Secondary prophylaxis for rheumatic heart disease: A case report

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CASE STUDY

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ABSTRACT

Rheumatic heart disease is an irreversible sequela of rheumatic fever which is a major cause of cardiovascular morbidity and mortality in developing countries. We report a case of a 22-year-old lady with underlying chronic rheumatic heart disease, underwent mitral valve repair, presented with a recurrence of acute rheumatic fever with new aortic regurgitation confirmed by echocardiography, upon defaulting oral penicillin prophylaxis. She was treated symptomatically and started on IV Penicillin 2.4MU for 14 days based on clinical suspicion of possible infective endocarditis although laboratory values were not suggestive. With the resolution of clinical symptoms and treatment completion, she was discharged with oral penicillin despite non-compliance and a referral to the tertiary cardiac centre for continuation of care. Medical management was continued without surgical intervention to date. There is no specific guideline available in Malaysia to manage rheumatic heart disease, therefore treatment relies on the physician's experience. Majority still prefer prescribing oral penicillin prophylaxis in Malaysia but the recommended choice of prophylaxis worldwide is IM penicillin. In my opinion, this patient should have been discharged with IM penicillin or, even better, initiated at the point of initial diagnosis. In this case report, we not only highlight the importance of secondary prophylaxis but also focus on the route of prophylaxis to halt the progression of the disease.

Key Words

Implications for Practice:

1. What is known about this subject?
Rheumatic heart disease, a sequela of rheumatic fever caused by delayed immune reaction from streptococcal pharyngitis is a serious cause of morbidity and mortality in developing countries.

2. What new information is offered in this case study?
Effectiveness of oral penicillin as a secondary prophylactic agent is questionable. Non-compliance and unpredictable therapeutic level of serum penicillin may contribute to a recurrence of rheumatic fever.

3. What are the implications for research, policy, or practice?
Oral penicillin is widely given as secondary prophylaxis of rheumatic fever in Malaysia albeit recommended prophylactic agent being IM Benzathine Benzylpenicillin.

Background

Rheumatic heart disease (RHD) is an irreversible, immune-mediated disease precipitated by group A β-haemolytic streptococcus (GAS) infection in the pharynx. RHD is one of the significant cause of valvular heart disease, predominantly affecting mitral valves followed by aortic, tricuspid and pulmonary valves.[1] The nature of the disease is progressive which eventually necessitates valvular surgery in many affected individuals once medical treatment fails or the patient deteriorates clinically.[1]

Primary prevention with penicillin halts the development of acute rheumatic fever (RF) after an episode of streptococcal pharyngitis.[2] Dilemma exists in distinguishing streptococcal pharyngitis from viral pharyngitis in the primary care but

general practitioners can safely exclude the former using the following modalities: McIsaac score, rapid antigen detection tests or throat culture.

The next imperative step in managing RF/RHD will be the initiation of secondary prophylaxis. There are various guidelines recommending an appropriate duration of prophylaxis based of factors such as history of recurrences, age, presence of carditis, environmental conditions. As a rule, secondary prophylaxis is given for 10 years from the onset of disease or until 18–21 years old.[2] Lifelong prophylaxis can be implemented for individuals with severe carditis that require valvular surgery. Penicillin is the primary choice of secondary prophylaxis and there are two forms available – intramuscular (IM) and oral.

This case report intends to highlight the superiority of IM Benzathine penicillin as oppose to oral Penicillin V to prevent recurrences or progression of the disease.

Case details

We present a case of a 22-year-old Malay lady, from a rural region in Negeri Sembilan with underlying chronic rheumatic heart disease, diagnosed at 13 years old. Subsequently, she underwent an uneventful mitral valve repair for severe mitral regurgitation at the age of 14; she has been on T. Penicillin V 250mg BD and T. Enalapril 2.5mg OD since.

She had a recurrence of acute RF, with symptoms fulfilling the Jones criteria - she presented with intermittent fever for one month followed by migratory joint pain for two weeks. Dry cough and sore throat were present for two days associated with painful swallowing. She defaulted on her penicillin prophylaxis approximately two weeks prior to the onset of fever. Examination revealed signs of aortic regurgitation with wide pulse pressure, collapsing pulse, early diastolic murmur in the aortic region and mid-diastolic murmur in the mitral region. Blood investigations showed normocytic normochromic anaemia, leucocytosis, elevated Antistreptolysin O titre, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Blood culture showed no growth. Echocardiogram showed evidence of mitral stenosis and aortic regurgitation as shown in Table 1. She was diagnosed as recurrent rheumatic carditis.

Clinical suspicion of possible infective endocarditis arose with a history of valvular involvement, presence of a new murmur and a fever. She completed IV Penicillin 2.4MU 6 hourly for 14 days. She was started on T. Prednisolone 20mg TDS for 2/52 followed by a tapering dose for another

two weeks; T. aspirin 450mg QID for six weeks; and T. Enalapril 2.5mg BD was continued. She was discharged on day 18 of admission with T. Penicillin V 250mg BD, T. aspirin 450mg QID, T. Pantoprazole 40mg OD and tapering regimen of prednisolone. A referral was given for continuation of care in a tertiary cardiac centre. She was on regular follow up for monitoring of mitral and aortic valve for intervention, if necessary. Oral prophylaxis was maintained with no surgical intervention until her last follow up. Prognosis of the patient depends on an effective secondary prophylaxis and satisfactory surveillance of the valves by the surgeon. The timely referral to a cardiac centre should detect any valve deterioration at an earlier onset in this patient. But the continuation of oral prophylaxis likely increases the risk of valve deterioration.

Discussion

The patient in this case presented with a recurrence of rheumatic fever with worsening of valvular involvement due to non-compliance to oral penicillin.

The prevalence of rheumatic heart disease is higher in areas with poor health care access or environmental conditions like overcrowding. Incidence of RHD has not been widely studied in Malaysia according to our literature search. There was a small prevalence study carried out in Kelantan 33 years ago on primary school children which concluded a prevalence rate of 0.11 per thousand.[3] The reliability of the statistics is questionable in the current setting as the nation has developed vastly in terms of healthcare. Although the patient described in the case was from a rural area, she still had access to clinics, however failed to seek immediate help at first presentation due to inadequate knowledge about the illness.

An outpatient audit on RHD encompassing about 47 patients carried out in Queen Elizabeth Hospital II, Sabah eight years ago reported that only about 44.7% of patients were on IM penicillin and 38.3% were not on any prophylaxis. Currently, there is no Malaysian guideline emphasising on the preferred route of secondary prophylaxis, and the choice of treatment relies on the treating physician's preference.[4] Many prefer prescribing oral penicillin because IM penicillin is not readily available in a lot of primary care clinics according to a cardiothoracic surgeon from a private hospital in Malaysia. IM injections of penicillin are superior to oral forms as steady serum drug levels can be maintained with regular injections as opposed to oral penicillin, wherein the serum drug levels cannot be accurately determined.[5] American Heart Association (AHA) further adds that even individuals who rightfully comply to

oral penicillin prophylaxis are noted to have an increased risk of recurrences as oppose to those on IM penicillin.[5,6] If our patient was started on IM penicillin at initial diagnosis, the recurrence of RF could be avoided. Many guidelines, including WHO and AHA recommend the use of IM Penicillin as the first line of secondary prophylaxis. AHA proposed three weekly IM penicillin in places with high incidence of RF, otherwise four weekly regimens suffice.[6] Oral penicillin is only considered for those at a lower risk of recurrence or if IM injections are refused.[6]

A critical aspect of this case was the continuation of oral penicillin despite non-compliance which is an indication to start IM penicillin. Daily intake of oral penicillin tablets pose great challenge in ensuring medication adherence in patients. On the contrary, IM Benzathine Penicillin 1.2MU injections are delivered by healthcare staff at monthly clinic visits.[3] The patients can be contacted if they do not attend an appointment. Having said that, patients need to have an accessible mode of transportation to attend regular appointments. Another important factor to consider when delivering IM Penicillin injection is the dose of required medication. Several studies in European countries have laid out the use of prophylaxis based on the body weight of their population.[7] But these values may not be applicable in our setting as Asians have a different body build compared to Europeans. To the best of our knowledge, no specific studies were carried out in Asian countries to provide exact specification in managing these patients. As secondary prophylaxis is important to abate disease progression, more studies on ideal dosages of IM penicillin for an Asian population to manage RHD will be helpful to reduce disease burden.

Conclusion

Primary prevention is the goal to eradicate streptococcal pharyngitis caused by GAS; however, this mode of prevention can take longer in developing countries. The progression of carditis can be prevented if secondary prophylaxis is started at an early onset and given for an appropriate duration at an adequate dose. Physicians should be encouraged to use IM Benzathine Penicillin as its effectiveness supersedes that of oral penicillin.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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PATIENT CONSENT

The authors, Ganesin R, Khan AA, declare that:

1. They have obtained informed consent for the publication of the details relating to the patient in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees which does not require ethical approval for individual cases. This study has been registered with the local research body for publication – NMRR-21-6-57971.

Table 1: Findings of an inpatient echocardiogram of a patient with a previously normal aortic valve

Chambers	Mildly dilated left atrium (4.1cm) No obvious hypokinetic area Left ventricular end diastolic diameter (LVEDD): 4.7cm (normal) Left ventricular end systolic diameter: 3.1cm (normal)
Ejection fraction	58%
Aorta	Normal
Main pulmonary artery (MPA)	Normal
RV Function	Normal (TAPSE[+] – 1.9cm)
Mitral valve Doppler	Thickened chordae and thickened posterior annulus due to repair. Diastolic doming of anterior mitral valve leaflet. Mild mitral stenosis (PHT[++] $1.72cm^2$ and MPG[+++] 13.1mmHg) and mild mitral regurgitation
Aortic valve Doppler	Prolapsed valve Moderate aortic regurgitation, no aortic stenosis
Tricuspid valve Doppler	Normal No tricuspid regurgitation
Pulmonary valve Doppler	Mildly thickened No pulmonary regurgitation
Others	No visible vegetation/ intracardiac clots/ pericardial effusion. Interatrial septum and Interventricular septum intact.

[+]TAPSE, tricuspid annular plane systolic excursion

[++]PHT, pressure half time

[+++]MPG, mean pressure gradient