



Case report

Rare presentation of infective endocarditis due to *Salmonella enterica* subspecies *salamae* (subgroup II) in a sickle cell anemia girl



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ABSTRACT

Sickle cell anemia (SCA) is a common inherited kind of hemolytic anemia in Africa and some areas of Asia. In Saudi Arabia, SCA is prevalent as well. The patient of SCA is prone to some bacteria species more than the others, and *Salmonella* is one of the most prevalent infections in SCA that were known to cause bacteremia, osteomyelitis, septic arthritis, and gastroenteritis. Herein, we report a 7-years old girl who presented with a history of fever for five days and jaundice with abdominal pain and mild respiratory distress. Later, the patient was diagnosed to have infective endocarditis due to *Salmonella enterica* subspecies *salamae* (subgroup II). The patient improved completely after receiving proper antibiotics. To the best of our knowledge, there is only one case of adult SCA that has been reported with infective endocarditis due to *Salmonella enterica* but no reported case in pediatric.

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Introduction

Salmonella species are gram-negative bacilli, and almost all are motile, indole-negative, and non-lactose fermenters [1]. Most of the clinical presentations are ranging from simple gastroenteritis to severe infections such as bloodstream infection, osteomyelitis, and meningitis especially in the high-risk group of infants and immunocompromised patients like sickle cell anemia patients [2]. Occasionally, it may metastasize and cause infection in organs with pre-existing anatomic abnormalities such as polycystic kidney, tumor, and hyperplastic lymph nodes [1]. Rarely, *Salmonella* can cause meningitis, peritonitis, urinary tract infection, jaundice, liver and spleen abscesses, pneumonia, and thrombocytopenia [1–3]. Cardiac involvement in salmonella infection is well known, and most of the cases present as myocarditis but endocarditis is so scarce [3]. Underlying cardiac diseases, such as congenital cardiac diseases and rheumatic heart diseases are responsible for most of the cases of endocarditis due to salmonella infection [3]. *Salmonella* is responsible for 0.01–2.9 % of bacterial infective endocarditis with the mean

age of 50–60 years [5]. Mitral valve salmonella infective endocarditis represents around a third of the cases of *Salmonella* infective endocarditis while *Salmonella* mural infective endocarditis stands for 26.4 %. The overall Mortality rate can reach 42.5 % [5].

Salmonella infection is quite common in patients with sickle cell anemia which belongs to many reasons. Infarction secondary to capillaries occlusion due to intravascular sickling allows the salmonella to get access to the bloodstream. Suppressed opsonization and complement function will allow salmonella to cause serious infections in these patients. For these reasons and others, salmonella is considered one of the significant causes of morbidity and mortality in SCA patients [4].

Herein we report a seven years old girl with SCA who presented to the emergency department with fever, jaundice, abdominal pain, and respiratory distress and was diagnosed later to have infective endocarditis due to *Salmonella enterica* subspecies *salamae* (subgroup II). After a broad review of the literature, we found only one reported infective endocarditis due to *Salmonella enterica* ss. *arizona* in adult SCA patients [7].

Case Data

A seven years old Saudi girl is known as a case of SCA. She presented to the emergency department with a history of fever for

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five days and jaundice with abdominal pain and mild respiratory distress. Also, she was complaining of left elbow pain for the preceding three days.

On examination, the patient was looking unwell, deeply jaundiced, highly febrile, with tachycardia and tachypnea. Blood pressure was normal. Chest examination revealed bilateral crepitation with bronchial breath at the base of lungs bilaterally. Cardiovascular system examination was normal. The abdomen was soft and lax with tender hepatomegaly while the spleen was just palpable. The left elbow was swollen with hotness and tenderness. No neurological deficits had been detected.

Initial workup showed :Hemoglobin: 7.5 g/dl, Mean Corpuscular Volume (MCV): 76 fL, White Blood Cells (WBC): $24 \times 10^9/L$, Platelets: $335 \times 10^9/L$, Prothrombin Time: 13 s., Partial Thrombotic Time: 33 s., Total Bilirubin (TB): 535 $\mu\text{MOL/L}$, Direct Bilirubin (DB): 434 $\mu\text{MOL/L}$, albumin: 24 G/L. Erythrocyte Sediment Ratio (ESR): 33 mm/hr. C-reactive protein (CRP):0.45. Chest X-ray revealed increased bronchovascular marking with bilateral basal lung opacities.

Hospital Course

Upon initial assessment in the first day, the patient was suspected of having liver complications of sickle cell anemia (like hepatic vasoocclusive crisis, viral hepatitis, intrahepatic cholestasis, or cholelithiasis) with acute chest syndrome and suspected septic arthritis.

First Blood culture, urine culture, influenza PCR, and Respiratory Syncytial Virus (RSV) rapid test had been sent and antimicrobials (cefotaxime, vancomycin azithromycin, oseltamivir) were started.

The patient was managed supportively with intravenous maintenance hydration, simple blood transfusion, analgesics. The rapid test came negative for RSV. Oseltamivir had been stopped after the result of negative influenza PCR.

Upon the second and third day of admission, the patient was still looking ill with respiratory distress and deep jaundice and received a simple blood transfusion. Pending first blood culture grew negative bacilli for more identification and a new sample was sent. Antibiotics were adjusted to meropenem and amikacin only.

On the fourth day, the patient deteriorated and was transferred to the intensive care unit for close observation and blood exchange. The final result of the first blood culture after using the automated machine and subsequent serological and biochemical tests showed the growth was *Salmonella enterica* subspecies *salamae* (subgroup II) which was sensitive to amoxicillin/clavulanic acid, ampicillin, cefepime, cefotaxime, ceftazidime, ciprofloxacin, levofloxacin, meropenem, piperacillin/tazobactam, tetracycline, tigecycline, trimethoprim/sulfamethoxazole.

Because of persistent high fever and the patient was deteriorating, diagnostic measures had been expanded to include CT chest, abdominal ultrasound, and echocardiography. CT chest showed bilateral basal airspace lung consolidations while abdominal ultrasonography revealed hepatomegaly with gallbladder mud and no signs of cholecystitis or any other intraabdominal infections. Echocardiography showed two vegetations at the inferior vena cava-right atrium junction (about 7 mm by 8 mm in diameter). As infective endocarditis was not suspected initially and the patient was looking very sick since admission, no frequent blood cultures were taken before starting antibiotics and all blood cultures after starting antibiotics came negative. However, the visualized vegetation and single growth in blood culture in addition to elevated ESR make IE is highly suspected according to Modified Duke criteria.

Despite pan-sensitivity of *Salmonella enterica* subspecies *salamae* (subgroup II), the patient showed a slow response to sensitive single antibiotics over the first 3–4 days. Also, a quick review of the literature showed high mortality among cases of IE

due to salmonella even with the use of sensitive antibiotics in some cases in addition to the unusual and serious presentation of salmonella, the patient was planned to receive ciprofloxacin and cefotaxime for six weeks with echocardiography follow up. Amikacin was continued for 2 weeks. Within the next three days, the patient showed significant clinical improvement. Repeated echocardiography during admission showed smaller vegetation size that then disappeared at the end of the antibiotics course and no surgical interventions were required.

Discussion

Salmonella infection is quite common in patients with sickle cell anemia and this belongs to some reasons. For instance, gastrointestinal tract infarction secondary to capillaries occlusion due to intravascular sickling allows the salmonella to get access to the bloodstream [1]. Furthermore, suppressed opsonization and phagocytosis raise the risk of salmonella infections in sickle cell anemia patients [1,4].

Infective endocarditis usually occurs in the diseased cardiac valves or artificial valves and *Salmonella* as a cause of endocarditis represents a small portion among all other bacteria. Atrial thrombus formation, myocarditis, and pericarditis are the most common presentation in cases of *Salmonella* infections of the heart. However, such complications, which are associated with a poor prognosis did not present in our patient. *Salmonella* serotypes that are common to cause endocarditis to include *S. choleraesuis*, *S. typhimurium*, *S. thompson*, and *S. derby* serotypes, and *S. typhi* while *Salmonella enterica* is very seldom to cause infective endocarditis [5,6].

This case also responded well to 3rd generation cephalosporin plus the ciprofloxacin antibiotic course. Although *Salmonella* is a common infection in sickle cell anemia which is very common in our area, we did not confront any case with infective endocarditis due to *Salmonella* infection. After an extensive review of the literatures, we found no reported case with infective endocarditis due to *Salmonella enterica* subspecies *salamae* among sickle cell anemia patients. This case shall attract attention toward the spectrum of salmonella infections in patients with sickle cell anemia which may extend to cause infective endocarditis.

No guideline suggested that one antibiotic or more treat SCA patients with IE due to *Salmonella*. Chen WL et al. had reviewed some cases of salmonella endocarditis. Some cases responded to single antibiotics while others responded to double or triple antibiotics [5]. One old lady with diabetes mellitus and end-stage renal disease (Yusuke Tsugawa et. al) was treated with double sensitive antibiotics, ciprofloxacin, and ceftriaxone, from the first day, then deteriorated after grading down the antibiotics to one sensitive antibiotic. Unfortunately, the patient passed away after she developed brain embolism [5]. Subsequent resistance of salmonella to long-duration single antibiotics could be the reason. On the other hand, Starakis I et al. reported one case of SCA with *Salmonella enterica* ss *arizonae* with successful treatment with double antibiotic coverage without surgical intervention [7].

As our patient responded to double coverage of antibiotics after initial delayed in clinical response to a single sensitive antibiotic, we may suggest that double coverage of sensitive antibiotics to treat salmonella in SCA patients with IE due to salmonella could be necessary till further data are available.

Furthermore, we recommend considering infective endocarditis in the patient with SCA if fever persisted without clear, obvious focus.

Conclusion

We are reporting this case to attract the attention of the clinicians to the spectrum of *Salmonella enterica* infections in SCA

that may be extended to include infective endocarditis. We suggest investigating for IE in any SCA patient with delayed clinical improvement after Salmonella infection. Early detection and treatment could reduce mortality and morbidity.

Authors Statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in (IDCases Journal).

Declaration of Competing Interest

No conflict of interest by all authors

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