CASE REPORT

Arthritis and adult respiratory distress syndrome: unusual presentations of typhoid fever

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SUMMARY

A middle-aged woman presented with fever of 1-month duration along with bilateral knee joint pain, swelling and difficulty in walking for 2 weeks. The patient's Typhidot test was positive for IgM antibodies. Her Widal test was negative, and blood culture and synovial fluid culture were sterile. She was started on ceftriaxone, to which her fever initially responded. However, after 4 days of treatment her disease course was complicated by relapse of fever and acute respiratory distress syndrome (ARDS). This settled with respiratory support and addition of azithromycin. Following recovery from ARDS and fever, her persistent knee arthritis responded to intra-articular methyl prednisolone instillation.

BACKGROUND

Typhoid fever continues to be a public health problem, particularly in developing countries. The disease usually begins to resolve by the third week but can have complications involving various organ systems. Arthritis and acute respiratory distress syndrome (ARDS) have been sparsely reported in association with typhoid fever. We report a case of typhoid fever presented to the rheumatology department because of acute arthritis and development of ARDS. The purpose of this case report is to highlight the fact that typhoid can present with highly unusual multiple complications and healthcare personnel should be well aware of these rare manifestations.

CASE PRESENTATION

A 47-year-old woman presented with pain in both knee joints, back pain, and standing and walking disability for 2 weeks. She also had history of fever (38–39°C), headache, abdominal pain, vomiting and anorexia for the past 1 month. There was no history of rashes, cough, diarrhoea or constipation. Medical history was unremarkable.

On physical examination her pulse was 99/min, blood pressure 110/70 mm Hg and respiratory rate 16/min. On admission, her temperature was 38.5°C. Both her knees were swollen and tender (figure 1). No abnormality was detected on abdomen and other systems examination.

INVESTIGATIONS

Her total leucocyte count was 15 350/mm³ (with 90% neutrophils), erythrocyte sedimentation rate was 120 mm/h and C reactive protein was 28.7 g/L. Her serum glutamic oxaloacetic transaminase (76 U/L) and serum glutamic pyruvic transaminase (80 U/L) were mildly elevated. Serological tests for malaria parasite and dengue virus were negative. Widal test

was negative (*Salmonella typhi* H, 1/160; *Salmonella typhi* O, 1/80). Synovial fluid examination showed 2000 cells/mm³ with 90% neutrophils. Synovial fluid gram staining and acid-fast bacilli staining were negative and no crystals were seen. Blood, urine and synovial fluid cultures were sterile. Stool culture was negative for *Salmonella typhi*. *Salmonella typhi* IgM antibody was positive by *Salmonella* Typhidot test. Montoux test showed 5 mm induration. X-rays of chest and both knee joints were unremarkable. Ultrasonography (USG) of the abdomen showed mild hepatosplenomegaly.

DIFFERENTIAL DIAGNOSIS

As our patient had fever, anorexia and arthritis; infections including tuberculosis, brucellosis, typhoid fever, septic arthritis, HIV, malaria and dengue and connective tissue diseases such as rheumatoid arthritis were the main differential diagnoses. Tuberculosis was excluded as there were no physical signs suggestive of tuberculosis and chest X-ray and USG of the abdomen were normal along with negative Montoux test. Possibility of septic arthritis was ruled out by synovial fluid examination, which was sterile on culture. Possibility of other infections such as brucella, malaria, HIV and dengue fever were ruled out by appropriate serological tests. Rheumatoid arthritis was excluded as there was no involvement of small joints of hands and tests for rheumatoid factor and cyclic citrullinated peptide antibody were negative. We considered typhoid fever as our final diagnosis because of clinical manifestations and a positive *Salmonella* Typhidot test.

TREATMENT

Considering the diagnosis of delayed presentation of untreated typhoid fever with arthritis, the

Figure 1 Bilateral knee arthritis.

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Figure 2 Chest X-ray showing bilateral lung infiltrates suggestive of acute respiratory distress syndrome.

patient was started on intravenous ceftriaxone 1 g twice a day, antipyretics (paracetamol) and a non-steroidal anti-inflammatory drug (aceclofenac 100 mg twice a day orally). The patient was afebrile after 48 h of treatment, however, her fever relapsed on the fifth day of treatment and she reported breathlessness. Her respiratory rate was 40/min and oxygen saturation dropped to 75% at room air. Chest examination revealed bilateral basal crepitations. After administration of oxygen (6 L/min) through nasal prongs, saturation improved to 90%. Arterial blood gas analysis showed pH=7.32, P_{CO_2} =51 mm Hg, and P_{O_2} = 89 mm Hg. Circulating fibrin degradation products and activated partial thromboplastin time were within normal limits. Chest X-ray showed bilateral lung infiltrates suggestive of ARDS (figure 2). The patient was managed in high dependency unit with oxygen support by venturi mask (6 L/min) and diuretics (furosemide). Azithromycin (1 g intravenously once a day) was started in addition to ceftriaxone. She responded well and recovered in 7 days. She became afebrile, her oxygen saturation improved to 99% on room air, infiltrates on chest X-ray resolved and liver enzymes became normal. She was switched over to oral azithromycin (1 g/day) and aceclofenac (100 mg twice a day). However, there was little decrease in knee joints pain and swelling, and the patient still had significant difficulty in walking due to bilateral knee arthritis. Intra-articular methylprednisolone (80 mg) was instilled in each knee. The patient had a dramatic improvement with the intra-articular steroid treatment and she was walking comfortably in 48 h. She was discharged on oral azithromycin for 5 days.

OUTCOME AND FOLLOW-UP

The patient was completely asymptomatic at the time of discharge and is doing well at follow-up of 4 months.

DISCUSSION

Although presenting with bilateral knee arthritis, our patient had many clinical features suggestive of typhoid including fever, abdominal pain, vomiting and hepatic involvement. At presentation, Widal test and cultures (blood and stool) were negative. In cases of typhoid fever, the organism can usually be cultured

during the initial 2 weeks of illness. Blood culture positivity decreases after the first week and becomes negative in the fourth week.¹ Urine and stool cultures are also less frequently positive after 4 weeks. As our case presented after 4 weeks, positive IgM antibody to *Salmonella* along with the clinical picture were the main criteria for diagnosis of typhoid fever. Sensitivity of the Typhidot IgM test has been reported from 61.1% to 92.3% and specificity from 40.6% to 98.8%, with higher values for Asian populations.^{2–3} Arthritis and ARDS were major complications seen during the course of disease in our patient. Arthritis is an uncommon manifestation of typhoid fever.^{4–5} Typhoid arthritis can be divided broadly into two categories: septic arthritis and reactive arthritis.⁵ Synovial fluid cell count and culture from affected joints ruled out the septic arthritis.

ARDS is rarely reported with typhoid fever although sepsis is a common manifestation.⁶ Our patient, during her hospital stay, developed the ARDS, which was successfully managed by adding a second antibiotic and supportive therapy. The multiresistant *Salmonella* typhi may be responsible for prolonged courses and atypical presentations of typhoid fever.⁷ Other reported rare pulmonary manifestations include bronchitis, pneumonia, lung abscess and empyema.

Learning points

- ▶ Arthritis and acute respiratory distress syndrome can be rare manifestations of typhoid fever.
- ▶ Typhoid fever should be considered in the differential diagnosis of polyarthritis or monoarthritis with fever, especially in tropical countries where the disease is endemic and drug resistant strains are prevalent.
- ▶ In cases of late presentation, clinical history and Typhidot test (with 75% specificity and 95% sensitivity) can be important for diagnosis of typhoid fever, as cultures may be negative.

Competing interests None.

Patient consent Obtained.

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