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# An Adult Woman Diagnosed with Recurrent Rheumatic Fever and Infective Endocarditis with Manifestations of Prolonged Fever and Heart Murmur

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## ABSTRACT

**Background and Aim:** Rheumatic Fever (RF) is a non-suppurative systemic inflammatory disease with a "delayed autoimmune" caused by Group A streptococcal infections. Inadequate RF treatment causes recurrent RF which is a predisposing factor for Infective Endocarditis.

**Case Presentation:** A 39-year-old woman was admitted to the hospital with chief complaints of intermittent fever since one month ago, shortness of breath during strenuous activities, weight loss, and easy fatigue. Heart examination palpable thrill, grade 3/6 systolic murmur at apex. Laboratory results were Hb 9.4 g/dl, ESR I: 61 mm, ESR II: 159 mm, ASTO 2563 IU/ml, and CRP 8.9 mg/l. Results of Transthoracic echocardiography revealed vegetation on the posterior mitral leaflet measuring 2.09 x 0.7 and blood culture identified Streptococcus alactolyticus.

**Conclusion:** Patients diagnosed with recurrent rheumatic fever and infective endocarditis received empirical antibiotic therapy for 2 weeks and corticosteroids, after follow-up the patient experienced clinical improvement and echocardiography showed reduced vegetation size.

**Keywords:** Recurrent Rheumatic Fever, Prolonged Fever, Infected Endocarditis

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## 1. Introduction

Rheumatic fever (RF) is a non-suppurative systemic inflammatory disease with a "delayed autoimmune" in collagen vascular disorders or connective tissue disorders caused by group A streptococcal infections in genetically susceptible individuals **(1, 2)**. RF can be found worldwide and affects all ages, but 90% of the first attacks occur in the age of 5-15 years. In 1994 an estimated 12 million RF and RHD patients worldwide with 3 million of them having to be treated repeatedly, and mortality in 2000 was 332,000 **(2)**.

Patients with acute RF often develop valvulitis in the first episode. However, chronic and persistent valvular disease after recovery from the initial episode of RF is usually considered a predisposing factor for Infective Endocarditis (IE) **(3)**. IE is an infection that occurs in natural valves and or prosthetic valves on the surface of the endocardium, or devices implanted in the heart. IE is an uncommon infectious disease with an annual incidence ranging from 3 to 10 cases per 100,000 people per year. In 2010, overall IE was associated with 1.58 million causes of death and non-fatal illness or disability **(4, 5)**.

## 2. Case Presentation

A 39-year-old female, working as a housewife, was admitted to the hospital with the chief complaint of intermittent fever 1 month ago. There was a history of fever at 7 months before admission, fever was accompanied by cough, painful swallowing, and joint pain, especially the joints of the knees, elbows, and fingers. Patients were treated with cefadroxil and paracetamol to be taken for 3 days. Two months later the patient felt intermittent fever accompanied by weakness and joint pain, and she was treated with antibiotics and paracetamol which was taken for 3 days. After that the fever reappeared 1 month ago, the patient was then referred for further examination because the doctor previously found a systolic murmur from the physical examination.

The patient also complained of shortness of breath during strenuous activities, decreased appetite, and decreased body weight (unknown how many kilograms), accompanied by easy fatigue during activities. The patient had a history of cavities and had a tooth extraction performed by a dentist 3 months ago. After the procedure, the patient received antibiotics for 3 days but did not know the name of the antibiotic given.

Physical examination revealed poor nutritional status (BMI 17.79 kg/m$^2$), blood pressure 100/60 mmHg, heart rate 106 beats/minute, respiratory rate 24 beats/minute, temperature 38.5˚C, and 99% O2 saturation. Heart examination palpable thrill, grade 3/6 systolic murmur at apex. The laboratory results were WBC 6.92x10^3/µL, Hb 9.4 gr/dL, PLT 200x10^3/µL, Erythrocyte Sedimentation Rate (ESR) I: 61mm, ESR II: 159 mm), ASTO 2563 IU/mL, CRP 8.9 mg/L. The chest X-ray shows a cardiomegaly. The patient's ECG showed within normal limits.

Results of transthoracic echocardiography in the patient obtained LV and RV systolic function both EF 60.5%, LA and LV dilatation, eccentric LVH, severe MR, vegetation in PML size 2.09 × 0.7 (**Figure 1**).

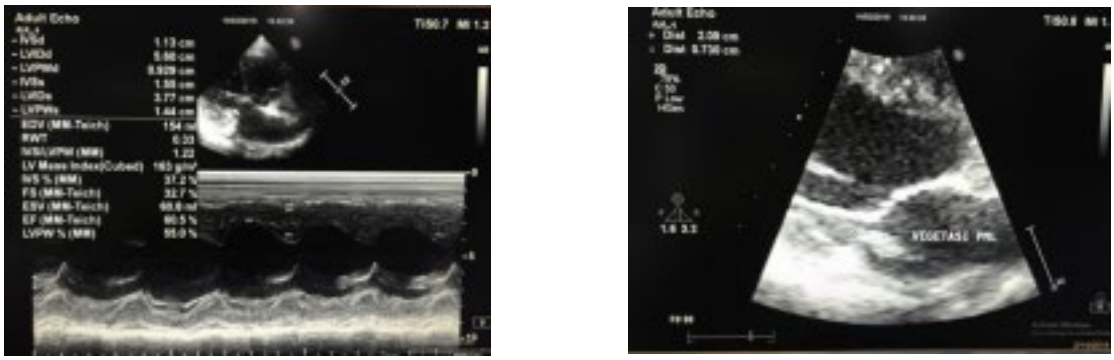

**Figure 1.** Initial echocardiography in RS. Wahidin Sudirohusodo. It looks like a stalked mass that is isolated on PML measuring 2.09 x 0.7

The patient was diagnosed with recurrent RF based on the 2015 Jones criteria which met one major criterion, namely carditis, two minor criteria, namely fever 38.5, ESR I 60 mm and/or CRP ≥ 3 mg/dL, and evidence of group A streptococcal infection, namely ASTO 2563.

The results of blood culture in a liquid medium showed bacterial growth, which after being isolated was identified as *Streptococcus alactolyticus*. In this patient, according to Modified Duke criteria, there were 2 major criteria, namely vegetation from echocardiography and positive culture, and 2 minor criteria, namely predisposing to heart conditions (rheumatic heart disease), intermittent fever, so the patient's diagnosis was Definitive Infective Endocarditis.

During treatment, the patient received 2 weeks of empiric antibiotic therapy and corticosteroids, after follow-up the patient had clinical improvement and echocardiography of the vegetation was still visible with reduced size.

## 3. Discussion

Rheumatic fever treatment has not changed over the years. Management includes anti-streptococcal treatment (primary and secondary prevention) and anti-inflammatory treatment. The drug of choice is oral phenoxymethylpenicillin in an adult dose, 2–3 MIU/day in 2 divided doses every 12 hours for 10 days. For penicillin-allergic patients, cefadroxil 1 gram/day in a single dose for 10 days can be given **(1)**. From the patient's anamnesis, the patient's treatment is inadequate, this may lead to recurrent RF.

Secondary prevention is the prevention of recurrent rheumatic fever with chronic anti-streptococcal treatment: phenoxymethylpenicillin benzathine benzylpenicillin or macrolides. The duration of

secondary prevention is determined individually, depending on whether the patient has developed carditis and complications of chronic valvular heart disease **(6)**. In the above cases, in addition to not receiving adequate antibiotic therapy for primary prevention, the patient also did not receive antibiotic therapy for secondary prevention. In cases of cardiac involvement, a glucocorticoid is given, namely prednisone at a dose of 1-2 mg/kgBW/day for 2-3 weeks, then the dose should be gradually reduced with a duration of glucocorticoid treatment for 6 weeks **(1)**. This patient was given methylprednisolone 62.5 mg/24 hours/intravenously for 2 weeks, then on discharge methylprednisolone 16 mg/12 hours/oral which was taped off for 4 weeks.

Infective endocarditis is a disease caused by bacterial infection of the endocardial lining of the heart. This disease is characterized by the presence of vegetation. IE generally occurs in congenital or acquired heart disease. Patients who have predisposing factors such as congenital heart disease, history of rheumatic fever with cardiac involvement, prosthetic valves, history of endocarditis, and other valvular diseases. In low-income countries, RHD is still a major risk factor for IE, accounting for two-thirds of all cases **(7, 8)**.

Bacteremia often occurs after dental procedures, especially when caries or gingivitis are present. In the anamnesis, the patient complained of cavities and had his teeth extracted by a dentist 1.5 months before the complaint appeared. If caries or gingivitis is present, the bacteremia may be triggered by activities of daily living, such as chewing or brushing teeth **(9)**.

Investigations to diagnose an IE start with a blood culture examination. Cultures were taken before the administration of antibiotics. According to the guidelines, blood samples support the diagnosis if at least 2 samples are culture positive which are taken at an interval of > 12 hours, or 3 samples or 4 separate samples where the first and last samples are 1 hour apart. The culture in this case report used VersaTREK Redox culture medium (Figure 2), using a system (TREK Diagnostic System, Cleveland, OH, USA) that detects bacterial growth by measuring changes in air pressure in the head chamber of the culture bottle. Blood samples were taken as much as 10 cc from 2 different venous puncture points, then the sample was put into a bottle containing 80 ml of broth.

The results of the patient's blood culture found Streptococcus alactolyticus which is a species of Streptococcus bovis/ Streptococcus equinus complex (SBSEC). SBSEC is a Gram-positive bacterium Streptococcus non-enterococcal group D which is divided into several species: *Streptococcus equinus*, *Streptococcus infantarius* subsp. infantarius, *Streptococcus lutetiensis*, *Streptococcus alactolyticus*, and three subspecies of *Streptococcus gallolyticus*, namely *S. gallolyticus* subsp. gallolyticus (SGSG), *S. gallolyticus* subsp. macedonicus and *S. gallolyticus* subsp. pasteuria (SGSP). SBSEC is a normal flora commonly found in the digestive tract of livestock and the human colon. Some SBSECs cause serious infections such as IE in humans, particularly the data from Southern Europe, where there is an increasing prevalence in animals and elderly patients **(10, 11)**.


**Figure 2.** VersaTREK Redox culture media

In addition, echocardiography was performed, and an oscillating stalked mass was found on the mitral valve. Echocardiographic features that can be found in IE patients are vegetations, abscesses, fistulas, valve perforations, valvular regurgitation, and prostheses valve dehiscence. Echocardiography is the initial modality of choice recommended for assessing either native valve infective endocarditis (NVE) or prosthetic valve infective endocarditis (PVE). In NVE patients, TTE has a sensitivity of 50 to 90% and a specificity of 90% **(4)**.

Based on 2015 ESC guidelines, antibiotic treatment of IE due to oral streptococci with normal renal function, the combination of penicillin or ceftriaxone plus an aminoglycoside for 14 days is considered safe and effective **(4, 12)**. This patient was given the empirical antibiotic ceftriaxone 2 grams intravenously and gentamicin 140 milligrams intravenously for 2 weeks.

According to ESC guidelines, mitral NVE with vegetation > 10 mm associated with regurgitation is an indication for surgery with a class IIa recommendation **(12)**. At the time of hospitalization, this patient did not agree to surgery so the treatment was carried out conservatively. In the second week after therapy, the patient was hemodynamically stable, clinical improvement occurred, and control echocardiography

showed a smaller vegetation size than the first echocardiography.

**Figure 3.** Echocardiography 2 weeks after administration of antibiotics

An oscillating stemmed mass appears on the PML valve with a size of 1.7 x 0.8.

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## 4. Conclusion

None.


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## Conflict of Interest

The authors declared no conflict of interest.