Abstract:

Reactive arthritis and erythema are uncommon presentations of tuberculosis (TB). Reactive arthritis in tuberculosis (TB) is known as Poncet’s disease, a rare aseptic form of arthritis observed in patients with active TB. We report a case of Poncet’s disease in a 20-year old man whose reactive arthritis overshadowed other clinical symptoms of TB resulting in delayed diagnosis and treatment. Although a conclusive diagnosis of Poncet’s disease is not possible, reactive immunologic reactions such as reactive arthritis and erythema nodosum even without respiratory symptoms should raise suspicion on possible TB. Thus, taking a thorough medical history as well as performing relevant examinations and investigations for possible TB will help expedite the diagnostic process.

Introduction

Tuberculosis (TB) is a major public health concern. It remains the leading cause of death attributed to infectious diseases. An estimated 1.2–1.5 million died from TB in 2010.1 Twenty one percent of the world’s notified TB cases are in the Western Pacific Region which includes Malaysia.2 In 2011, the World Health Organization (WHO) declared that global incidence rate of TB has decreased. However, in Malaysia, TB control has not reached a satisfactory level despite national control efforts.3 In 2005, the incidence rate of TB was 86 per 100,000 persons and it has only dropped slightly to 82 per 100,000 in 2010.1,3 Delayed diagnosis and low index of suspicion are the main reasons why the incidence of TB remains high.4 Atypical presentation of TB can also be a contributing factor. Associated rheumatologic diseases such as reactive arthritis may overshadow typical clinical features of TB.

The clinical feature of reactive arthritis (also known as Reiter’s syndrome) consists of joint inflammation often as a result of extra-articular bacterial infections, mostly originating from the urogenital, gastrointestinal and respiratory system.11,12 It’s estimated prevalence is 30-40 per 100,000 adults.8,9 It is clinically described as asymmetrical oligoarthritis, usually in joints of the lower limbs.10 This has posed a challenge to clinicians in establishing early diagnosis of reactive arthritis.12 This case report describes reactive arthritis accompanying pulmonary tuberculosis.

Case summary

A 20-year old college student presented to an outpatient clinic with progressive painful ankle swelling for the past two weeks. This was preceded by an upper respiratory infection a week prior to the onset of the joint swelling. There was no history of fall or injury. His past medical history was insignificant; there were no symptoms of urinary infection or sexually transmitted infections. On examination, both
the ankles were mildly inflammed from distal part of the lateral malleoli to proximal part of the ankle joints. He had limited ankle movements. There was no vascular or neurological deficit.

He was treated with non-steroidal anti-inflammatory drugs (NSAIDs) and asked to rest in bed. A week later, a mildly-raised, ill-defined and tender purplish blue rash appeared on the antero-lateral side of the shins. He was investigated for connective tissue disease, rheumatoid arthritis and erythema nodosum.

The patient was prescribed co-amoxycillin and clavulanic acid 625mg twice a day for a week in view of the possible diagnosis of reactive arthritis following a history of upper respiratory tract infection (e.g. streptococcal pharyngitis). He did not return for the next follow up visit. One month later, the patient returned to the clinic with loss of weight (3kg) and painless lumps at the left posterior cervical region. There were neither respiratory symptoms nor history of contact with TB patients. The ankle swelling and erythema nodosum over the shins had subsided. Examination of the neck revealed small lymph nodes on the left posterior cervical region with the biggest measuring 2x2 cm in diameter. They were firm, not tender and fixed. His full blood count was within normal range and the erythrocyte sedimentation rate was greater than 100mm per hour. Anti-nuclear antibody and rheumatoid factor were negative. The chest radiograph showed haziness over the left upper zone. The patient had a Mantoux reaction of more than 15mm with blistering. Biopsy of the lymph nodes revealed inflammatory lymphadenopathy with no acid-fast bacilli. Similarly, three sputum specimens were tested negative for acid-fast bacilli.

Subsequently, the patient developed cough and the chest radiograph revealed left upper lobe consolidation. A repeat chest radiograph showed left upper zone cavitation. The fourth sputum sample was tested positive for acid-fast bacilli. Standard anti-tuberculosis treatment regimen consisting of ethambutol, isoniazid, rifampicin, pyrazinamide (EHRZ) was initiated for the first two months followed by isoniazid, rifampicin (HR) biweekly for the subsequent four months. He responded positively to the treatment.

Discussion

This was a rare case of pulmonary tuberculosis with reactive arthritis and erythema nodosum. A diagnosis of TB made in more than 30 days from the initial consultation is considered a delay. Diagnosis was delayed in this patient by 30 days due to lack of awareness, mixed presentations and lack of pulmonary involvement in the early stage of the disease. The possibility of Poncet’s disease was considered as patient presented with reactive arthritis followed by active TB. Poncet’s disease is not a typical presentation of TB and is, therefore, not a well discussed topic in Malaysia. Even in an established private institute of rheumatology, Poncet’s disease was the diagnosis made in 14% of the patients receiving treatment for some form of musculoskeletal problems and has concurrent TB. Even in countries with high TB prevalence, diagnosis remains challenging due to atypical presentation of Poncet’s disease. A review of 50 cases of Poncet’s disease showed differences in characteristics: 30% of patients showed some features of oligoarthritis and the rest, polyarthritis. Even though the majority of patients had lower limb involvement, some patients reported pain in the small joints of hands and feet.

The diagnosis of tuberculous arthritis demands a high index of suspicion in order to secure joint functions; late treatment may result in joint damage. Case studies of Poncet’s disease highlight the need to differentiate tuberculous septic arthritis from TB-related reactive arthritis. However, a review of 50 cases reports found that 70% of those diagnosed with Poncet’s disease did not undergo a synovium examination. TB septic arthritis often involves single joint and it requires evidence of acid-fast bacilli in the synovial fluid and synovial tissue biopsy. Sometimes, polymerase chain reaction-based tests are needed to assist the diagnosis.
However, TB-related reactive arthritis are mostly aseptic.\textsuperscript{15,16} Evidence of increased mycobacterial activity can be challenging. In this patient, synovial fluid examination or x-ray of the ankles was not done since there was no clinical indication of joint effusion or joint destruction. The diagnosis of reactive arthritis and Poncet’s disease were made based on clinical suspicions, especially when synovial fluid examination was not possible. Furthermore, close observation for recurrence is important. Synovium examination, though helpful, may not be necessary in all cases of arthritis.\textsuperscript{5} Therefore; investigations must be geared towards early diagnosis of TB.

In this case, arthritis was initially considered because of possible streptococcal infection. In retrospect, the diagnosis could not be confirmed because no throat swab or anti streptolysin-O titre was done. Moreover, a week’s course of co-amoxycillin and clavulanic acid would not have changed the course of post-streptococcal reactive arthritis because the treatment regime prescribed was shorter than the recommended 10-day duration.\textsuperscript{17} The patient showed clinical signs of TB within six weeks of developing arthritis in the ankles. Studies have reported that immunologic response usually takes about six weeks, starting from the infection with TB bacilli.\textsuperscript{18} Thus; TB is a more likely cause for the reactive arthritis than streptococcal infection.

Patients often respond quickly to the treatment of tuberculous reactive arthritis in Poncet’s disease compared with tuberculous septic arthritis.\textsuperscript{6,19} In this case, the arthritis subsided completely before the respiratory symptoms emerged and commencement of the anti-TB treatment. Many case reports documented the disappearance of reactive arthritis upon initiation of anti-TB treatment.\textsuperscript{19} However, there was a case of Poncet’s disease whereby the patient had intermittent episodes of polyarthritis (with remission in between) before developing cough and dyspnoea. This occurred before the commencement of TB treatment and the arthralgia disappeared completely after six weeks of anti-TB treatment.\textsuperscript{20} This suggests that the course of illness for TB-associated reactive arthritis may vary.

TB can also trigger erythema nodosum, a skin inflammation that results in reddish, painful, tender skin lesions. It can also occur as a result of sarcoidosis, streptococcal infection, histoplasmosis, and as reaction to drugs such as oral contraceptives, penicillin and sulphonamides.\textsuperscript{14,21} Due to low prevalence of sarcoidosis among Asians, it was not considered in this patient.\textsuperscript{22} Moreover, erythema nodosum is a presentation of an underlying septal panniculitis, a reactive process to several stimuli and thus, inconclusive of any particular illness.\textsuperscript{20} Therefore, no chest x-ray was performed when there were signs of erythema nodosum. Tuberculin reaction to TB was postulated as tuberculo-protein hypersensitivity. Erythema nodosum aggravated the reaction as seen in the Mantoux tuberculin skin test.\textsuperscript{14,15} A negative result on the other hand, may strengthen the evidence of excluding TB as a diagnosis.\textsuperscript{15}

In conclusion, the diagnosis of TB in some patients is delayed because of multiple presentations involving non-pulmonary sources. Even though it is not possible to come to a conclusive diagnosis of Poncet’s disease, immunologic reactions such as reactive arthritis and erythema nodosum, even without respiratory symptoms, should alert primary care physicians to search for symptoms and signs of TB. Thus, taking a thorough medical history, performing relevant examinations and investigations may help expedite the diagnostic process.

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References