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Poststreptococcal Reactive Arthritis in Children: A Serial Case

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***Abstract*—**Infection by group A streptococci (GAS) can trigger an autoantibody that cause a poststreptococcal reactive arthritis (PSRA). Four patients with PSRA aged 10 years to 14 years old with the main complaint of joint pain for five days to 10 days after suffering a fever and sore throat. The joint pain was persistent, additive, and non migratory. All patients revealed an increase in erythrocyte sedimentation rate (ESR) and anti-streptolysin O (ASLO), but the chest x-ray, electrocardiography, and echocardiography were normal. Bone imaging showed no destruction on the affected joint. Jones Criteria were not fulfilled in all patients. Erythromycin and ibuprofen were given in all patients and an improvement was shown. Erythromycin was continued for one year and routine controls were conducted for cardiac evaluation. The prognosis of all the patients was good.

***Keywords*—**Arthritis, group A streptococcus, autoantibody, Jones criteria.

I. Introduction

ARTHRITIS is an inflammation reaction of the joint caused by autoimmune or non-autoimmune process, and can be the primary feature of disease or secondary to the main disease. PSRA is a recurrent arthritis characterized by immune mediated arthritis caused by autoantibody after pharyngeal streptococcal infection. The arthritis is non-migratory, persistent, with duration less than three weeks, and symptoms free of carditis [1], [2].

The age distribution of PSRA appears to be bimodal with a peak at ages eight years to 14 years, and another at age 21 years to 37 years, in the 47% of cases that were children. PSRA is a rare case that systematic review identified 188 cases published in the literature over 20 years around the world. Case reports derived mainly from developed countries, about 60 cases from United State, 20 cases from Asia but no data from Indonesia which may be the result of an under-diagnosis of cases [2], [3].

PSRA is a poorly understood clinical syndrome that has generated much controversy about clear diagnostic criteria and lacking of therapeutic recommendations. Current knowledge supports that PSRA is a distinct entity of disease based on clinical findings, response to therapy and lack of cardiac involvement in almost all cases [2], [4].

The important considerations of patient with PSRA are related to the diagnosis and management that include antibiotics prophylactic. Whether carditis is a late sequalae of PSRA is still being debated, and antibiotic for prophylaxis must be given to patients with PSRA for late carditis because of the current low level of evidence supporting prophylaxis in PSRA [3], [5].

We report a series of cases of PSRA in children focusing on diagnosis and management based on available data and the current evidence base.

II. Case Report

The first case, a 14 year old boy who suffered from a fever lasting eight days and a sore throat, which was followed by joint pain in the right and left elbow, knee, and ankle in the second day after the fever. The pain was persistent and worsened during activity, but there was no stiffness. The patient also had a sore throat and fever two months prior, which was followed by bilateral knee and ankle joint pain, and had a relapse a month prior which was coupled with elbow pain while moving.

A physical examination showed normal heart rhythm, a temperature of 38°C, tenderness and warm to touch around the joints on the elbow, knee and ankle. Laboratory tests found elevated ESR was 60 mm/hr (normal range is 0-20 mm/hr), the C-reactive protein (CRP) level was 11.5 mg/L (normal range is 0-.9 mg/L) and the ASLO level was 400 IU/mL (normal range is less than 200 IU/mL). The chest x-ray, electrocardiography and echocardiography results were normal. The radiologic imaging of the shoulder, elbow and knee were also normal.

The patient did not fulfill the Jones Criteria and was assessed as having PSRA. Treatment was ibuprofen 300 mg three times daily and erythromycin 500 mg four times daily for two weeks. In the follow up after two weeks, there was no complaint, but the patient still had mild pain in the elbow, knee, and ankle joints, with an elevated ESR of 60 mm/hr, and CRP of 11.5 mg/L.

The second case, a 11 year old girl with a complaint of right and left elbow, knee, and ankle joint pain without migratory and stiffness for five days. The patient had fever and sore throat for five days ago. The patient had the first right ankle pain about eight months prior accompanied by the previous symptoms of sore throat and cough for three days. The patient then had had recurrent fever and pain in the right and left elbow, knee, and ankle joint four months later and was admitted to the emergency department for fever and ankle joint pain.

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From the physical examinations were found tenderness, warm to touch and pain without worsening during movement of the affected joints.

The laboratory examination revealed, ESR was 40 mm/hr, CRP level was 102 mg/L and ASLO level was 800 IU/mL. The chest x-ray, electrocardiography and echocardiography results were normal. The radiologic imaging of the right and left elbow, knee, and ankle joint were also normal. The patient did not fulfill the Jones Criteria and the diagnosis was PSRA.

The third case, a 10 year old boy who was complaining of joint pain in the left knee, which worsened during activity, without stiffness and migratory pain and lasting for three weeks. The patient had sore throat and fever one week prior to the joint pain. In an examination of the history of illness, the patient had twice experienced episodes of joint pain following a fever.

A physical examination of left knee revealed tenderness and warm to touch of the tissue and joint. The laboratory tests found leukocyte was 16.500/uL, ESR was 84 mm/hr, and the ASLO level was 800 IU/mL. The chest x-ray and electrocardiography results were normal, as was the radiologic imaging of left knee.

The patient did not fulfill the Jones Criteria and the assessment was PSRA.

The fourth case, a 10 year old boy complaining of joint pain that worsened during activity and constant pain in the right shoulder, elbow, and foot phalanges for the past five days. The patient had fever about four weeks previously, which was followed by joint pain 10 days later. The fever and sore throat reoccurred one week ago. The physical examination revealed joint pain in the right shoulder, elbow, and foot phalanges with tenderness and warm to touch tissues and joints. The laboratory results were ESR was 23 mm/hr, CRP level was 4.9 mg/L, and ASLO level was 400 IU/mL. The chest x-ray and electrocardiography results were normal. The radiologic imaging of the right shoulder, elbow, and foot phalanges were also normal.

The patient did not fulfill the Jones Criteria and was diagnosed with PSRA.

According to anamnesis, physical examination, and laboratory results, all patients were diagnosed with PSRA, and were treated with therapies of erythromycin and ibuprofen. Patients also continue with regular follow ups until one year after diagnosis.

TABLE I
SYMPTOMS AND EXAMINATIONS OF ALL CASES

Symptoms/examination	Case 1	Case 2	Case 3	Case 4
Age	14	11	10	10
Fever	Yes	No	No	No
Sore throat	Yes	Yes	Yes	Yes
Onset of joint pain	7 days	5 days	7 days	10 days
Affected joint	>1, bilateral	>1, bilateral	Knee joint	>1, unilateral
Non-migratory	Yes	Yes	Yes	Yes
Swollen	Yes	Yes	Yes	Yes
Stiffness	No	No	No	No
Sign of carditis	No	No	No	No
ESR	60 mm/hr	40 mm/hr	84 mm/hr	23 mm/hr
ASLO titer	400 IU/mL	800 IU/mL	800 IU/mL	400 IU/mL
Chest x-ray	Normal	Normal	Normal	Normal
Imaging of bone	Normal	Normal	Normal	Normal
Echocardiography	Normal	Normal	Normal	Normal
Echo evaluation	Normal	Normal	Normal	Normal
Jones Criteria	Not fulfill	Not fulfill	Not fulfill	Not fulfill

III. DISCUSSION

Arthritis is a form of joint disorder that involves inflammation because an immune or nonimmune process of one or more joints that can be the primary feature of disease or secondary cause of the primary disease. The pain in arthritis is due to inflammation that occurs around the joint. The joint pain in all patients was persistent, migratory, without stiffness and increased pain during activity. In this case, the joint pain was considered to be the primary cause of the disease. The causes of arthritis in children are shown in Table II [6].

Hemophilia, acute lymphocytic leukemia, lymphoma, and neuroblastoma can be present with joint pain and arthritis. Expansion of lymphoblast in bone metaphysis results in pain, which is typically severe, and may awaken the child from sleep. Thrombocytopenia and anemia are sometimes found in children with malignancy but is rare in children with PSRA, thus its presence suggests the possibility of leukemia. Lymphocytosis is also uncharacteristic of patients with PSRA and raised lymphocytosis suggests the possibility of leukemia, particularly when neutropenia is present [2], [6], [7].

In this case, all patients had previously complained of fever, but there were no complaint of paleness and no history of bleeding. The physical examination revealed no hematoma in the joint, no palpable mass, and no organomegaly was noted. The laboratory results of a complete blood count were also normal. Thus, arthritis caused by hemophilia, acute lymphoblastic leukemia, lymphoma, and neuroblastoma can be excluded.

Arthritis can be caused by tuberculosis; it is usually affected only one joint. Tuberculosis symptoms like recurrent fever, chronic cough (more than two weeks), history of weight loss,

decreasing of appetite, family member that has tuberculosis, palpable lymph node enlargement, chest x-ray with tuberculosis, and bone imaging with destruction of affected joint [6].

TABLE II
CAUSES OF ARTHRITIS IN CHILDREN [6]

Causes of arthritis in children	
Idiopathic	Juvenile idiopathic arthritis
Hematological/malignancy	Hemophilia Acute lymphoblastic leukemia Lymphoma Neuroblastoma
Reactive	Poststreptococcal arthritis Rheumatic fever Post-viral
Infection	Septic arthritis Osteomyelitis Tuberculosis

All of our patients have a history of fever and cough of less than two weeks, no history of weight loss, and no family history of chronic or bloody cough. The physical examination of all patients was normal without palpable lymph node enlargement. The chest x-ray and radiologic imaging of affected joint were also normal. From all these result, tuberculosis in the bone as a cause of arthritis could be excluded in all patients.

The cause of the arthritis in osteomyelitis and septic arthritis can be associated with streptococcal infection. Both of the disorders may produce a similar clinical picture, with warm to touch, acute joint pain less than three days after streptococcal infection, and a severely painful range of motion. Osteomyelitis is usually acute and affects the long bone of arms and legs in children. The bacteria can infect bone through haematogenous or directly through an open wound. A patient may experience fever and chills, and the bone infected by streptococcus is usually unilateral, sore, red, and swollen skin. The bone x-ray may show a sign of infection. Laboratory tests may reveal an increase of leukocyte and CRP. Septic arthritis is a purulent invasion in the joints which produces arthritis in an acute onset usually less than three days. If untreated, it may destroy the joint in a period of days and spread to other parts of the body. Septic arthritis causes pain during movement, joint swelling, warm to touch, and redness. Usually only one joint is affected [6], [8].

The characterization of the joint pain in all patients was mild swollen, and also mild painful on range of motion. From the history, all the joint pain was recurrent and the time of onset of the joint pain after suffering from a fever was more than five days. The affected joints from all the patients were more than one, with the exception of the third patient with only one affected joint. Thus, from anamnesis, the physical and laboratory examination did not support evidence of osteomyelitis and septic arthritis.

Juvenile idiopathic arthritis (JIA) is the most common form of arthritis in children less than 16 years of age. Juvenile idiopathic arthritis is an autoimmune joint disease of more than six weeks duration in children and refers to a condition with no defined cause. Hereditary, genetic mutation and environmental factors may influence the etiopathology, but the mechanism is still not clear, and a virus can trigger this process. A history of the findings in children with JIA may include joint pain and stiffness in the morning or after taking a nap. Swelling is a common first symptom affecting a large joint such as the knee, which may involve one or more joints and may affect other body tissue including swollen lymph nodes, rashes, and eye inflammation. Children with persistent join pain, swelling, and stiffness can have a limited ability to participate in physical activity for months or for the rest of their lives. The bone imaging of the joint shows an inflammation process, erosive, destruction, and deformity [6].

All of the patients had complained of joint pain without stiffness lasting less than two weeks; however, they also suffered recurrent joint pain with complete relief between episodes. The physical examination showed mild swelling of the joint. The laboratory examinations of the ANA test and rheumatoid factor were negative, and C3 was normal. The bone imaging of the affected joint was also revealed to be normal. According to these findings, the diagnosis of JIA can be excluded.

Elevated titer of the anti-streptococcal antibody is of value for identifying a preceding GAS infection. The most commonly used and commercially available are ASLO and anti-deoxyribonucleic B (anti-DNase B). The ASLO titers begin to rise approximately one week, and a peak of three to six weeks after the initial GAS infection. Titers of anti-DNase B starting to rise around one to two weeks and reach a peak of six to eight weeks after GAS infection. Those elevated titers may persist for several months or even years after infection by GAS. The value of the anti-streptococcal antibody examination to confirm a GAS infection in a child is between 300-800 IU/ml for ASLO and 200-800 IU/ml for anti-DNase-B. Elevated ASLO titers more than two standard deviations that repeated two to three weeks after the initial test confirm recent streptococcal infection [4], [7], [9].

The ASLO of all patients was elevated more than 200 IU/mL. Thus, the arthritis was caused by GAS infection, and therefore, viral infection was also least likely to be the cause of the arthritis.

GAS are the most common bacterial cause of pharyngitis and primarily affects school-aged children five to 15 years of age. The vast majority of GAS diseases are superficial infections of the throat and skin, resulting in pharyngitis and impetigo, respectively, and serious infections such as necrotizing fasciitis and streptococcal toxic shock syndrome. Furthermore, repeated GAS infections may trigger serious post infectious immune-mediated conditions affecting a diverse set of organs and tissues, including the heart, kidneys, joints, brain, eyes, and skin, cause disease including PSRA, acute poststreptococcal glomerulonephritis (APSGN), acute rheumatic fever (ARF), and rheumatic heart disease (RHD). The clinical symptoms and diseases epidemiology of GAS infection are shown in Table III [9], [11]-[13].

From history taking, physical examination, and laboratory test results all of the patients revealed repeated GAS infection that triggers a sequel of immune mediated disorders with the

chief complaint being arthritis. GAS infection is associated with several immune-mediated conditions affecting a diverse set of organs and tissues, including the heart, kidneys, joints, brain, eyes, and skin. According to the description in Table III, the sequelae of GAS immune mediated disorder with chief complaint arthritis are PSRA and rheumatic fever.

TABLE III
CLINICAL SYMPTOMS AND EPIDEMIOLOGY OF THE MAJOR GAS INFECTIONS [9]

Disease	Sign and Symptom	Estimated global incidence	Associated M types
Superficial			
Pharyngitis	sore throat, malaise, fever	> 600 million/year	1,3,5,6,12,14
Scarlet fever	deep red rash, strawberry tongue, exudative pharyngitis		17,19,24
Impetigo	impetigo pustules mature into honey-colored scabs	111 million/year	33,41,42,52,53,70
Sequela			
ARF	Polyarthritis migraine, carditis, rash, subcutaneous nodule	> 471.000/year	1,3,5,6,11,12,14,17,18,19,2
Acute post streptococcal glomerulo nephritis	Edema, hypertension, urine sediment abnormality	> 470.000/year	4,27,29,30,32,41
Post streptococcal reactive arthritis	Arthritis non migratory, no carditis		1,4,12,49,55,57,60,1,5,18
Invasive			
Bacteremia	High fever, nausea, vomiting		
Puerperal sepsis	Fever, chills, abdominal pain in pregnant or early postpartum		28
Cellulitis	Acute, tender, erythematous and swollen area skin		
Necrotizing fasciitis	Fever, tender skin lesion, toxemia, tissue destruction		1,3,28
Streptococcal toxic shock syndrome	High fever, rapid onset hypotension, rapid multisystem failure		1,3

The classic condition related to arthritis following throat infections with GAS is ARF. The diagnosis of ARF is established largely on clinical grounds. The description of the clinical manifestations, known as the Jones Criteria, is shown in Table IV. Since 1959, there are reports of patients who present arthritis after GAS infection but do not fulfill the classical Jones Criteria. Furthermore this condition is designated as PSRA [3], [4], [14].

TABLE IV
JONES CRITERIA FOR THE DIAGNOSIS OF ACUTE RHEUMATIC FEVER [4]

The five major manifestations are:
- Polyarthritis (predominantly involving the large joints)
- Carditis, valvulitis and pericarditis (e.g., pancarditis)
- Central nervous system involvement (e.g., sydenham chorea)
- Erythema marginatum
- Subcutaneous nodules
The four minor manifestations are:
- Arthralgia
- Fever
- Elevated acute phase reactants (ESR; C-reactive protein, CRP)
- Prolonged PR interval
Supporting evidence of antecedent GAS infection
Positive throat culture or rapid streptococcal antigen test
Elevated or rising streptococcal titer

The age distribution of PSRA appears to be bimodal, with a peak at ages eight years to 14 years, and another at age 21 years to 37 years. In contrast, ARF has a single peak incidence in childhood at around 12 years, but can affect children aged five years to15 years old. Both genders are equally affected in all age groups of PSRA and ARF [4], [8].

The average age range of the patients in this case was 10 years to 14 years old. The first patient was 14 years old, the second was 11 years old, and the third and fourth were 10 years old. All patients had additive, persistent, and non-migratory joint pain. Post streptococcal reactive arthritis is usually additive and persistent, also typically non-migratory. In contrast, for the patient with ARF, the arthritis is characterized with migratory or flitting and transient joint pain [8], [14].

Post streptococcal reactive arthritis can involve large joints, small joints, or the axial skeleton, particularly those of the lower limb. ARF usually involves the large joints. Involvement of small and axial joint may occur, but is uncommon. Monoarthritis, oligoarthritis, and polyarthritis are equally represented in patients with PSRA, but usually polyarthritis is present in patients with ARF. Table V shows the summary of characteristic joint involvement in patients with PSRA [3], [4].

In this case, the first patient complained of pain in both of the elbows, knees, and ankles. The second patient complained of pain in the left hand, both knees, and the left foot. The third patient complained of joint pain in the left knee. The fourth patient complained of joint pain in the shoulder, elbow, and knee. The most affected was the knee joint and also both of the joints or bilateral.

Patients with both PSRA and ARF have arthritis that follows a symptom after an episode of GAS pharyngitis or tonsillitis. In ARF, arthritis usually occurs 10-28 days after the GAS pharyngitis, while in PSRA arthritis appears after a shorter incubation period, approximately seven-10 days after the infection [3], [4].

All patients had history of recurrence sore throat with fever and were followed by joint pain. In all of patients, the interval between fever and joint pain was less than 10 days. For the first and second patients it was five days later, the third patient was seven days, and for the last patient it was 10 days.

According to the literature, the ESR and CRP levels were significantly higher in ARF (92.2 mm/h and 10.7 mg/dL,

respectively) compared to the PSRA patients (57 mm/h and 2.3 mg/L, respectively) [8]. But in our cases, some patients also had high CRP and ESR.

The first patient had high ESR and CRP (60 mm/h and 11.5 mg/L) on the first laboratory evaluation. The second patient had high CRP (102 mg/L) with a mild increase level of ESR (40 mm/h). The third patient had high ESR (84 mm/h) but only a slight increase in the level of CRP (2.5 mg/L). The last patient had a slight increase in ESR and CRP (23 mm/h and 4.9 mg/L, respectively).

The diagnostic criteria for PSRA are based on these clinical features: 1) Arthritis of acute onset, symmetric or asymmetric, usually non-migratory, can affect any joint, persistent or recurrent. The arthritis is at best only poorly responsive to salicylates or nonsteroidal anti-inflammatory drugs; 2) Evidence of antecedent GAS infection; and 3) Failure to fulfill the modified Jones Criteria for the diagnosis of ARF [1], [3], [4].

None of the patients complained of dyspnoea. Neither a physical cardiac examination, nor an additional examination such as electrocardiography, chest x-ray, and echocardiography revealed any cardiac abnormality. According to the descriptions of the patient's condition above, the diagnosis of rheumatic fever was not found in all the patients. Thus, PSRA was the appropriate diagnosis. The comparison between PSRA and ARF were shown in Table V [4].

PSRA is an immune mediated disease caused by antistreptococcal antibody to cartilage and synovium of the joint. The concept of molecular mimicry between microbial antigens and self proteins in the joint may activate self cross-reactive, thus 'triggering' pathogenic autoreactivity. However, although the phenomenon of self cross-reactivity can be demonstrated in a variety of systems, the extent to which this 'triggers' autoimmune disease remains uncertain [10], [11], [13].

GAS express cell surface M proteins which have an important role in virulence as antigens for host antistreptococcal immunity. There are over 100 different M protein serotypes. For example, some M types have inducing outbreaks of ARF such as 1, 3, 5, 6, 14, 18, 19, 24, 27 and 29. Other M types 2, 49, 57, 59, 60, and 61, are associated with pyoderma and acute glomerulonephritis. Some studies have shown the M types associated with PSRA are 1, 5, and 18 [13], [15].

The C-terminal half of M proteins, which is highly conserved between M serotypes, contains sequences homologous with mammalian proteins (including tropomyosin) suggesting that the opportunity for activating self cross-reactive. M proteins can elicit antibodies which are cross-reactive with a variety of tissues including joints; there is potential for cross reactive recognition as a result of molecular mimicry. Human M protein-specific antibodies M1, M5, and M18 are cross-reacted with chondrocytes, cartilage, and synovium thus can trigger and activated significant levels of complement. The pathogenesis of streptococcal infection induce immune disease was shown by Fig. 1 [15].

TABLE V
COMPARISON OF POST STREPTOCOCCAL REACTIVE ARTHRITIS AND ARF [4]

	PSRA	ARF
Epidemiology		
age (years)	bimodal: 8-15 and 21-37	5-15 with peak incidence 12 years
sex ratio (male: female)	1:1	1:1
Chorea	0	0-30%
Erythema marginatum	0	0-13%
Carditis	*	30-90%
Nodules	0	0-8%
Arthritis		
Flitting/migratory	-	+++
Persistent	+++, additive	-
Large joint	+++	+++
Small joint	+++	+-
Salicylate response	Inconsistent, poor or moderate	+++, dramatic
Deforming	-	-
Erosive		-
Preceding streptococcal infection	+++	+++
Acute phase reactants	Moderately elevated	Markedly elevated
Approximate interval between infection and disease (days)	10	21
Association with B-cell Alloantigen D8/17	*	+++
Genetic marker	Increased frequency of HLA DRB1*01	Increased frequency of HLA DRB1*16allele
Antibiotic prophylaxis	For 1 year if echocardiogram is normal	Long term secondary antibiotic prophylaxis

*not known

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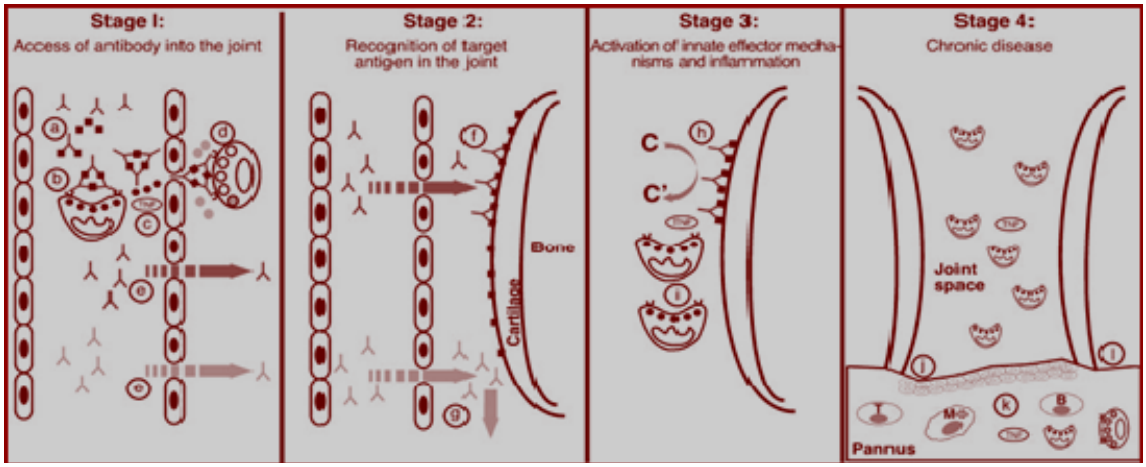

Fig. 1 A four-step model of autoantibody induced arthritis. Stage 1: Access of Ab into the joint triggering the release of vasoactive mediators such as TNF (oval), resulting in a local increase in vascular permeability, Stage 2: Recognition of target Ag in the joint, bind to GPI present on the cartilage surface, Stage 3: Activation of innate effector mechanisms and inflammation. Abs bound to the cartilage surface activate the alternative pathway of complement producing the anaphylatoxin then activates multiple cell types (neutrophils, mast cells, macrophages, and endothelial cells) to produce proinflammatory molecules (i.e., TNF-_, IL-1, and chemokines), thereby causing inflammation. Stage 4: Chronic disease [15]

The ability of GAS to cause diseases with multiple clinical manifestations also results from different host susceptibilities. The correlation between agent and host susceptibilities is shown in Fig. 2 [9], [11].

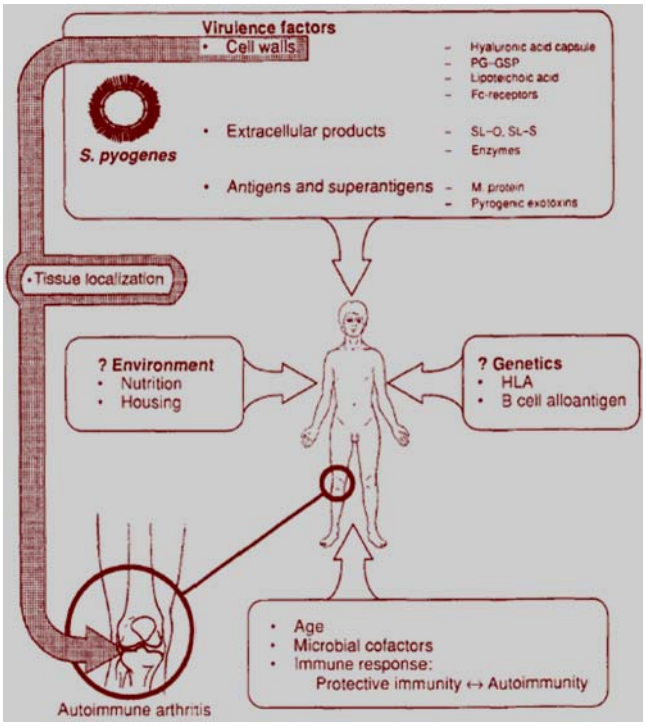

Fig. 2 The correlation between agent and host susceptibilities with patient with arthritis [13]

Host susceptibility may be an important factor in the production of toxic streptococcal syndrome. Susceptibility to streptococcal reactive arthritis may be associated with major histocompatibility antigens or class II molecules expressed by patients developing this syndrome. Recent studies suggested that there was an increased frequency of the HLA-DRB1*01 allele in streptococcal reactive arthritis compared with normal individuals or patients with rheumatic fever. The HLA-B27 allele was not found more frequently in streptococcal reactive arthritis than in normal individuals. Rheumatic fever patients were shown to have an increased frequency of the HLA-DRB1*16 allele, not theHLA-DRB1*01 allele, which was increased in streptococcal reactive arthritis cases [15].

The arthritis of ARF responds dramatically to acetylsalicylic acid or NSAIDs like naproxen. In contrast, the response in PSRA is inconsistent, poor, or not dramatically like in patients with ARF. The resolution of arthritis after treatment occurred in ARF patients about two days compared to seven days in the PSRA group. Relapse occurred in 7% of the ARF group, compared with 21% of the PSRA group. In the cohort study, after take acetylsalicylic acid reveal 33% of PSRA patients continued to have active arthritis after six weeks of follow-up, and the other study reported the mean duration to the resolution of symptoms was 54 days. Arthritis is treated symptomatically by non-steroidal anti-inflammatory drugs (NSAIDS). Ibuprofen helps to reduce inflammation and to reduce pain. Ibuprofen works by blocking the production of some of the body chemicals that cause inflammation, pain, stiffness, tenderness, swelling and increased temperature. By reducing inflammation in conditions affecting muscles and joints, ibuprofen helps to improve movement. Ibuprofen will

normally be prescribed at the lowest possible dose for the shortest time to reduce the chance of side effects [16].

All of patients were prescribed ibuprofen for pain relief, with the dose of 10 mg per kg of body weight three times daily.

Once a diagnosis of PSRA is made, antimicrobial therapy should be given to eradicate the GAS. Intramuscular penicillin G benzathine and oral penicillin V are the recommended antimicrobial drugs for the treatment of GAS, except in individuals with histories of penicillin allergy. The oral antibiotics of choice are penicillin V and amoxicillin [16], [17].

The use of an oral macrolide (erythromycin or clarithromycin) or azalide (azithromycin) is reasonable for patients allergic to penicillins. Ten days of therapy is indicated, except for azithromycin, which is given for five days. The worldwide surveillance revealed geographic heterogeneity in macrolide resistance, whereas there was absence of resistance in Indonesia. The dose of therapy is 10 mg per Kg body weight four times daily, and 250 mg twice daily for dose of prophylaxis; however, the literature shows that this varies. Macrolides (erythromycin and clarithromycin), and to a much lesser extent azalides (azithromycin), can cause prolongation of the QT interval in a dose dependent manner [16]-[18].

In our case, we use erythromycin for the antibiotic therapy and prophylaxis. We use a dose of 10mg erythromycin per kg of body weight four times daily for therapy and continued for a year with at a dose of 250 mg twice daily for prophylaxis.

The 2009, the American Heart Association (AHA) Scientific Statement recommended that patients with PSRA should be observed carefully for several months for clinical evidence of carditis. They suggest that secondary prophylaxis be given for up to one year after the onset of symptoms and discontinued if there is no evidence of carditis. If a recent streptococcal infection can be proved, then cardiac evaluation with echocardiography should be undertaken. The secondary prevention of rheumatic fever is shown in Table VI [17], [19].

Erythromycin was continued for one year, and all patients were to undergo a planned routine cardiac evaluation, such as electrocardiography, echocardiography, and chest x-ray for early detection of carditis.

TABLE VI
SECONDARY PREVENTION OF RHEUMATIC FEVER [17]

Agent	Dosage	Evidence rating*
Penicillin G benzathine	Patients weighing 27 kg (60 lb) or less: 600,000 units IM every 4 weeks† Patients weighing more than 27 kg: 1,200,000 units IM every 4 weeks†	1A
Penicillin V potassium	250 mg orally twice daily	1B
Sulfadiazine	Patients weighing 27 kg or less: 0.5 g orally once daily Patients weighing more than 27 kg: 1 g orally once daily	1B
Macrolide or azalide antibiotic (for patients allergic to penicillin and sulfadiazine)‡	Varies	1C

The patient with PSRA was shown to be at risk of developing rheumatic carditis. Patients with a normal baseline echocardiogram may have developed findings of abnormality in the echocardiogram after 12 months of follow-up, such as left ventricular systolic dysfunction, mitral, tricuspid and pulmonary insufficiency [19].

If valvular disease is detected, the patient should be classified as having had ARF and should continue to receive secondary prophylaxis. However, the effectiveness of this strategy is not well established. The level of evidence for this recommendation is only the consensus opinion of experts, case studies, or standard of care, and that usefulness or efficacy less well established by evidence. The duration of secondary rheumatic prophylaxis is shown in Table VII [17].

TABLE VII
DURATION OF SECONDARY RHEUMATIC FEVER PROPHYLAXIS [17]

Category	Duration after last attack
Rheumatic fever with carditis and residual heart disease (persistent valvular disease)	10 years or until 40 years of age (whichever is longer), sometimes lifelong prophylaxis
Rheumatic fever with carditis but no residual heart disease (no valvular disease*)	10 years or until 21 years of age (whichever is longer)
Rheumatic fever without carditis	5 years or until 21 years of age (whichever is longer)

*clinical or echocardiographic evidence

Joint Paint in PSRA can improve and not cause bone destruction, because the inflammation process is virtually less than three weeks. Also, there is no evidence of cardiac abnormality and no sign of inflammation in other tissue. Thus, almost all the patients with PSRA have good prognosis [14], [19].

After receiving ibuprofen, the joint pain decreased in almost all of the patients. Also, after being administered erythromycin, none of the patients complained of fever and sore throat again. There were no complications to other parts of the body, and the patients also revealed normal physical examinations. Thus, the prognosis of all patients with post streptococcal arthritis was good.

IV. SUMMARY

A report on serial cases of post streptococcal reactive arthritis in children aged 10 years to 14 years old has been reported. All of the patients came in with the chief complaint of joint pain about five days to 10 days after suffering from a sore throat and fever. The characteristic of the joint pain in all patients were persistent, but non-migratory. All of patients revealed normal physical examinations, normal complete blood count, an increase of ESR and ASLO, normal chest x-ray and also normal imaging of affected joints. Neither the physical cardiac examination, nor additional examinations (chest x-ray, electrocardiography, and echocardiography) revealed any cardiac abnormality. All patients revealed a GAS infection that was proven by an elevated ASLO titer. The applying of Jones Criteria was not fulfilled in all patients. All of the patients were administered erythromycin and ibuprofen and showed improvement. These therapies were continued for

a year for evaluation of the complication of carditis. All patients will undergo a planned cardiac evaluation in a year. The prognosis for all patients was good.

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