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CASE REPORT

Salmonella typhi soft tissue abscess in a patient with myelodysplastic syndrome

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ABSTRACT

We describe a 59-year-old Filipino male patient with myelodysplastic syndrome (MDS) who developed a *Salmonella typhi* leg abscess, presenting with a two-week history of right leg swelling and fever. The infection was treated successfully with a combination of surgical drainage and a three-week course of intravenous antibiotics. MDS predisposes patients to severe *Salmonella* infections ranging from infected subdural empyema to aortitis, empyema thoracis and splenic abscesses. To our knowledge, this is the first reported case of *S. typhi* soft tissue abscess in MDS. *Salmonella* infections should be considered in the differential diagnosis of soft tissue abscesses, especially among immunocompromised patients such as patients with MDS.

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Introduction

Salmonella enterica serotype *typhi* (*S. typhi*) causes typhoid fever that usually presents as an acute systemic infection. Typhoid fever is most common in developing countries and has been associated with low socioeconomic levels and poor sanitary conditions.[1] Transmission occurs through the faecal-oral route with contaminated food or water.

Globally, typhoid fever has about 21 million cases with 216,510 deaths yearly.[2] South-Central Asia and South-East Asia are the regions with the highest incidence of typhoid fever, affecting more than 100 people per 100,000 population each year.[2]

Risk factors for *Salmonella* infection include malnutrition, sickle-cell and malarial anaemia, and immunocompromise from conditions such as HIV infection, steroid use, malignancy, renal disease, and hepatic disease.[3] Newborns and elderly patients are also at increased risk of *Salmonella* infections. Moreover, living or traveling in *Salmonella*-endemic country increases the risk of typhoid fever.

Soft tissue abscesses from *S. typhi* infections are rare. Few case reports and series have been published involving both immunocompetent and immunocompromised patients. *Salmonella* soft tissue abscesses have been reported in patients with systemic lupus erythematosus, lymphoma, HIV infection, and rheumatoid arthritis.[4-7] These reports suggest that MDS should also predispose patients to severe *Salmonella* infections, which may present with infected subdural empyema,[8] aortitis,[9] empyema thoracis,[10-11] or splenic abscesses.[10,12] To our knowledge, this is the first reported case of an *S. typhi* soft tissue abscess in MDS.

Case report

A 59-year-old Filipino male patient was diagnosed with myelodysplastic syndrome with a subtype of refractory anaemia with excess blasts (RAEB) one year prior to admission based on bone marrow findings. Immediately after diagnosis, he was maintained on danazol, vitamin B_{12}, omeprazole, and low-dose prednisone. He did not receive any other chemotherapeutic agents. He required frequent admissions for transfusion of 2–3 units of packed red blood cells every 1–2 months. Prior to this admission, the patient did not have underlying neutropenia. There was no antibiotic use for the past year. He denied any skin lesion or chronic wound aside from the present lesion over his right leg.

The patient presented with two weeks of pain and swelling of the right leg that was worse with ambulation. He also had intermittent fever (highest recorded temperature 39°C). There was no headache, abdominal pain, bleeding, diarrhoea, vomiting, dysuria, or altered mental status. On the day of admission, he complained of a cough with "whitish" sputum. He was diagnosed with pulmonary tuberculosis four years prior, for which he completed a six-month treatment of anti-tuberculosis medications. He had no other medical comorbidities. He also underwent an appendicectomy 40 years ago. He is an ex-smoker and occasionally drinks alcohol. He drank and used water from the community water system. He denied having pets at home or any contact with animals. There were no known reported cases of *Salmonella* infections in his rural community.

On examination, he was alert and orientated but in mild respiratory distress with a blood pressure of 60/40 mmHg, heart rate of 160 beats/min, respiratory rate of 28 breaths/min, temperature of 37.7°C, and an oxygen saturation of 96% on 6 L/min of oxygen via simple face mask. He had pale conjunctivae and crackles in the left lung base. A 5 × 8 cm tender, erythematous, fluctuant mass was noted on his right anterior leg. The remainder of the examination was normal. Hypotension persisted despite adequate fluid resuscitation and vasopressors were eventually required. His haemoglobin was 38 g/L (reference range 120–180 g/L), haematocrit was 11.3% (reference range 40–54%), platelet count was 16,000 × 10^6/L (reference range 150,000–450,000 × 10^6/L), white cell count was 2,510 × 10^6/L (reference range 4,500–11,000 × 10^6/L), with 52% neutrophils (reference range 50–70%), 14% lymphocytes (reference range 20–50%), and 34% monocytes (reference range 2–9%). The blood level of sodium was 128 mmol/L (reference range 136–144 mmol/L), potassium was 3 mmol/L (reference range 3.6–5.1 mmol/L), chloride was 96 mmol/L (reference range 101–111 mmol/L), albumin was 25 g/L (reference range 35–48 g/L). Absolute neutrophil and lymphocyte counts were 1,305 cells/μL and 351 cells/μL respectively. Arterial blood gas showed respiratory alkalosis with good oxygenation. Urinalysis showed 8–12 red blood cells per high power field, 0–2 white blood cells per high power field, 2–6 hyaline casts

per low power field, and 0–1 coarse granular casts per low power field. The remainder of the urinalysis, coagulation function tests, and the blood levels of calcium, creatinine, glucose, and magnesium were normal. An electrocardiogram showed sinus tachycardia with normal axis. Ultrasonography of right leg revealed a complex fluid collection in the subcutaneous and muscular layers with floating medium-level echoes exhibiting Brownian movement. Culture of intraoperative wound aspirate grew *S. typhi* with sensitivity to ceftriaxone, chloramphenicol, cefotaxime, cotrimoxazole, and intermediate sensitivity to ciprofloxacin. Wound aspirate was negative for acid-fast bacilli. Sputum culture showed light growth of *Pseudomonas aeruginosa* (sensitive to amikacin, aztreonam, ceftazidime, ciprofloxacin, gentamicin, imipinem, meropenem, and piperacillin-tazobactam) and *Enterobacter aerogenes* (sensitive to amikacin, ampicillin, ampicillin-sulbactam, aztreonam, ceftazidime, ciprofloxacin, gentamicin, meropenem, piperacillin-tazobactam, and cotrimoxazole). Blood culture grew *P. aeruginosa* after 9.12 hours of incubation from one site (sensitive to amikacin, aztreonam, cefepime, ceftazidime, ciprofloxacin, gentamicin, meropenem, and piperacillin-tazobactam) and methicillin-resistant *Staphylococcus epidermidis* (MRSE) after 3.15 days of incubation from another site (sensitive to chloramphenicol, ciprofloxacin, clindamycin, erythromycin, linezolid, tetracycline, and cotrimoxazole; resistant to oxacillin and penicillin G). Urine and stool cultures were negative.

He was transfused with packed red blood cells and platelet concentrate units. Electrolytes were corrected. Surgical drainage was performed for the leg abscess. Intravenous piperacillin-tazobactam was given and shifted to a combination of a two-week course of intravenous ceftazidime and oral clindamycin when culture results were available. A seven-day course of intravenous amikacin was added after the results of repeat intraoperative wound aspirate grew a heavy growth of *Escherichia coli* (sensitive to amikacin; resistant to ampicillin-sulbactam, aztreonam, cefazolin, cefepime, cefoxitin, ceftazidime, cefuroxime, clindamycin, gentamicin, imipinem, meropenem, piperacillin-tazobactam, and cotrimoxazole). He was discharged after three weeks. The patient was not tested for HIV status.

Case discussion

Myelodysplastic syndromes (MDS) are clonal disorders of haematopoietic stem cells and are associated with a risk of severe infections.[13] Infection is the most common cause of death in MDS, affecting 38% of patients followed by AML transformation (15%) and haemorrhage (13%).[14] This risk of infection has been attributed primarily to both quantitative and qualitative defects in neutrophils.[15-17] Other potential mechanisms predisposing MDS patients to infections include a reduced number of peripheral B cells, impaired antibody production,[18-20] lymphocytopenia[18,21] and NK cell impairment.[22-23]

Our patient presented to the emergency room with profound bacterial co-infections involving the lungs, bloodstream, and soft tissue of the leg. The patient's susceptibility to these bacteria can be attributed to MDS (evident from the neutropenia and lymphopenia in the blood count) and possibly to the effects of chronic steroid use. Neutropenia likely represents the major reason for the increased risk of infection in MDS.[13] However, functional neutrophil defects, antibody-related effects and NK cell defects related to MDS were not demonstrated due to inaccessibility and impracticality of these tests. The infecting organisms in our patient, which include *Enterobacteriaceae* and coagulase-negative *staphylococci*, are similar to the infecting organisms seen in febrile neutropenia and MDS patients.[24] On the other hand, other uncommon pathogens in MDS such as mycobacteria and fungal agents were not seen in our patient.[25]

There were no abdominal complaints such as abdominal pain, vomiting, or diarrhoea in our patient to raise suspicion of typhoid fever in the emergency room, although abdominal pain is present only in about 30–40% of typhoid fever patients at presentation. In most cases of *S. typhi*, the purported initial site of infection is frequently the gastrointestinal tract which, in severe cases, spreads haematogenously to reach distant sites, such as the soft tissues of the leg. Reported extra-intestinal *Salmonella* infections in MDS are rare. Cases reported include infected subdural empyema,[8] aortitis,[9] empyema thoracis,[10-11] and splenic abscesses.[10,12] In our patient, co-infections of *Pseudomonas*, *Staphylococcus*, and *Enterobacter* are present aside from *S. typhi*. These multiple co-infections were present in the blood and the lungs and have more grave clinical implications compared to a leg abscess from *S. typhi*. However, it is

important to treat all these infections at once with a targeted antibiotic therapy: initially with empirical broad-spectrum antibiotics and, eventually, with a more streamlined treatment. Moreover, source control of infections with surgical drainage cannot be over emphasized.

Quinolones, macrolides, and third-generation cephalosporins are preferred for empirical therapy for presumed *Salmonella* infections until susceptibility reports are available. In this patient, we empirically started piperacillin-tazobactam for broad-spectrum coverage for gram-positive, gram-negative, and anaerobic bacteria, and clindamycin to cover for possible community-acquired MRSA. We then stepped down to a combination of ceftazidime and clindamycin to address the patient's polymicrobial infection, covering for *S. typhi* (soft tissue abscess), *Pseudomonas aeruginosa* (pneumonia, bacteraemia), *Enterobacter aerogenes* (pneumonia) and MRSE (pneumonia and bacteraemia). The bacterial growths from our patients are most likely community-acquired because of the highly susceptible sensitivity patterns. Often, nosocomial infections exhibit multi-drug resistant species.

Recent sensitivity patterns report that at least 95% of *S. typhi* is susceptible to ceftazidime, ceftriaxone, cotrimoxazole, chloramphenicol, and amoxicillin-clavulanic acid, with 80% resistance rate to nalidixic acid and decreased susceptibility to ciprofloxacin.[26] The *S. typhi* isolate in our patient had intermediate sensitivity to fluoroquinolones; this phenomenon has been described in previous studies.[27-30] In the Philippines, *S. typhi* isolates are highly susceptible to ampicillin, chloramphenicol, and cotrimoxazole.[31] Resistance to ampicillin and cotrimoxazole is 0.8% and none for chloramphenicol. There has been a report of five unconfirmed isolates with poor susceptibility to ciprofloxacin and one isolate resistant to ceftriaxone. Increasing antimicrobial resistance is a compelling problem.

Conclusion

To our knowledge, this is the first reported case in the world of *S. typhi* soft tissue abscess in a patient with MDS. *Salmonella* infections should be considered in the differential diagnosis of soft tissue abscesses, especially in patients with MDS.

What is known already:	What this study adds/ highlights:
• Risk factors for *Salmonella* infections include extremes of age (newborns and elderly), malnutrition, sickle-cell and malarial anaemia, and immunocompromised conditions such as systemic lupus erythematosus, non-Hodgkin's lymphoma, chronic steroid use, and HIV infection. • Reported *Salmonella* infections in MDS are rare. These include infected subdural empyema, aortitis, empyema thoracis and splenic abscesses. • Culture and drug-sensitivity testing of collected samples from suspected and known sites of infection are crucial to the diagnosis and treatment of infections especially in immunocompromised patients.	• *Salmonella typhi* abscess should be a differential diagnosis among MDS patients who present with soft tissue abscess. • Both surgical drainage and medical interventions such as appropriate antibiotics and supportive therapy are important in successfully managing *S. typhi* abscesses. • To our knowledge, this is the first reported case of *S. typhi* soft tissue abscess in a patient with MDS.

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