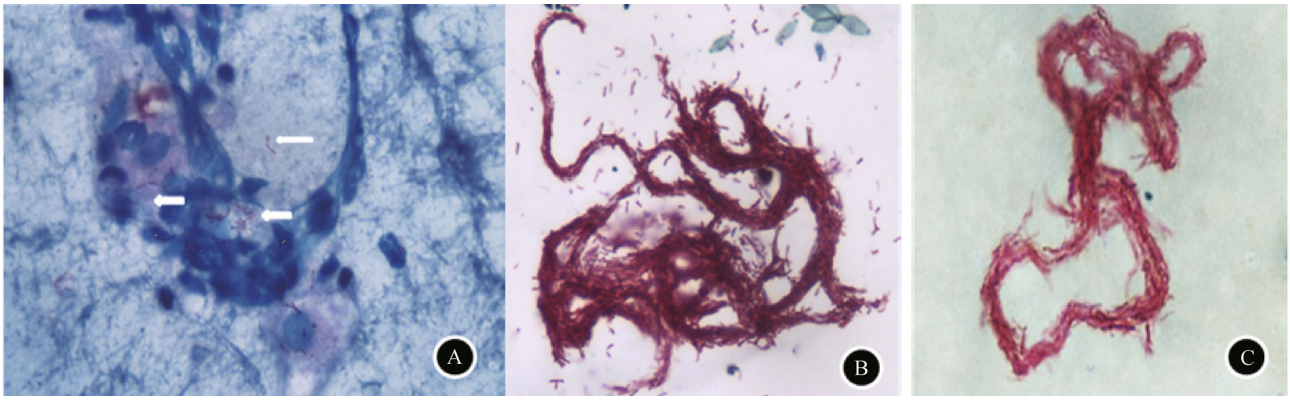

Fig. 3 Identification of acid-fast bacilli from sputum and bone marrow. (A) Acid-fast bacilli could be found in the sputum smear (arrows). (B and C) Bone marrow (B) and sputum (C) culture were both positive for *M. tuberculosis,* with the cord factors being found.

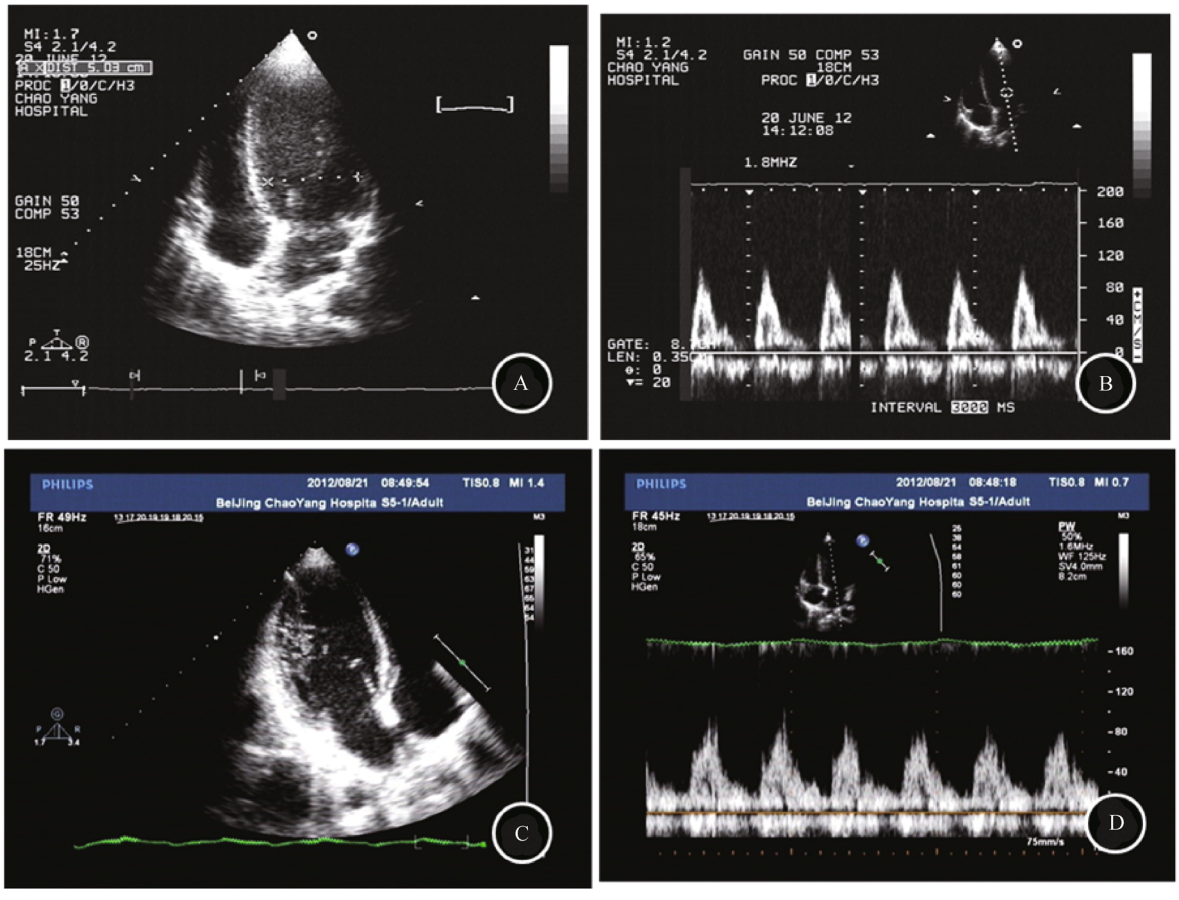

Fig. 4 Two-dimensional echocardiogram before antituberculosis (June 20, 2012) (A, B) and after 2 months of antituberculosis treatment (C, D). (A, B) The left ventricular chamber was slightly enlarged, with decreased motion of both ventricles, and no vegetation was noticed. (C, D) Fibrosis changes were found in the left ventricular wall (arrow), with the left ventricular ejection fraction at 66%.

patients. Only three of them underwent echocardiography, resulting in normal, mild concentric ventricular hypertrophy, and right ventricular intracavitary mass, respectively [7–10]. The three patients recovered with treatment of anti-tuberculosis drugs and anti-arrhythmia agents. Of the 4 patients who died, 2 were diagnosed postmortem with tuberculosis, whereas the other 2 patients died from tuberculous sepsis and ventricular fibrillation during anti-tubercular treatment,

respectively [10,11]. In summary, the heart (including pericardium) is involved in all patients of disseminated tuberculosis, presenting ventricular tachycardia or fibrillation. It has a higher incidence in patients with myocardial tuberculosis than tubercular pericarditis. For pericarditis and the nodular type of myocardial tuberculosis, echocardiography proved to be an effective assistant examination, but it was limited in the detection of military or infiltrative type of myocardial tuberculosis. In several reports, MRI proved to be a useful tool for those with normal echocardiogram [5].

Cardiovascular (including pericardium) involvement occurred in about 1% to 2% of the TB patients, whereas the incidence of myocardial tuberculosis discovered during autopsy was about 0.25% [5]. Diagnosis of myocardial tuberculosis is now, mainly based on invasive procedures to obtain the diagnostic specimen. Positive PCR, TB culture, or acid-fast bacilli isolation were believed to provide definitive diagnosis [5]. Although histological diagnosis was not performed in the patient described in this report, myocardial tuberculosis was strongly considered based on the clinical, radiological, and laboratory features. However, based on the available evidence for our patient, tuberculous endocarditis could not be absolutely excluded. Presently, no consensus for the management of myocardial tuberculosis is in place, and treatment is mainly based on empirical guidance.

Ventricular tachycardia or fibrillation in TB patients has been occasionally reported previously, but severe disseminated MDR-TB patients who responded well to reserve antitubercular drugs have not been reported. This case is a good example demonstrating the considerable challenge of an immune-competent college student suffering from disseminated MDR-TB with the rare manifestation of ventricular fibrillation. As for patients with ventricular tachycardia, particularly in cases complicated with tubercular poisoning symptoms, the differential diagnosis of myocardial tuberculosis should be taken into account.

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Compliance with ethics guidelines

Hui Li, Ran Li, Jiuxin Qu, Xiaomin Yu, Zhixin Cao, Yingmei Liu, and Bin Cao declare that they have no conflicts of interest. Informed consent was obtained from the patient for inclusion in this study.

Electronic Supplementary Material Supplementary material is available in the online version of this article at http://dx.doi.org/10.1007/s11684-014-0321-7 and is accessible for authorized users.

References

1. Hillemann D, Rüsch-Gerdes S, Richter E. Evaluation of the GenoType MTBDRplus assay for rifampin and isoniazid susceptibility testing of *Mycobacterium tuberculosis* strains and clinical specimens. J Clin Microbiol 2007; 45(8): 2635–2640
2. Dye C, Williams BG. The population dynamics and control of tuberculosis. Science 2010; 328(5980): 856–861
3. Zhao Y, Xu S, Wang L, Chin DP, Wang S, Jiang G, Xia H, Zhou Y, Li Q, Ou X, Pang Y, Song Y, Zhao B, Zhang H, He G, Guo J, Wang Y. National survey of drug-resistant tuberculosis in China. N Engl J Med 2012; 366(23): 2161–2170
4. Wang JY, Hsueh PR, Wang SK, Jan IS, Lee LN, Liaw YS, Yang PC, Luh KT. Disseminated tuberculosis: a 10-year experience in a medical center. Medicine (Baltimore) 2007; 86(1): 39–46
5. Liu A, Hu Y, Coates A. Sudden cardiac death and tuberculosis — how much do we know? Tuberculosis (Edinb) 2012; 92(4): 307–313
6. Schnitzer R. Myocardial tuberculosis with paroxysmal ventricular tachycardia. Br Heart J 1947; 9(3): 213–219
7. Khurana R, Shalhoub J, Verma A, Assomull R, Prasad SK, Kooner JS, Sethi A. Tubercular myocarditis presenting with ventricular tachycardia. Nat Clin Pract Cardiovasc Med 2008; 5(3): 169–174
8. Behr G, Palin HC, Temperly JM. Myocardial tuberculosis. BMJ 1977; 1(6066): 951
9. O'Neill PG, Rokey R, Greenberg S, Pacifico A. Resolution of ventricular tachycardia and endocardial tuberculoma following antituberculosis therapy. Chest 1991; 100(5): 1467–1469
10. Kirchhof P, Eckardt L, Haverkamp W, Baba HA, Seidl KH, Borggrefe TM, Breithardt G. Intracardiac tuberculoma causing "idiopathic" ventricular tachycardia in a patient without detectable heart disease. J Cardiovasc Electrophysiol 2001; 12(1): 118
11. Zhu Q, Sun G, Qian Y, Li N. Oxalate crystallization and atrioventricular block: a case report. Bulletin of Jinling Hospital (Jinling Yi Yuan Xue Bao) 1991; 2: 175–176 (in Chinese)
12. Zhimin Huang, Weihong Wu, Xiaoying Huang. Ventricular tachycardia caused by tubercular pericarditis: a case report. Jiangsu J Pract Electrocardiol (Jiangsu Xin Dian Yu Lin Chuang Za Zhi) 2000; 3:180 (in Chinese)