Case Report

Pericardial tamponade secondary to *Salmonella enterica* serovar Enteritidis

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ABSTRACT

Nontyphoidal *Salmonella* species usually cause self-limiting gastroenteritis. Extra-intestinal manifestations can occur, and purulent pericarditis is an extremely rare manifestation. It is potentially life-threatening, and a high index of suspicion is required to prevent morbidity and mortality. We report a case of *Salmonella enterica* serovar Enteritidis infection manifesting as life-threatening pericardial tamponade in a woman living with advanced HIV. It highlights a life-threatening manifestation of invasive nontyphoidal *Salmonella* species and the importance of appropriate treatment.

Keywords: Invasive nontyphoidal Salmonella, HIV, South Africa, Pericardial tamponade

INTRODUCTION

Purulent pericardial effusion is a rare condition with a significant mortality risk.(1) Risk factors include pneumonia, endocarditis, direct contamination via thoracic surgery or chest trauma, and immunosuppressive conditions, such as co-infection with human immunodeficiency virus (HIV).(1)

Commonly implicated organisms are *Staphylococcus aureus* and *Streptococcus pneumoniae*, but any organism can spread from the bloodstream to the pericardium and cause purulent pericardium[1]. Nontyphoidal *Salmonella* (NTS) species are an extremely rare cause of purulent pericarditis[1]. The most important risk factors for NTS bacteraemia and subsequent pericardial effusion in sub-Saharan populations are HIV co-infection, malaria and malnutrition.(2)

Pericardial tamponade is an extremely uncommon and potentially fatal manifestation of invasive NTS and has only been described in case reports.(1,3)

We report a case of *Salmonella enterica* serovar Enteritidis infection manifesting as life-threatening pericardial tamponade in a woman living with advanced HIV.

CASE DESCRIPTION

A 40-year-old woman presented to the emergency department of a public hospital in Johannesburg, South Africa with a four-day history of cough, palpitations, bilateral swelling of the legs and diarrhoea. Upon examination, she had a low blood pressure of 90/60 mmHg, a heart rate of 126 beats per minute, and dyspnea with room air saturation of 88%. She was ill-looking with marked bitemporal wasting. Her jugular venous pulsation was elevated to the angle of the jaw with soft first and second heart sounds on auscultation. Bilateral crackles were present on pulmonary examination, and moderate bipedal oedema was present in the lower limbs. Her chest X-ray showed a globular heart. A point-of-care ultrasound confirmed clinical suspicion of pericardial tamponade.

Ultrasound-guided emergency pericardiocentesis drained 200mls of purulent pericardial fluid with immediate symptomatic and hemodynamic improvement. The patient was initiated on empiric amoxicillin-clavulanate and admitted to a high-care setting for therapeutic pericardiocentesis and further work-up. Two months prior to her current presentation, she had presented to the same hospital with mild gastroenteritis and was newly diagnosed with HIV co-infection. At that time, she had a CD4 count of 26 cells/uL and a viral load of 514,000 copies/mL. She refused further hospital treatment and was lost to follow-up.

Her blood cultures from the previous hospital presentation and the pericardial fluid from her current admission grew a non-lactose fermenting Gram-negative bacillus on MacConkey agar. (Figure 1 & 2) The serotype was

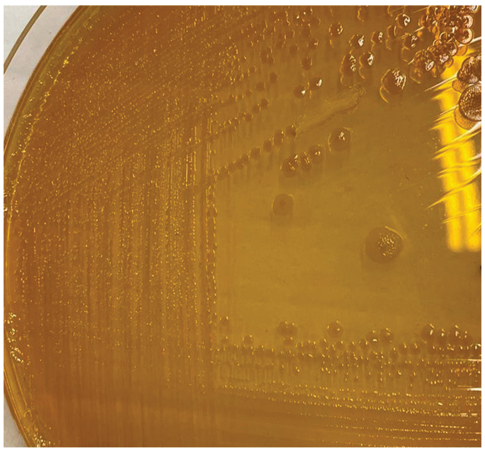

Figure 1: Pericardial fluid cultures on MacConkey agar of *Salmonella* species.

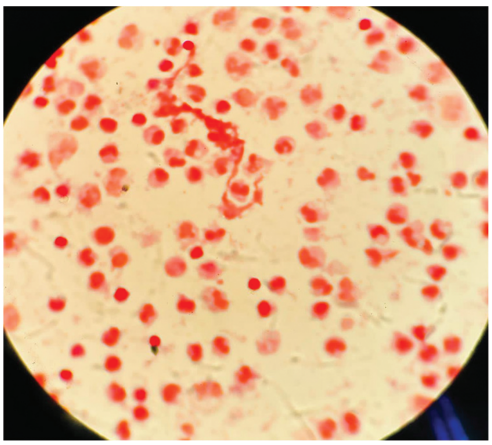

Figure 2: Gram stain of pericardial fluid showing multiple leucocytes and gram-negative bacilli.

determined as *Salmonella enterica* serovar Enteritidis using the Kauffmann-White Scheme, based on the antigenic formulae of somatic 'O' and flagellar 'H' antigens.

Ceftriaxone was initiated based on antimicrobial susceptibility testing and continued for 14 days. Antiretroviral treatment (ART) with tenofovir, lamivudine and dolutegravir was initiated soon after multiple tests ruled out TB co-infection. (Table 1)

The patient showed marked clinical and biochemical improvement over the next two weeks. Subsequent blood cultures over the next three weeks were negative. Serial echocardiography showed no evidence of fluid re-accumulation.

She received extensive counselling regarding adherence to ART and was discharged with a close follow-up plan with the cardiology and infectious diseases departments.

DISCUSSION

NTS has a faecal-oral transmission route and usually causes a self-limiting disease in immunocompetent hosts.(2,4) In people living with HIV (PLWHIV), however, it more frequently causes severe disease manifestations.

The gastrointestinal tract is a site of early and profound CD4 T-cell depletion in HIV infection. Loss of T-helper 17 cells and its associated cytokine interleukin-17 is critical to the systemic invasion of *Salmonella* bacteria.(2) The early innate response of neutrophils and monocyte recruitment is essential to prevent spread to lymphoid tissue.(5) Our patient, who had low CD4 T-lymphocyte, neutrophil and monocyte counts with mild gastrointestinal symptoms on her initial presentation, presented initially with bacteraemia, which in turn progressed to pericardial empyema with pericardial tamponade eight weeks later.

Dysregulated cytokine function during intracellular infection leads to the persistence and recurrence of invasive NTS. In one study, bone marrow and blood cultures at the time of infection initially showed equal amounts of Salmonella. However, during subsequent relapse, the concentration of NTS in the bone marrow was six times greater. (2) Again, the role of adaptive immunity, in particular CD4 T-lymphocytes, is crucial in preventing Salmonella burden and associated mortality. Inflammatory cytokines such as interferon-gamma and tumour necrosis factor-alpha also play an essential role by inhibiting the ongoing proliferation secondary to macrophage activation.(5)

Ineffective serum killing of nontyphoidal *Salmonella* strains has been described in PLWHIV. In a Malawian study, despite the presence of IgG antibodies against Salmonella polysaccharide, impaired serum killing of the bacteria was observed mainly due to the interaction of IgG antibodies against polysaccharide with coexisting bactericidal antibodies directed against *Salmonella* outer membrane proteins.(2)

The lack of CD4 T-lymphocytes and subsequent imbalance of protective cytokines in our patient led to the ongoing intracellular bacterial proliferation with subsequent bacteraemia and the rather dramatic presentation of pericardial tamponade. She denied treatment on her initial visit but showed marked symptomatic improvement with two weeks of intravenous ceftriaxone on her subsequent admission. There was no evidence of recurrent pericardial effusion on repeated echocardiography. Further, given the normal bone marrow aspiration and trephine results (Table 1), concern for subsequent relapses remains low. However, should she present with a relapse, we would consider pericardiectomy (or a less invasive pericardial window) to avoid the risk of severe tamponade.

The rate of recurrence of invasive NTS prior to the advent of ART was 20–40%.(2) Recurrence is caused by recrudescence rather than reinfection, which was evident in another Malawian study where index and recurrent paired isolates were identical in genotyping and

Table 1: Laboratory Investigations

Test	Patients Result (2-months prior to current admission)	Patient's result during current admission	Normal Values
Absolute CD4	26 cells/uL	-	
HIV Viral Load	514000 copies/mL	-	
Blood Culture & Serotype	*Salmonella* Enteritidis	*Salmonella enterica*	
Pericardial Fluid Protein LDH Leucocytes Culture & serotype GXP	-	49g/L >750 >10000 *Salmonella enterica* serovar Enteritidis Negative	
TB Bactec	Negative	Negative	
White cell count	1.09 × 109/L	5.89 × 10 9/L	3.90–12.60
neutrophils	0.82 × 109/L	4.25 × 109/L	1.60–8.30
lymphocytes	0.19 × 109/L	0.42 × 109/L	1.40–4.50
Haemoglobin	7.1g/dL	7.0g/dL	11.6–16.4
MCV		99.9fL	78.9–98.5
Platelet count	45 × 109/L	58 × 109/L	186–454
Iron	2.0 umol/L	-	9.0–30.4
Ferritin	4997 ug/L	-	10–291
Sodium	134 mmol/L	135 mmol/L	136–145
Potassium	3.6 mmol/L	4.0 mmol/L	3.5–5.1
Chloride	99 mmol/L	101 mmol/L	98–107
Urea	21 mmol/L	23.7 mmol/L	2.1–7.1
Creatinine	133 umol/L	129 umol/L	49–90
Hepatitis A IgM	Negative	Negative	
Hepatitis B SAntigen	Negative	Negative	
Hepatitis C Antibody	Negative	Negative	
CRP	195 mg/L	129 mg/L	<10
Bone Marrow Trephine and Aspiration	No evidence of Salmonella infection		

phenotyping.(6) Due to the high risk of invasive NTS bacteraemia recurrence, the preferred treatment duration is 10–14 days.(6) Should there be suspicion of an endovascular complication, the duration of therapy is usually extended to 4–6 weeks.(6)

Given the well-described role of ART in immune reconstitution, we would expect to see a significant decline in subsequent infection in PLWHIV. However, large multi-centre studies are needed to establish such a fact.

CONCLUSION

Salmonella enterica serovar Enteritidis is known to be the major cause of invasive NTS. Its presentation in immunocompromised patients is varied and occasionally life-threatening. This case study reports on an extremely rare and potentially fatal complication of invasive NTS. It highlights the importance of appropriate treatment of NTS bacteraemia in PLWHIV and timely initiation and compliance to ART. Research efforts towards vaccine development and non-vaccine prevention measures for preventing NTS invasive disease should also be considered.

ETHICAL CONSIDERATION

Informed consent was obtained from the patient. Ethical approval was obtained from Helen Joseph Hospital and Wits HREC (ethical clearance number M230569).

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