

Case Report

Subcutaneous Nodules and Delayed Diagnosis in Acute Rheumatic Fever: A Case Report

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Abstract

Acute Rheumatic Fever (ARF) is the sequelae of Group A Beta-Hemolytic Streptococcus (GABHS) infection and commonly present as arthritis and carditis. Subcutaneous nodules (SCN) is one of the major criteria as per the Revised Jones Criteria. It is rare, hence the delay in diagnosing ARF. We report three cases with delayed diagnosis of ARF presenting with SCN. All had prolonged fever with arthritis and carditis preceding the development of SCN which demonstrated complete resolution after initiation of treatment for ARF. Presence of SCN should increase awareness amongst healthcare providers the possibility of ARF as a differential diagnosis albeit of its rarity.

Keywords

- Subcutaneous nodules
- Acute rheumatic fever
- Delayed diagnosis
- Prolonged fever

ABBREVIATIONS

ARF: Acute Rheumatic Fever; SCN: Subcutaneous Nodules; PIP: Proximal Interphalangeal; MCP: Metacarpophalangeal; IVIG: Intravenous Immunoglobulin; ECHO: Echocardiography; ECG: Electrocardiography; ASOT: Anti-Streptolysin O Titre, CT: Computed Tomography; LLSE: Lower Left Sternal Edge

INTRODUCTION

Acute Rheumatic Fever (ARF) is a non-suppurative sequelae that occurs two to four weeks following group A Beta-Hemolytic Streptococcus (GABHS) infection. Revised Jones major criteria include carditis, arthritis, Sydenham chorea, erythema marginatum and subcutaneous nodules (SCN). Two major criteria or one major with two minor criteria along with evidence of GABHS infection is required to establish diagnosis of ARF. Carditis and arthritis are the two most common features whilst SCN is rare, with reported incidence of <1% to 21% of cases [1].

The incidence of ARF is high in countries with poor socio-economic status ranging from 100-200 per 100,000 population worldwide in the 5-15 year-old age group [2]. In Malaysia, admissions in the 1980s ranged from 2 to 21.2 per 100,000 paediatric population per year. Although there is a gradual decline in the incidence of ARF in our population, the disease burden remains significant. Incidence of SCN is reported at 11%, consistent with worldwide reporting [3]. We report three cases of delayed diagnosis of ARF who presented with fever initially, followed by arthritis, carditis and SCN.

CASE PRESENTATION

Patient A

A, 6-year-old girl presented with fever for two months

followed by joint swelling, limited range of movement of fingers and small nodular swellings over the fingers and wrist joints one week prior to admission. Symptoms persisted despite seeking medical advice from several private GPs.

Physical examination revealed multiple nodules over bilateral proximal interphalangeal (PIP) joints, extensor surface of right elbow, fifth toe of right leg and second toe of left leg. There was ulnar deviation and fixed flexion deformity over both wrists and PIP joints (Figure 1). Her apex beat was displaced with presence of grade 3/6 diastolic murmur at the second upper left sternal edge and grade 3/6 systolic murmur at the mitral area. She had a positive ASOT 1:800 with raised inflammatory markers, ESR 45mm/1hr and CRP 12.3mg/L respectively. Radiograph of hands showed generalized osteopenic bone with normal joint space. Chest X ray revealed cardiomegaly while echocardiography demonstrated thickened mitral and aortic valves with severe regurgitation and moderate tricuspid regurgitation. She was managed as acute on chronic rheumatic heart disease and was



Figure 1 Left- Subcutaneous nodules with fixed flexion deformity noted over PIP joints of both hands. Right- Subcutaneous nodule seen on the extensor surface of right elbow.

given oral prednisolone, penicillin V, and frusemide. Aspirin was added while tapering off prednisolone. Monthly prophylactic intramuscular Benzathine penicillin was started one month later. She made forward progress and SCN resolved within 3 weeks.

A defaulted follow up after 6 months and presented 10 months later with recurrent ARF. There were nodules over bilateral MCP joints of the hand and elbow with evidence of arthritis. Grade 3/6 pansystolic murmur over mitral area and grade 2/6 early diastolic murmur over aortic area was present. Both her inflammatory markers were raised with positive ASOT titre 1:400. ECG revealed sinus rhythm with bifid P wave and prolonged PR interval. ECHO showed thickened valve leaflets with moderate aortic regurgitation, severe tricuspid and mitral regurgitation. She was given a course of IV C Penicillin, and started on oral aspirin, frusemide and enalapril. She showed remarkable improvement within a week whereby the nodules and joint swelling had resolved.

Patient B

B, a 10-year-old Bidayuh boy presented with fever for two days associated with joint pain, abdominal pain, vomiting, and diarrhea and bitemporal headache. He was admitted to a district hospital on day two of illness. Fever was intermittent in nature and he developed urticarial rash on day four of illness. Physical examination was unremarkable. He was managed as typhoid fever and given IV Ceftriaxone for ten days. His fever persisted and he was investigated extensively for prolonged fever. Most investigations were insignificant except the raised ESR 103mm/1hr, thrombocytosis 750,000/ul and hypochromic microcytic anemia. His serum ASOT titre was normal and Widal tests taken twice was negative. His ECG was normal with no prolonged PR interval. ECHO showed presence of mild aortic regurgitation.

On the third week of illness, he developed painless occipital, temporal and frontal SCN whilst his fever continued to spike and joint pain persisted. Skull X ray and CT brain were normal. Both dorsum of his hands were oedematous with desquamation over the knuckles. He was managed as incomplete Kawasaki disease with IVIG and showed transient response to IVIG infusion and high dose aspirin. Bone marrow aspiration done and report showed increase in megakaryopoiesis with no other changes.

The district hospital team referred him to the Paediatric Rheumatologist to rule out connective tissue disease. Assessment revealed multiple firm SCN over the scalp, right elbow and extensor surface of left second MCP joint which were mobile and non-tender (Figure 2,3). Multiple hyperpigmented macules with indistinct margin (erythema marginatum) were seen over the trunk and extremities (Figure 4). Apex beat was displaced with grade 3/6 ESM over LLSE and grade 3/6 EDM at LLSE. He had hepatomegaly but no splenomegaly.

He was referred to a Paediatric Cardiologist for an echocardiography. ECHO by Paediatric Cardiologist revealed dilated left atrium and ventricle with evidence of rheumatic valvular heart disease. The mitral leaflets were thickened with decreased mobility resulting in severe mitral regurgitation whilst the aortic valves were also thickened with severe aortic regurgitation. ECG was normal. A repeat ASOT done yield



Figure 2 (Left and right) Subcutaneous nodules seen on the MCP joint of left hand and right elbow.



Figure 3 Subcutaneous nodules on the scalp.



Figure 4 Erythema marginatum seen on the trunk and extremities.



Figure 5 Subcutaneous nodules seen on right foot.

positive result. He was managed as acute on chronic rheumatic heart disease and given oral Penicillin V, prednisolone, frusemide with aspirin added on upon discontinuing prednisolone. His general condition improved and SCN resolved completely after two weeks of treatment.

Patient C

C, a 13-year-old boy presented with one week history of fever associated with knee and ankle joint pain, with subsequent involvement of the finger joints. The arthralgia was worse in the morning and was not migratory in nature. His arthralgia worsened limiting his functional ability despite treatment. He was admitted for few days for further evaluation but lost to follow up upon discharge.

He presented 1.5 months later with heart murmur and worsening of joint pain. His ASOT was raised 1:800, CRP 8.8mg/L and ESR 31mm/1hr. Ultrasound of the knee joints, suprapatellar bursae and elbow joints showed minimal effusion. ECHO revealed prolapsed floppy mitral valve tip with moderate mitral regurgitation. He was treated as rheumatic fever with oral Penicillin V and high dose aspirin. Albeit of treatment, his wrist joint swelling, pain, and restricted movement persisted. He was referred to a Paediatric Rheumatologist for further assessment of the arthritis.

Review by Paediatric Rheumatologist four months after onset of fever revealed multiple nodules over first right MTP joint, third right MTP joint, olecranon process, and the left fourth flexor tendon (Figure 5). His apex beat was displaced with presence of grade 3/6 pansystolic murmur over mitral area radiating to axilla and a grade 3/6 diastolic murmur over the same region. ECG showed prolonged PR interval and P mitrale. Repeat CRP was normal with persistently raised ASOT 1:800. Echocardiography by a second Paediatric Cardiologist showed dilated left atrium and ventricle, thickened anterior and posterior mitral valve leaflets with severe mitral regurgitation. He was diagnosed with acute on chronic rheumatic carditis, and managed with oral penicillin V and prednisolone followed by high dose aspirin. He made remarkable progress with alleviation of the joint pain and complete resolution of SCN after one week.

DISCUSSION

Studies showed that carditis and arthritis are two most common features [4,6]. Whilst SCN is the least common manifestation with reported incidence of <1% to 21%. Presence of SCN is frequently associated with carditis [1]. A prospective study revealed that a total of 90.4% of SCN were associated with carditis, while 9.5% occurred with no evidence of carditis. An average number of 18 nodules was observed with 30.9% had less than 10 nodules [4].

Case reports of ARF with SCN revealed typical history of preceeding fever followed by development of arthritis and carditis. SCN often emerged after onset of arthritis and carditis suggesting that it is a late manifestation of ARF [1,5]. This finding

is observed in all our cases. The presence of SCN with preceding fever should raise suspicion of ARF.

SCN is painless, firm, mobile nodule, measuring 0.5cm to 2cm and is usually located over extensor surfaces of the joints [7]. SCN should be differentiated from erythema nodosum which is an acute, nodular, erythematous eruption which is usually limited to the extensor aspects of the lower legs.

SCN is not exclusive to ARF and is occasionally observed in juvenile rheumatoid arthritis and other connective tissue diseases. Excisional biopsy of SCN reveal fibrocollagenous tissue with interstitial spindle cells, collagen degeneration and associated histiocytic reaction with occasional neutrophil [5]. In contrary, SCN found in juvenile rheumatoid arthritis is described as a central zone of fibrinoid necrosis surrounded by a prominent rim of epithelioid histiocytes and numerous lymphocytes and plasma cells. Fibrin may be deposited in the center of the granulomas [8].

There is no specific treatment for SCN. With initiation of treatment for rheumatic carditis, majority of SCN (69%) disappear within 4 weeks [4]. Early diagnosis and treatment of ARF is indeed crucial to minimise heart valve damage and progression to rheumatic heart disease [9].

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REFERENCES

1. Anil Kumar Singhi, Prashant Bobhate, Mahesh Kappanayil. Acute Rheumatic Fever: Subcutaneous Nodules and Carditis. *Circulation*. 2010; 121: 946-947.
2. Tibazarwa KB, Volmink JA, Mayosi BM. Incidence of Acute Rheumatic Fever in the world: a systematic review of population-based studies. *Heart*. 2008; 94: 1534-1540.
3. Hung Liang-Choo, Nadia Rajaram. A review of Acute Rheumatic Fever and Rheumatic Heart Disease Research in Malaysia. *Med J Malaysia*. 2016; 71: 79-86.
4. Behera M. Subcutaneous Nodules in Acute Rheumatic Fever: an analysis of age old dictums. *Indian Heart J*. 1993; 45: 463-467.
5. Dinesh Kumar J. Subcutaneous Nodules in Acute Rheumatic Fever: a case report. *SRJM*. 2011; 4: 40-41.
6. Simone Manso de Carvalho, Ivete Dalben José Eduardo Corrente, Claudia Saad Magalhães. Rheumatic Fever Presentation and Outcome: a case-series report. *Rev Bras Reumatol*. 2012; 52: 236-246.
7. Binotto MA, Guiherme, Tanaka AC. Rheumatic Fever. *Images Paediatr Cardiol*. 2002; 4: 12-31.
8. Smith MT, Zurynski Y, Lester-Smith D. Rheumatic fever: Identification, management and secondary prevention. *Aust Fam Physician*. 2012; 31-35.
9. Paresh HB, Birare SD, Dantkale SS. Juvenile Idiopathic Arthritis: A Case Report. *J Evol Med Dental Sci*. 2012; 737.

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