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A Case Report of Recurrent Rheumatic Fever: Considerations and Comments

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ABSTRACT

Rheumatic fever (RF) is a prevalent healthcare problem in the developing countries. Recurrence of this disorder is often observed in childhood and adolescence. RF can mimic the presentations of infective endocarditis, and clinicians are not really familiar with this issue. Herein, we present a case of recurrent acute rheumatic fever in a patient suspicious of acute bacterial endocarditis due to her previous RF. Finally, she was definitively diagnosed and underwent valvular replacement surgery and received prophylaxis antibiotics besides regular follow-up.

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Introduction

Acute rheumatic fever (ARF) is a common, preventable health problem in the developing countries (1). It causes 30-35% of cardiovascular admissions in these countries and is an important indication for cardiac surgery (2). ARF is prevalent in subjects in age group of 5-15 years old. It also is a rare complication of carriers of group A streptococcal infection (3). Disturbed immunological response to group A streptococcal infection may lead to ARF in predisposed cases. Although few local outbreaks were observed in many developed countries, it causes a significant burden to healthcare systems (4). Rheumatic heart disease is the complication of rheumatic fever, which can promote susceptibility to acute infective endocarditis (5). Clinical presentations of recurrent rheumatic fever can simulate acute endocarditis and might lead to misdiagnosis. Here, we present the case of a patient with endocarditis manifestations that was followed up and finally diagnosed with recurrent rheumatic fever.

Case Presentation

A 39-year-old female with a previous history of rheumatic fever (15 years ago) was referred to our department with provisional diagnosis of infective endocarditis. According to prophylaxis against recurrent streptococcal infection, she regularly received intramuscular penicillin injection for 10 years every month and was followed up thereafter. During this period of 15 years, she had not experienced any major problems except for mild dyspnea and fatigue. She attended the local general physician's office with one-week history of fever, arthralgia,

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progressive fatigue, and dyspnea and received oral antibacterial agent (ciprofloxacin 500 mg twice a day). She presented with fatigue, asthenia, arthralgia, and palpitation in this period with no chest pain, cough, orthopnea, or any episode of paroxysmal nocturnal dyspnea. Considering the lack of improvement in symptoms and signs and prolonged fever, she was referred to a local hospital with provisional diagnosis of infective endocarditis.

In the work-up, there was no obvious vegetation in transthoracic echocardiography. For more evaluation and performing trans-esophageal echocardiography (TEE), the patient was referred to our center. On admission, she presented with fever (axillary temperature=37.8 °C), blood pressure of 120/85 mmHg, heart rate of 104/minute, and respiratory rate of 20/minute. She had no cardiovascular risk factors. The patient or her family did not have history of pharyngitis. She had no complaints of neurologic symptoms or skin or subcutaneous lesions. She had not travelled out to endemic regions and had not undergone any invasive medical or dental procedures.

We found loud S1 in cardiac auscultation, holosystolic murmur, and opening snap. Diastolic rumbling murmur resumed in pre-systole in the apex. In addition, we detected holodiastolic decrescendo murmur in the left sternal border examination. Primary laboratory findings included white blood cell (WBC) count of 12×10^3/L (with neutrophil dominance [80%]), hemoglobin level of 11.7 g/dL, normal coagulation tests, erythrocyte sedimentation rate (ESR) of 70 mm/first hours, and qualitative C-reactive protein (CRP) test of 3+. Her blood culture was negative two times.

Her chest X-ray showed left atrium (LA) enlargement and mild lung parenchymal congestion. Electrocardiogram revealed a mitral P-wave with sinus tachycardia. She underwent TEE for more evaluation of infective endocarditis. Mildly increased left ventricle size with ejection fraction of 55-60% was detected. Severe LA enlargement, LA volume index of 74 cc/m^2, and dilated left atrium appendix were noted.

Mitral valve showed rheumatismal changes with significant thickening of leaflets tip resulting in severe mitral stenosis (MS; Figure 1) and severe mitral regurgitation (MR). Tricuspid aortic valve was detected with marginal leaflet thickening and commissural fusion between right coronary cusp and non-coronary cusp with no AS, severe aortic insufficiency (AI; holodiastolic flow reversal in descending aorta, vena contracta: 6 mm; Figure 2). There was moderate to high pulmonary insufficiency with moderate tricuspid regurgitation

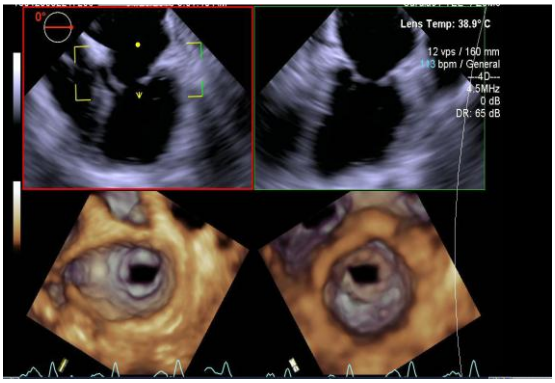

Figure 1. Trans esophageal echocardiography severe MS

and severe pulmonary artery hypertension up to 70 mmHg. Interatrial septum was aneurysmal. No obvious vegetation was seen in TEE.

Due to negative blood culture, as well as no vegetation or history of rheumatic fever (RF), we checked antistreptolysin O (ASO; 400 IU) and anti-DNase (45 U/mL) that were positive. Autoimmune factors and rheumatoid factor were negative. Anti-inflammatory dose of aspirin (Tab ASA 625 mg/every 4 hours in a day), prednisolone (50 mg/twice a day), and penicillin g benzathine (1,200,000 U/stat/IM) were started for the patient. After a week, her condition improved and symptoms of the patient suppressed dramatically; furthermore, ASO was decreased to 200 IU. We discharged the patient with advice of medication therapy and regular follow-up. One month after discharge, she had ASO of lower than 100 IU and negative anti-DNase. We continued the treatment protocol as ASA-Tab 625 mg/three times a day and prednisolone tablet 25mg/twice a day.

After six weeks, echocardiography was performed again, showing dramatic reduction in AI grade (mild AI). Due to severe MS and severe MR, she was referred to a cardiac surgeon for mitral valve replacement (MVR). After operation, no organisms were detected on microscopy of the valve, and all cultures of the valve were negative. Histopathological exam of the valve showed nonspecific inflammation with neutrophil

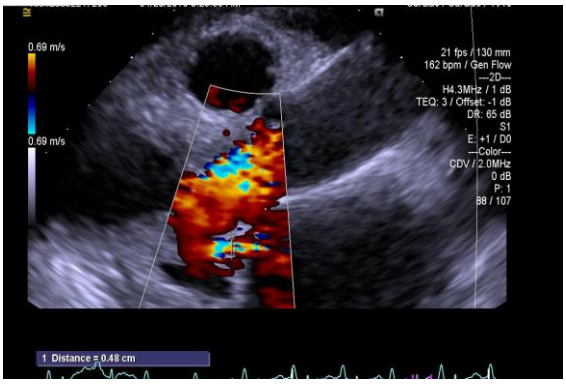

Figure 2. Trans esophageal echocardiography severe AI

infiltration, and fibrin formation was consistent with RF.

Discussion

Rheumatic fever is the cause of cardiac disorder in young age subjects and can lead to adverse events like severe disability and also mortality. Moreover, the frequency of RF has been grown increasingly in developing countries (6, 7). In according to improvements in general health and antibiotic prescription, the increasing rate of RF is tended to be lowered in developed countries (8). The risk of carditis is near to sixty percent of RF patients (9). It should be noticed to recurrence of RF even in mild type of it (10). Prior rheumatic fever and findings of rheumatic heart disease were the most important subheadings in Jones criteria, in the past (11). Subsequently, this manifestation gradually omitted from its criteria. Despite of this change during the time, any new cardiovascular presentation in patient with positive history of rheumatic fever should be considered for relapse (12). Auscultation of new murmur is the necessity of carditis diagnosis, based on Jones criteria. In our case, we have an uncommon age for recurrent RF, and this issue besides prolonged fever at admission shifted our diagnosis to infective endocarditis.

After complementary evaluation, we detected murmur and positive laboratory data plus echocardiography findings compatible with RF and no vegetation. The age of our case was high for RF relapse. Similarly, Kadir et al. presented a case of recurrent acute rheumatic fever in a 20-year-female patient who was initially thought to be suffering from acute bacterial endocarditis on her previously diseased rheumatic aortic valve (13). Rayamajhi et al. performed a cross-sectional study on 51 patients (aged under 14 years). In that study, 26 cases had first-episode RF and 25 had recurrent RF. They noted that arthritis occurred in a significantly large number of first-episode patients, while aortic regurgitation occurred mostly in recurrent RF patients (1). As it can infer, the occurrence of recurrent RF or first-episode of RF is prevalent in very young patients.

We performed TEE and the results encouraged our suspicion to recurrence of RF, which was confirmed with specific laboratory findings. Here, we had one major criterion (carditis), three minor criteria (fever, arthralgia, and elevated acute phase reactions: ESR, CRP), and a high titer of ASO, which verified the diagnosis. Thus, we definitively diagnosed the recurrence of RF.

For prevention of RF, secondary prophylaxis should be considered in such cases. Benzathine benzylpenicillin with a dose of 1,200,000 units for adult patients is recommended by single intramuscular injection every 3-4 weeks. Other regimens are oral penicillin V, sulfonamides, and erythromycin. After valve surgery, lifelong prophylaxis is indicated (14). As the patient was at high risk due to two episodes of RF, MVR and lifelong prophylaxis were deemed necessary.

In the current study, we introduced a rare case of recurrent RF in an adult in a developing country. Although its prevalence is decreasing worldwide, it should be considered in a patient with a previous history of first-episode of RF presenting with fever. Recurrent attacks of RF occur significantly more often in older children, but in the current study we showed it in an adult female. Infective endocarditis is similar to the attack of RF and clinicians should consider it as a differential diagnosis besides the importance of recurrent RF. Therefore, clinicians should be aware of this relapse and include it in their differential diagnosis of febrile patients with a previous history of rheumatic fever.

Patient permission

The patient completed patient permission consent and signed it. We told the patient that the information will be published without her name attached and every attempt will be made to ensure anonymity.

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Conflict of Interest

The authors declare no conflict of interest.

References

1. Rayamajhi A, Sharma D, Shakya U. First-episode versus recurrent acute rheumatic fever: is it different? Pediatr Int. 2009; 51:269-75.
2. Bhardwaj R, Kandoria A, Marwah R, Vaidya P, Singh B, Dhiman P, et al. Prevalence of rheumatic fever and rheumatic heart disease in rural population of Himachal a population based study. J Assoc Physicians India. 2012; 60:13-4.
3. Murray RC, Chennupati SK. Chronic streptococcal and non-streptococcal pharyngitis. Infect Disord Drug Targets. 2012; 12:281-5.
4. Esposito S, Bianchini S, Fastiggi M, Fumagalli M, Andreozzi L, Rigante D. Geoepidemiological hints about *Streptococcus pyogenes* strains in relationship with acute rheumatic fever. Autoimmun Rev. 2015; 14:616-21.
5. Gerber MA, Baltimore RS, Eaton CB, Gewitz M, Rowley AH, Shulman ST, et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis. Circulation. 2009; 119:1541-51.
6. Metzgar D, Zampolli A. The M protein of group A Streptococcus is a key virulence factor and a clinically relevant strain identification marker. Virulence. 2011; 2:402-12.

7. Lee JL, Naguwa SM, Cheema GS, Gershwin ME. Acute rheumatic fever and its consequences: a persistent threat to developing nations in the 21st century. Autoimmun Rev. 2009; 9:117-23.
8. Toor D, Vohra H. Immune responsiveness during disease progression from acute rheumatic fever to chronic rheumatic heart disease. Microbes Infect. 2012; 14:1111-7.
9. World Health Organization. Rheumatic fever and rheumatic heart disease: report of a WHO expert consultation, Geneva, 20 October-1 November 2001. Geneva: World Health Organization; 2004.
10. Carvalho SM, Dalben I, Corrente JE, Magalhães CS. Rheumatic fever presentation and outcome: a case-series report. Rev Bras Reumatol. 2012; 52:241-6.
11. Carapetis JR, Mayosi BM, Kaplan EL. Controlling rheumatic heart disease in developing countries. Cardiovascr J S Afr. 2006; 17:164-5.
12. Jones TD. The diagnosis of rheumatic fever. J Am Med Assoc. 1944; 126:481-4.
13. Kadir IS, Barker TA, Clarke B, Denley H, Grötte GJ. Recurrent acute rheumatic fever: a forgotten diagnosis? Ann Thorac Surg. 2004; 78:699-701.
14. Rémond MG, Coyle ME, Mills JE, Maguire GP. Approaches to improving adherence to secondary prophylaxis for rheumatic fever and rheumatic heart disease: a literature review with a global perspective. Cardiol Rev. 2016; 24:94-8.