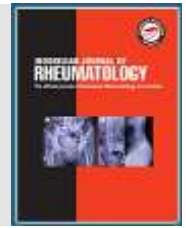




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RECURRENT RHEUMATIC FEVER

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ABSTRACT

Rheumatic fever (RF) may often be encountered in developing country including in Indonesia. RF is autoimmune disease resulted from Group-A Streptococcus upper respiratory tract infection. RF diagnostic criteria underwent some changes since it was first arranged. Patients with RF episode history have a higher risk to experience recurrence following Group-A Streptococcus pharyngeal infection and need long-term antibiotic prophylaxis to prevent severe disease and RHD. Here we present a Case report about patient who has RF and RHD history since the age of 10 years old. This case is reported to show the management and prophylaxis treatment for recurrent RF that can be done next to prevent recurrence of RF in the future.

1. Introduction

Rheumatic fever (RF) prevalence is quite high and more common in children and rarely in adults. RF is autoimmune disease resulted from Group-A Streptococcus upper respiratory tract infection. This Streptococcus is gram positive extracellular pathogen that usually infects pharynx.¹ RF evokes general inflammation involving heart, joints, skin, and brain, either simultaneously or selectively. RF can usually cause rheumatic heart disease later in life.

In the case of rheumatic heart disease (RHD), with heart valve damage, the proper management can be implemented, RHD be controlled.² RF diagnostic criteria have changed from the beginning. Currently,

World Health Organization (WHO) classifies RF diagnostic criteria into primary episode, recurrent episode, and rheumatic chorea with chronic valve lesion. RF is diagnosed based on Jones Criteria consisting major and minor criteria. Supporting evidence of Streptococcus infection becomes one of the diagnostic criteria used.³ Patients with RF episode history have a higher risk to experience recurrence following Group-A Streptococcus pharyngeal infection and need long-term antibiotic prophylaxis to prevent severe disease and RHD.⁴

We hereby submit a case report about RF and RHD suffered by a patient since the age of 10 years old. He also has undergone routine treatment and has been declared cured since the age of 18 years old. He never experiences any symptoms for 2 years until finally at the age of 20, he experienced RF and pharyngitis symptoms caused by Group-A Streptococcus. Based on the diagnostic evaluation, it was considered as recurrent RF. After the treatment was done, his condition improved and he was allowed to go outpatient. This case was reported to show recurrent RF management and prophylaxis treatment can be done next to prevent recurrence of RF in the future.

Case Illustration

Twenty-year old male patient complaint about legs and arms pain which is felt getting worse 1 day prior to admission (PTA). These symptoms occurred when he was doing ordinary activities. There was no traumatic history before. These symptoms first appeared 2 weeks PTA, started with fever, cough, and rhinorrhea. Suddenly high fever occurred accompanied by sore throat and non-productive cough. He also felt lumps in several area of his body, such as plantar part of left foot, left edge of left foot, dorsal-part of right foot, upper left quadrant of abdomen, and near the left elbow. These lumps were painful, mobile, and felt a bit soft. He experienced limitation during movement because of these painful symptom. Two days PTA, due to fever symptoms, he was treated in a private hospital. There, echocardiography and ASTO examination were done, and he was referred to the Cipto Mangunkusumo hospital.

Ten years on PTA, the patient had experienced the same symptoms accompanied by joints pain in the arms and legs. He also complained

palpitations and fatigue. He was diagnosed with RF and RHD by paediatrician. He routinely went to the doctor and get *Penicillin G benzathine* injection until the age of 18 (for 8 years). He was also prescribed analgesic medication. Two-years PTA, general evaluation, including echocardiography, was carried out, and the results were good. He was declared cured of RHD and RF.

For the past 2 years, he no longer went to doctor, all drugs have been stopped, and no symptoms have been appeared. He does his usual daily activities, including climbing mountains. He did not consume drugs or suffer from diseases such as diabetes, hypertension, kidney disease, asthma, and all kinds of allergic reactions. He is the first child of two siblings.

Currently he is a student. He became a smoker and has a history of alcoholic beverages. He has stopped consuming alcohol for the last 4 months. He does not engage in promiscuity or taking drugs. His dietary habit was nutritious. He lived with his parents and used national health insurance.

Physical examination showed vital signs and body mass index within normal limits. General physical examination such as conjunctiva, pharynx, heart, lungs, abdomen, and examination of the extremities is normal. Capillary filling time < 2 seconds. On local physical examination, there are several lumps in several areas such as the left leg, right leg, left arm, right arm, and upper left abdominal quadrant. The lumps are soft, easy to move, warm, and painful when touched. The lumps are considered as erythema nodosum.

Based on laboratory findings there are Hemoglobin 16,2 g/dL, hematocrite 46%, leucocyte 20.300/ μ L, thrombocyte 310.000/ μ L, electrolyte Na/K/Cl 141/3,8/105 mg/dL; PT/APTT 10,7" (10,4") / 37,8" (30,6") ; urea/creatinine 17/1,0 mg/dL; LED 68 mm AST/ALT 10/5,5 / μ L; MCV/MCH: 82/29. Urinary findings are within normal limits. Some

antibiotics such as Cotrimoxazole, Tetracycline, Amoxicillin/Clavulanic acid, Ceftriaxone, Meropenem, Levofloxacin, and Moxifloxacin-were found to be still sensitive to *Klebsiella pneumonia* from pharyngeal swabs. Gram staining examination found Gram negative bacteria, leucocyte 0-1, epithelial cells 0-1. Chest X-ray (figure 2.1), and electrocardiography (figure 2.2) are normal. Echocardiographic examination results in 2014 (figure 2.3) were obtained within normal limits, no valve abnormalities, global normokinetic wall movements, and no pleural effusion. Re-evaluation of echocardiographic examination found global

normokinetic wall movement, TR trivial, good systolic LV and RV function (EF 71%, TAPSE 26.3), good diastolic function, no vegetation (figure 2.4). His ASTO positively resulted 400 and reactive.

Therefore, this patient's assessments were multiple erythema nodosum, recurrent RF, acute tonsilopharyngitis. The management given were soft diet 1700 kcal/day, room air O₂, IVFD Normal Saline 500mL/8 hours, Benzathine penicillin 1x1,2 M unit IM (in emergency department), Clindamycin 4x600mg (po), Sodium diclofenac 2x50mg (po), Methylprednisolone 3x8 mg (po), Lanzoprazole 1x30 mg (po).



Figure 2.1. Chest X-Ray (7th March 2018)

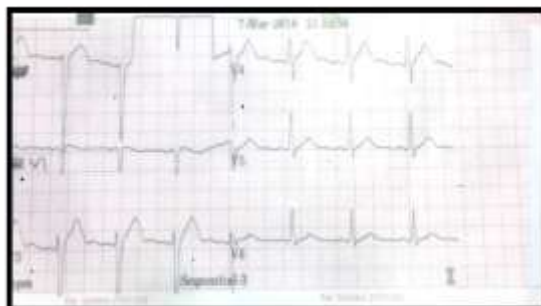




Figure 2.2. Electrocardiography (7th March 2018)



Figure 2.3. Echocardiography (2014)



Figure 2.4. Echocardiography (12nd March 2018)



Figure 2.5. Photo of patient (with patient's permission)



Figure 2.6. Erythema nodosum (with patient's permission)

4. Definition

Rheumatic fever (RF) is non-suppurative sequelae and inflammatory response to *Streptococcus pyogenes* (group A beta-hemolytic streptococcus [GABHS]) infection which commonly occurs 2-3 weeks after a throat infection, affecting mainly children and young adults.¹

Etiology

Streptococci is a group of gram-positive bacteria that is morphologically characterized by coccus and its chains. *Streptococcus pyogenes*, which belongs to GABHS, has the ability to produce toxins capable of lysing the red blood cells. The cytoplasmic membrane is surrounded by a thick layer of peptidoglycan of which is surrounded by S layer consists of carbohydrates, proteins, and glycoproteins. There is also specific type of carbohydrates, rhamnose-N-acetyl-glucosamine dimers with the ability to cross-react with the glycosides of heart valves.⁵

The S layer also contains M proteins that have varying molecular structure. The GABHS has more than 130 serotypes of M proteins. M proteins play an important role in the pathogenesis of streptococcal infection, each of which can cause different clinical manifestation. Some M serotypes are associated with acute RF. M proteins may also escape from immune system by inhibiting the complement activation and phagocytosis. M-like proteins bind to Fc part from IgG and IgA molecules, thus exposing the immunoglobulin layer around the bacteria with Fab part facing outward. This mechanism can inhibit phagocytosis and immune recognition. The bacteria cell walls are surrounded by hyaluronic acid capsules. Since its molecular structure is very similar to human hyaluronic acid, it gives additional protection against human innate immunity. Some rheumatogenic M serotypes have thick capsules and produce mucus when grown on blood agar.⁵ Streptococci produces many extracellular products, such as erythrogenic toxin, streptolysin O, streptolysin S, streptokinase, diphosphoridyl nucleotidase, and deoxyribonuclease.

Streptolysin O may trigger antibody response, antistreptolysin O (ASO), which forms the basis of antibody testing. The antigenicity of which is inhibited by lipid layer of the skin that explains the least association between streptococcal infection of the skin and RF. Streptococci has many antigens similar with mammalian tissues and can cross-reacts with joints, heart (myocardium and heart valves), skin, kidneys, and brain.⁵

Epidemiology

The prevalence of RF is high especially in developing countries. The global incidence of acute RF is estimated at 471,000 cases per year with incidence in children aged 5-15 years between 10 to 374 cases per 100,000 in pacific region.⁶ The peak incidence of acute RF is children aged 5-15 year.^{2,7} Rheumatic heart disease (RHD) is the most common complication of RF. The number of deaths due to RHD is around 233,000 deaths per year. It is estimated that there are 15 million people with RHD worldwide, affecting mainly children and young adults.^{1,8} Recurrent RF is associated with the increased frequency of carditis and other cardiac abnormalities. The incidence of recurrent RF is about 15–34%. The recurrence is high in people with the history of carditis as well as young age.⁸ Individual with family history of acute RF have five-fold greater risk of developing RF.⁷

Pathogenesis

RF is a consequence of *Streptococcus pyogenes* pharyngeal infection. The antigen mimicry of the organism and proteins from the human body can cause both humoral and cell-mediated autoimmune reaction leading to RF. It takes about 3 weeks after the *S. pyogenes* infection to induce a RF as well as causing inflammation of the brain, joints, skin, heart, and other organs.⁷ *S. pyogenes* contains M, T, and R proteins which are associated with the attachment of bacteria to the epithelial cells of the throat. M serotype proteins have the highest rheumatogenicity amongst the other serotypes. The class II HLA molecules, which contributes in antigen

presentation of T-cell receptors) appears to be more associated with an increased risk of acute RF and RHD compared to class I HLA molecules, although there has not been any single or combination of HLA molecules which consistently associated with rheumatic disease susceptibility. The molecular mechanism of class II HLA molecules and its effect to the rheumatic disease susceptibility has not been fully understood.⁷

The autoimmune reaction of RF occurs when the antibodies of GABHS react to human heart. After binding to antigen peptides, the HLA complex initiates an inappropriate T-cell activation. Molecular mimicry of M protein and other heart proteins (myosine, tropomyosine, creatine, laminine, and vimnetin) as well as T-cell cross-recognition of antigen have been identified as the underlying mechanism of RF.⁹ Mannose-binding lectin (MBL) is acute phase inflammatory protein that functions as soluble pathogen recognition receptor. MBL binds various type of sugars on the pathogen's surface and has important role in innate immunity due to its ability to attack pathogen, enhance phagocytosis, and activate complement cascade through lectin pathway.¹⁰ Cytokines (IL-1, IL-6, TNF- α) also have a role in acute RF.

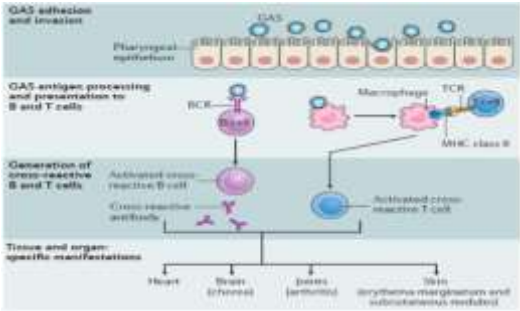


Figure 3.1. Acute Rheumatic Fever Pathogenesis¹¹

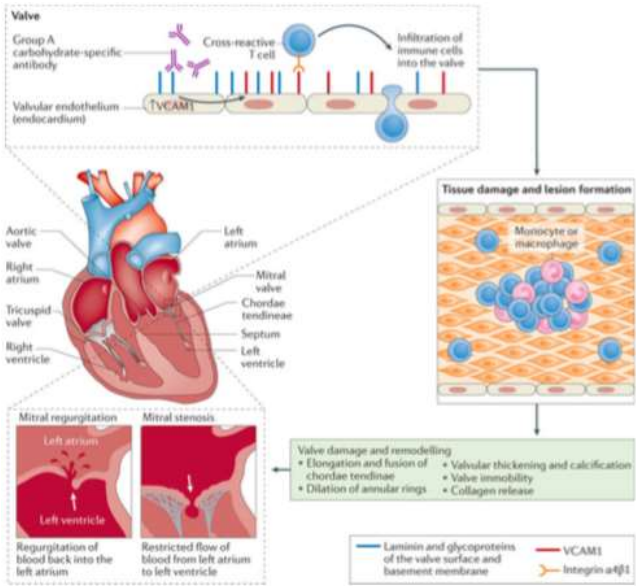


Figure 3.2. The immune cross-reaction response between GABHS and heart¹¹

Clinical Manifestation

Acute RF is usually preceded by GABHS pharyngitis. All clinicians, especially in high-risk populations must thoroughly distinguish GABHS pharyngitis from other pathogens.



Figure 3.3. GABHS acute tonsilopharyngitis¹²

Table 3.1. Clinical features and diagnosis of GABHS pharyngitis¹³

Clinical features of suspected GABHS infection:
<ul style="list-style-type: none"> • Abrupt sore throat • Odynophagia • Fever • Headache • Scarlet fever rash • Nausea, vomiting, and abdominal pain • Hyperemic tonsils and pharynx • Exudates on tonsils and pharynx • Soft palate petechiae (doughnut-like lesions)

<ul style="list-style-type: none"> • Hyperemic and swollen uvula • Tender anterior nodules • 5-15-year old patient • previous exposure history
Clinical features of viral infection: <ul style="list-style-type: none"> • Conjunctivitis • Coryza • Hoarseness • Cough • Diarrhea • Exanthema • Anathema

Generally, major clinical features of acute RF first episode are carditis (50-70%) and arthritis (35-66%).¹⁴ Carditis (valvulitis), which is one of acute RF major criteria, can be clinically diagnosed by finding the murmur in auscultation indicating mitral regurgitation (systolic murmur) or aorta regurgitation (diastolic murmur). Mitral valves are the most common affected valve. Pericarditis and myocarditis may rarely also be affected. Classic RF-related arthritis symptom is migratory asymmetrical polyarthritis which commonly affected big joints.²

The other symptoms of RF are sydenham chorea (10-30%) which commonly affects women, subcutaneous nodules (0-10%), and erythema marginatum (<6%).¹⁴ Subcutaneous nodules and erythema marginatum are very rare findings but very specific in diagnosing acute RF.¹³ Erythema marginatum is a hyperemic skin lesion with pale center, round (serpiginous) margins. A non-pruritic or painful rashes usually occur on the body trunk or proximal extremities. Subcutaneous nodules are non-painful nodules commonly found on the extensor joints, especially knee, elbow, wrist, as well as thoracic and lumbar vertebrae joints. Sydenham chorea is involuntary and non-stereotypical movements of the trunk and extremities. Other symptoms are speech disturbances, frequent dropping of objects, impaired writing ability, and emotional disturbances.^{2,14} Sydenham chorea is a self-limiting symptom which usually takes few weeks to 6 months to heal while some may take 2-3 years. Mild to moderate chorea does not need specific therapy. Chorea

can be triggered by stress and overstimulation.¹⁵

Diagnosis

Diagnostic Criteria

Jones criteria is commonly used to diagnose acute RF. In high-risk population, these criteria are commonly used, while in the low-risk population, these criteria cannot be used. Moreover, the criteria have tendency to overdiagnose and made further specific examination required, such as echocardiography. Hence in 2015 American Heart Association revised the criteria. The diagnosis acute rheumatic heart disease could be made if there are two major criteria or one major with two minors.¹⁴

Table 3.2. Revised Jones Criteria (2015)

First episode of acute rheumatic fever: - Two majors - One major + 2 minors	Recurrent RFL - Two majors - One major + two minors, or 3 minors
Criteria	
Low-risk population	Moderate and high-risk population
Major criteria: - Carditis (clinical and/or subclinical) - Arthritis (polyarthritis only) - Chorea - Erythema marginatum - Subcutaneous nodules	Major criteria: - Carditis (clinical and/or subclinical) - Arthritis (monoarthritis, polyarthritis and/or polyarthralgia) - Chorea - Erythema marginatum - Subcutaneous nodules
Minor criteria: - Polyarthralgia - Fever ($\geq 38,5^{\circ}\text{C}$) - Increased ESR (≥ 60 mm in the first hour) and/or CRP (≥ 3 mg/dL or more than normal value) - Prolonged PR interval (unless carditis is major	Minor criteria: - Monoarthralgia - Fever ($\geq 38,5^{\circ}\text{C}$) - Increased ESR (≥ 60 mm in the first hour) and/or CRP (≥ 3 mg/dL or more than normal value) - Prolonged PR interval

criterion)	(unless carditis is major criterion)
Evidence of preceding GABHS infection (positive throat culture, positive rapid antigen detection test (RADT), increased of anti-streptococcal antibodies titer).	

Table 3.3. The comparison of echocardiography

involvement in diagnosis guidelines :

Year	Guidelines	Perform echo in all-confirmed cases of ARF without clinical carditis?	Perform echo in all suspected cases of ARF?	Use echo to confirm carditis as major criterion in absence of murmur?
1992	Jones Criteria	No	No	No
2000	Jones Criteria Workshop	No	No	No
2001	WHO guidelines	Yes	No	No
2008	Indian working group	Yes	No	No
2008	New Zealand guidelines	Yes	Yes	Yes
2012	Australia guidelines	Yes	Yes	Yes
2015	Jones Criteria 2015	Yes	Yes	Yes

Diagnostic tools

Echocardiography and Doppler

In an era where auscultation ability tend to be decreasing and the availability of more advanced cardiac ultrasound is increasing, echocardiography combined with Doppler

should be used as a diagnostic tool for all cases of suspected acute rheumatic fever.

Table 3.4. Doppler assessment in rheumatic valvulitis

Pathological mitral regurgitation (all 4 criteria met)
- Seen in at least 2 views
- Jet length ≥ 2 cm in at least 1 view
- Peak velocity > 3 m/s
- Pansystolic jet in at least 1 envelope
Pathological aortic regurgitation (all 4 criteria met)
- Seen in at least 2 views
- Jet length ≥ 1 cm in at least 1 view
- Peak velocity > 3 m/s
- Pan diastolic jet in at least 1 envelope
Loading conditions should be accounted for at time of echocardiography/doppler assessment .

Table 3.5. Echocardiogram in rheumatic valvulitis

Acute mitral valve changes
- Annular dilation
- Chordal elongation
- Chordal rupture resulting in flail leaflet with severe mitral regurgitation
- Anterior (or less commonly posterior) leaflet tip prolapse
- Beading/nodularity of leaflet tips
Chronic mitral valve changes: not seen in acute carditis
- Leaflet thickening
- Chordal thickening and fusion
- Restricted leaflet motion
- Calcification
Aortic valve changes in either acute or chronic carditis
- Irregular or focal leaflet thickening
- Coaptation defect
- Restricted leaflet motion
- Leaflet prolapse
On occasion, particularly early in the course of acute rheumatic fever, mitral or valve morphology may be normal on echocardiogram while Doppler shows regurgitation. These findings can also seen in chronic rheumatic heart disease.

Laboratory examination

Elevated *erythrocyte sedimentation rate* (ESR) and/or *C-reactive protein* (CRP) is one of rheumatic fever criterion. Leukocytosis and mild anemia are often found but not specific for ARF. The diagnosis of preceding streptococcal

infection could be established if one of the following criteria is found:

- Increased anti-streptolysin O (ASTO) titre or other streptococcal antibodies (anti-DNASE B)
- A positive throat culture for group A β -hemolytic streptococcus
- A positive rapid group A streptococcal carbohydrate antigen test in a child whose clinical presentation suggests a high probability of streptococcal pharyngitis.

Usually, ASTO is checked first and if the result is negative then anti-DNASE B test can be done. ASTO titer will increase after one week of infection, and reach its peak level on the third week to sixth week post infection. The increase in titer of ASTO and anti-DNASE B may persist for several months after GABHS infection.

Treatment

First-line treatment of RF is to eradicate the agent of infection, which is GABHS. The preferred choice of antibiotics is penicillin G benzathine 1,200,000 IU intramuscularly (IM) for children weighed >20 kg or 600,000 IU for children weighed \leq 20 kg. Other alternatives include:¹³

- Patients which cannot receive intramuscular injection due to hemorrhagic disease can be given oral penicillin V (50 mg/kg/day, 4 times/day) or amoxicillin (50 mg/kg/day, 3 times/day) for 10 days
- Patients allergic to penicillin and its derivatives can be given erythromycin (40 mg/kg/day, 4 times/day for 10 days) or azithromycin (20 mg/kg/day, once daily for 3 days). Tetracycline (high risk of resistance), sulfonamide (cannot eradicate the agents), and chloramphenicol (high toxicity) should not be used.

Other clinical manifestations can also be treated:

- Arthritis: *nonsteroidal anti-inflammatory drugs* (NSAID) for 7-10 days, preferred via oral route:¹⁶
 - Acetylsalicylic acid (80-100 mg/kg/day)
 - Naproxen (10-20 mg/kg/day)
 - Ibuprofen (30 mg/kg/day)
 - Ketoprofen (1.5 mg/kg/day)

- Carditis: prednisone (1-2 mg/kg/day), preferred via oral route, maximum dosage 60 mg/day. The full dosage can be divided into 2 or 3 dosage/day for 15 days and then tapered 20-25% of the dosage for every following week.¹³
- Chorea: Mild to moderate chorea does not need specific therapy besides enough rest and avoiding stressors.¹⁵ Severe chorea can be treated with oral haloperidol (1 mg/day divided to 2 times/day), the dosage can be titrated 0.5 mg every 3 days until the desired effects is reached or maximum dosage 5 mg/day. The treatment is given for 3 months.¹⁷ Extrapyrimal symptoms commonly occur when the dosage is close to maximum dosage. The alternative is valproate acid (30 mg/kg/day, starting from 10 mg/kg/day titrated 10 mg/kg/week).¹⁸ The acute RF guidelines by Australia and New Zealand prefer the valproate acid and carbamazepine as the first-line therapy for chorea due to its fewer side effects.¹⁵

Complication

Mild to moderate carditis, the valve regurgitation can be stable and get better 12 months after diagnosis. Individuals with severe carditis in the first or recurrent episode is at higher risk of developing chronic RHD, associated with higher risk of heart failure, infective endocarditis, pregnancy complication, stroke, arrhythmia, and premature deaths.²

Recurrent rheumatic fever

The diagnosis of recurrent rheumatic fever can be established in individuals with history of acute RF or have been diagnosed with RHD and documented GABHS infection (2 major criteria or 1 major and 2 minor criteria or 3 minor criteria, or 2 minor WHO criteria).¹⁴ Risk factors of higher risk of RF recurrence:^{8,19}

- Young age (\leq 23 years old)
- Inadequate secondary prophylaxis
- History of heart failure

Prevention

The strategy of RF prevention divided into primary and secondary prevention, which are very important to reduce

the incidence of RHD.

Primary prevention

The ideal prophylaxis should be able to prevent acute RF episodes, especially when given immediately after the diagnosis of pharyngitis. Primary prophylaxis aims to eradicate GABHS infection through pharyngitis screening and oral or IM antibiotics. All patients suspected of GABHS pharyngitis (Table 1) is recommended to have throat swab culture or rapid antigen detection test (RADT). Recommended antibiotics for primary prevention are the same antibiotics given for the treatment of RF.¹³

Table 3.6. Primary prevention of RF (streptococcal tonsillopharyngitis)¹³

Therapy	Dosage	Route	Duration
Penicillin:			
Penicillin V (phenoxymethyl penicillin)	Children (BW ≤27 kg): 250 mg, 2-3 times/day Children (BB >27 kg), adolescence, dan adults: 500 mg, 2-3 times/day	Oral	10 days
Amoxicillin	50 mg/kg/day (max. 1 g)	Oral	10 days
Benzathine penicillin G	600,000 IU (BW ≤27 kg), or 1,200,000 IU (BW >27 kg)	IM	Single dose
Alternatives when allergic to penicillin:			
Cephalosporin narrow spectrum (cephalexin, cefadroxil)	Varied	Oral	10 days
Clindamycin	20 mg/kg/day divided into 3	Oral	10 days

	dosages (max. 1.8 g/day)		
Azithromycin	12 mg/kg/day, once daily (max. 500 mg)	Oral	5 days
Clarithromycin	15 mg/kg/day divided into 2 dosages	Oral	10 days
Sulfonamide, tetracycline, and fluoroquinolone are not recommended.			

3.10.2. Secondary prevention

Secondary prevention aims to prevent the recurrence or chronic RF. Recurrent RF can also occur even in patients who have undergone optimal therapy thus the secondary prevention is continuously given to prevent the recurrence.¹³

Table 3.8. Secondary prevention of RF (prevention of recurrence)¹³

Therapy	Dosage	Route
Benzathine penicillin G	600,000 IU (BW ≤27 kg), 1,200,000 IU (BW >27 kg) every 4 weeks	IM
Penicillin V	2x250 mg	Oral
Sulfadiazine	0.5 g/day (BW ≤27 kg), 1 g/day (BW >27 kg)	Oral
Alternatives when allergic to penicillin or sulfadiazine: Macrolide or azalide	Varied	Oral

Table 3.8. Duration of secondary prophylaxis for RF¹³

Category	Duration after last episode
RF with carditis and residual heart disease (persistent valve disorder)	10 years or until 40 years old, some cases need lifelong treatment

RF with carditis without residual heart disease (no valve disorder)	10 years or until 21 years old
RF without carditis	5 years or until 21 years old

Patients' compliance of taking secondary prophylaxis is very important. Doctors should provide enough information to the patients or parents about the benefits and importance of adherence in order to achieve treatment success, ensure patients about the effectivity of the treatment, using the control cards, optimize support from the family and environment to help the patients take medication regularly. The patients need supervisor to ensure the patients take the medicine regularly until the schedule is finished.¹⁹

Discussion

Based on evaluation, it was obtained several assessments such as recurrent RF, multiple erythema nodosum, acute tonsillopharyngitis.

Recurrent RF

The patient is 20-year old male. His chief complaint was painful lumps 2 weeks PTA. This symptom is immunologic phenomenon that is called Erythema Nodosum. This symptom was preceded by acute pharyngitis episode, accompanied by childhood RF history. Erythema nodosum is not cardinal symptom of RF. Distinguished from rheumatic nodule, erythema nodosum characteristically has pain on palpation. Erythema nodosum appearance does not necessarily leads to recurrent RF disease until the other causes related to this lump were excluded.

In this case, recurrent RF diagnosis was made by the elevated ASTO titer showing evidence of Group-A Streptococcus's infection. The RF minor criteria in this case were fever, polyarthrititis, elevated ESR, and previous RF history. Although there is no evidence of carditis due to normal result of electrocardiography and echocardiography, based on Jones criteria, this patient can be diagnosed as recurrent RF based on the presence of polyarthrititis as the major criteria and additionally presence of fever, elevated ESR, elevated ASTO titer as the minor criteria. This patient has been diagnosed RHD and

had routinely gotten treatment for 8 years. The risk factor of recurrent RF is inadequate secondary prophylaxis. Secondary treatment for carditis related-RF must be given for 10 years. The other recurrence risk factor is RHD as RF complication. Patients who have RHD tend to have a higher recurrence risk compared with the others without RHD history. This patient has also been gotten an intramuscular injection of benzathine penicillin with dose 1x1.2 M unit. This treatment should be continued as the secondary prophylaxis for 5 years.

Clindamycin was used to eradicate Group-A Streptococcus. Clindamycin is effective for Group-A Streptococcus, and this antibiotic can be given orally. NSAID was given to relieve erythema nodosum-related pain symptom. Erythema nodosum is a lump with characteristically pain on palpation symptom. It can grow in any part of body, but some were related with systemic disorder. Although erythema nodosum was not included in RF diagnostic criteria, its prevalence was fairly high.

Multiple Erythema Nodosum

The pain at both leg and arm were felt since 2 weeks PTA. There are multiple lumps in hand, foot, and abdominal. These lumps were characteristically pain on palpation, and slightly soft. There was RHD history. We considered it as erythema nodosum because its characteristic was different, either from erythema marginatum or subcutaneous nodule which do not have pain on palpation symptom. We excluded other systemic diseases by performing several examination such as chest X-ray to exclude Tuberculosis, and sputum examination cannot carried out from patients and we don't do the biopsy because at this time patient have a good respond for our treatment. Group-A Streptococcus infection evident showed that this pathogen can cause erythema nodosum. Based on these findings, we considered there was relation between erythema nodosum, Group-A Streptococcus infection, and RF.

Acute Tonsillopharyngitis

The patient experienced fever, sore throat, cough, and rhinorrhea. Physical examination showed hyperemic pharynx. Laboratory findings show elevated leucocyte

count 20.300/μL and from pharyngeal swab we found *Klebsiella pneumonia* that sensitive to cotrimoxazole, tetrasiklin, amoxicillin/ clavulanic acid , ceftriaxone, meropenem, levofloxacin and moxifloxacin. Gram staining examination showed negative-gram bacteria, with slightly increase the number of leucocyte, and epithelial cells. The treatment for this acute tonsillopharyngitis was Clindamycin 4x600mg orally.

Conclusion

Rheumatic fever is a rare case, especially recurrent case in adulthood. Besides immediate treatment, the patients also needs prophylactic therapy to prevent disease recurrence. With the good history taking, physical examination, and comprehensive investigation, diagnosing and treating RF and RHD can be done.

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