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INTRODUCTION

- Invasive non-typhoidal *Salmonella* (NTS) infection is a well-recognised clinical syndrome in immunocompromised patients, particularly with HIV infection and Sickle Cell anaemia. The incidence in other at-risk groups is less well described.^{1,2}
- Less than 1% of enteric infections with NTS result in bacteraemia. *Salmonella* serotype and host factors affect the risk of bacteraemia. Risk factors include; extremes of age, immunosuppression, haemoglobinopathies, liver disease, atherosclerosis & diabetes.¹⁻⁴
- The presence of prosthetic material (eg. cardiac valves, articular replacements and intra-vascular stents) is a risk factor for metastatic complications.¹⁻⁴
- In addition, disruption of the lining of the GI tract, for instance in Inflammatory Bowel Disease, predisposes to progression from enteric to systemic salmonellosis.⁵
- Risk assessment of patients presenting with enteric NTS infection is crucial, as appropriate treatment reduces the risk of developing invasive disease and metastatic complications.⁶
- We present a case of prosthetic joint septic arthritis, bacteraemia and sepsis associated with *Salmonella typhimurium*, in a patient with insulin-dependent diabetes, inflammatory bowel disease and corticosteroid usage.

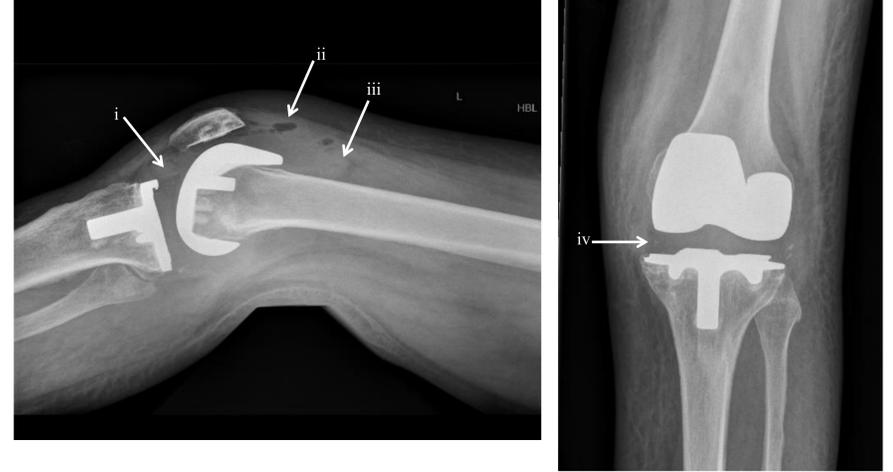


Figure 1. Lateral and AP radiographs of the left knee revealing intra-articular effusion (i), gas locules anterior to the patella (ii), soft tissue oedema (iii) and increased joint space (iv),

CASE DISCUSSION

- This 71 year old man presented to our Emergency Department with a hot, swollen left knee, fever and high inflammatory markers (Figures 1 & 4). Past history included insulin-dependent type 2 diabetes, ulcerative colitis, ischaemic heart disease and left total knee replacement 20 years previously.
- 10 days prior to this presentation he had been admitted for 5 days with diarrhoea and vomiting. Treatment had been commenced for ulcerative colitis flare, including a 3-week tapering course of prednisolone. Stool culture sent from his GP had identified *Salmonella* species, however cultures sent whilst in hospital were negative. As he was asymptomatic by the time of discharge, antimicrobial therapy was not initiated.

- On the date of readmission, knee aspiration was performed without preceding antibiotics. Frank pus was aspirated and gram-negative rods seen on microscopy. Treatment commenced with ceftriaxone 2g OD. After 12 hours blood cultures also flagged positive, with gram-negative rods on microscopy (Figures 2 & 3). Open washout and debridement of the infected knee joint was performed in theatre the following day.
- MALDI-TOF and API testing of isolates from blood, synovial fluid, debrided tissue and stool revealed *Salmonella* species, further characterised by agglutination reactions as *Salmonella typhimurium*. The organism was confirmed by whole-genome sequencing at the reference lab.

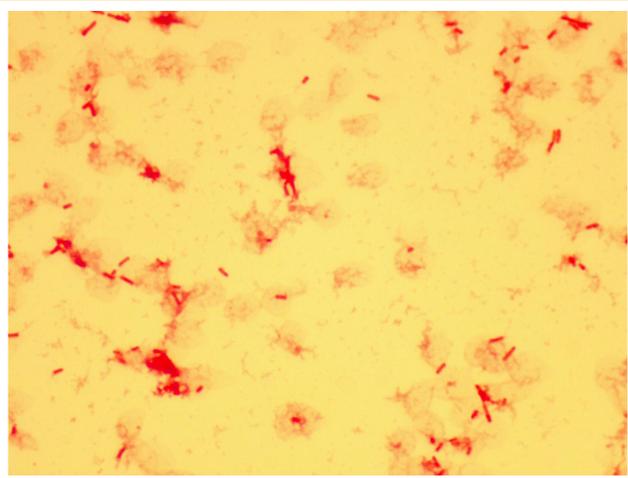


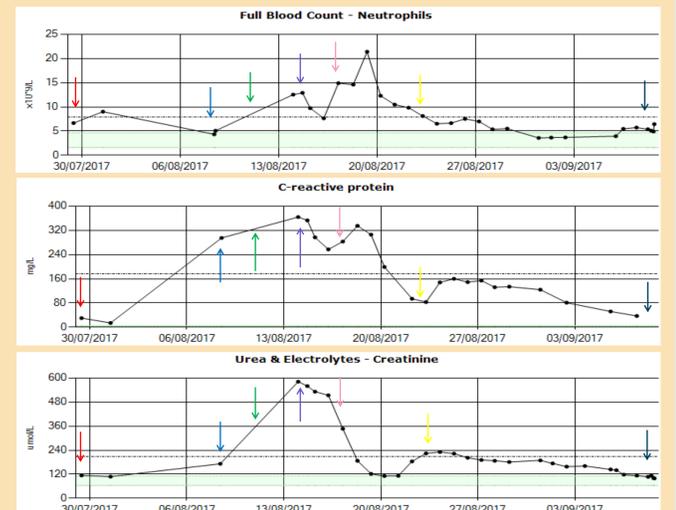
Figure 2. Gram stain of blood culture revealing gram-negative staining bacilli.



Figure 3. Bacterial colonies with black centres on Xylose lysine deoxycholate (XLD) agar, typical of *Salmonella* species.

Figure 4. Trends in inflammatory markers and renal function over time.

(i) 1st presentation (ii) 2nd presentation & ceftriaxone started (iii) Knee debridement (iv) ITU admission (v) Prosthesis removal (vi) changed to ciprofloxacin (vii) died.



- Despite appropriate antibiotics the patient developed septic shock, acute kidney injury (peak creatinine = 580μg/ml) and metabolic acidosis, requiring ITU admission on day 6 for haemofiltration, intubation and inotropic support.
- CT angiogram of the thorax, abdomen and pelvis showed no evidence of vascular aneurysms or other endovascular source of infection.
- Seven days into admission a first stage joint revision was performed. The prosthesis was removed, with >1L pus. Intra-operative tissue & pus cultured the same organism.
- On day 13 antimicrobial therapy was changed from ceftriaxone to ciprofloxacin in response to hepatic dysfunction (peak ALT = 313IU/L and Alk Phos = 1267IU/L) and isolation of multi-resistant *E. Coli* in samples from broncho-alveolar lavage. MIC testing confirmed sensitivity to ciprofloxacin and ceftriaxone.
- The patient responded with defervescence, reduction in inflammatory markers and improvement in renal and hepatic function (nadir creatinine 120μg/ml and ALT 72IU/L) (Figure 4). He was extubated, weaned off inotropes and discharged from ITU.
- Further debridement was planned at 30 days; however the patient suffered cardiac arrest intra-operatively and died. Post-mortem was not performed, in accordance with the family's wishes.
- Cause of death was suspected to be a sudden cardiac event precipitated by severe sepsis in the context of multiple underlying comorbidities.

CONCLUSIONS

- This case reiterates the risk of invasive NTS in patients with recognised risk factors including diabetes, atherosclerosis, corticosteroid usage and inflammatory bowel disease.¹⁻⁵
- The presence of prosthetic joint material (as a nidus for metastatic spread) should alert clinicians to the risk of complications secondary to bacteraemia. Similarly, the presence of intra-vascular and intra-cardiac material would be a red flag feature.^{3,4}
- In cases of gastroenteritis associated with non-Typhoidal *Salmonella*, where such risk factors exist clinicians must consider prompt antimicrobial treatment to reduce the risk of bacteraemia and secondary invasive NTS disease.⁶
- This case also highlights the potential severity of NTS disease and its association with septic shock and renal failure, particularly in the context of patients with significant comorbidities.

Acknowledgements

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References

- Ao TT, Feasey NA, Gordon MA, Keddy KH, Angulo FJ, Crump JA. Global burden of invasive nontyphoidal *Salmonella* disease, 2010(1). *Emerg Infect Dis.* 2015;21(6).
- Gordon MA. *Salmonella* infections in immunocompromised adults. *J Infect.* 2008;56(6):413.
- AU Hung TY, Liu MC, Lin YC. Rotavirus infection increases risk of bacteraemia in children with nontyphoid *Salmonella* gastroenteritis. *Eur J Clin Micro Infect Dis.* 2009;28(4):425.
- AUCohen PS, O'Brien TF, Schoenbaum SC, Medeiros AA. The risk of endothelial infection in adults with salmonella bacteraemia. *Ann Intern Med.* 1978;89(6):931.
- Benenson S, Ravesh D, Schlesinger Y, Alberton J, Rudensky B, Yimmon AM. Risk of vascular infection in adult patients with nontyphoid *Salmonella* bacteraemia. *Am J Med.* 2001;110(1):60.
- Mattila L, Peltola H, Simula I. Short-term treatment of traveler's diarrhoea with norfloxacin: a double-blind, placebo-controlled study during two seasons. *Clin Infect Dis.* 1993;17(4):779.