An unusual dual infection with *Salmonella bredeney*, including bacteraemia, and enterohaemorrhagic *Escherichia coli* O157 that posed a therapeutic dilemma

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In this case report, we describe an unusual case of a patient who had a dual infection with *Salmonella bredeney* including bacteraemia and enterohaemorrhagic *Escherichia coli* O157 following travel to Cyprus. This posed a therapeutic dilemma. We delayed treatment of the *Salmonella* infection until signs of colitis had resolved.

**Introduction**

*Salmonella* species are one of the most important causes of foodborne infection with over 8000 cases of non-typhoidal *Salmonella* infection reported by the Health Protection Agency (HPA) in the UK in 2010. Of these, nearly 50% were caused by *Salmonella enterica* serovar Typhimurium or *Salmonella enterica* serovar Enteritidis. *Salmonella bredeney* is a rare serotype and represented just 0.06% of *Salmonella* serotypes in the USA’s Center for Disease Control surveillance system in 2009 (Newell et al., 2010). Bacteraemia with non-typhoidal *Salmonella* is even less common, occurring in fewer than 5% of cases, and is often associated with immunosuppression (Cohen et al., 1987).

Enterohaemorrhagic *Escherichia coli* (EHEC) is an important but less frequent cause of foodborne infection with the added complication of haemolytic uraemic syndrome (HUS). Most treatment guidelines advise against the use of antibiotics in EHEC infections due to the increased risk of HUS, although this has not been definitively proven (Panos et al., 2006). A simultaneous infection with these pathogens has not previously been reported to our knowledge.

**Case report**

A 62-year-old British woman was admitted to a district general hospital in July 2011 with an 18-day history of watery, bloody diarrhoea that had commenced 4 days into a holiday in Cyprus. On her return to the UK, 3 days prior to admission, she developed severe bloody diarrhoea with stool frequency of 8–10 times daily, central abdominal cramps, nausea, anorexia, fevers, rigors and postural dizziness. She had not received any antibiotic therapy in Cyprus or the UK.

A provisional diagnosis of infective diarrhoea was made, and stool samples and blood were sent for culture. The patient was barrier nursed and started on intravenous rehydration therapy.

Her blood cultures became positive for Gram-negative rods on day 2 of admission, after 16 h of incubation, and the organism was subsequently identified as *Salmonella* sp. The isolate was sent for further identification to the Laboratory for Gastrointestinal Pathogens, Centre for Infections, HPA, London, UK, and was identified as *S. bredeney* by 16S rDNA restriction analysis. The isolate was susceptible to amoxicillin and co-trimoxazole. Stool cultures after 24 h incubation grew *Salmonella* sp from direct culture on XLD agar (Oxoid) and a suspected *E. coli* O157 was identified by direct non-fermenting growth on sorbitol-MacConkey agar and agglutination with O157 antisera. These stool isolates were further identified as *S. bredeney* and *E. coli* O157: H7 by the reference laboratory. The *E. coli* O157 isolate was identified as phage type 31 and had the stx2 and eae (intimin) genes.

The patient was initially treated conservatively. She was stable and the finding of a possible VTEC in stools raised the possibility of worsening the risk of HUS if antibiotics were used. After 7 days of conservative treatment, the patient was still spiking temperatures of 38.0 °C and had rigors. The bloody diarrhoea was improving, however, and had reduced to twice-daily motions. By day 10, she had reverted back to passing normal stools, and the C-reactive protein had reduced to 40 mg l⁻¹. Her renal function had

**Abbreviations:** EHEC, enterohaemorrhagic *Escherichia coli*; HPA, Health Protection Agency; HUS, haemolytic uraemic syndrome.
initially worsened on day 4 of admission (urea 8.7 mmol l\(^{-1}\), creatinine 103 \(\mu\)mol l\(^{-1}\)) but had improved by day 7 (urea 4.3 mmol l\(^{-1}\), creatinine 81 \(\mu\)mol l\(^{-1}\)). Haemoglobin gradually decreased over the course of her admission from 12.5 g dl\(^{-1}\) to 7.5 g dl\(^{-1}\) on day 9 of admission and she received a 2 unit blood transfusion.

On day 10 of her admission, it was decided to start her on antibiotics as the colitis appeared to be resolving and because of the concern about the Salmonella bacteraemia possibly giving rise to further complications. She was started on amoxicillin 500 mg i.v. 8 hourly for 7 days and was discharged home on oral ciprofloxacin 500 mg on day 14 of admission to complete a total of 4 weeks of treatment. At discharge she was afebrile with a significant improvement in her general clinical condition and she was discharged from outpatient follow-up 6 months later.

Discussion

This patient posed a therapeutic dilemma as she had a dual infection with pathogens for which there is divergent guidance about the use of antibiotics. Current HPA guidance is to avoid antibiotics in EHEC infection due to the increased risk of HUS. Severe non-typhoidal Salmonella infection with bacteraemia requires antibiotic treatment due to the risk of complications such as endovascular infection (Cohen et al., 1987).

Fewer than 5% of non-typhoidal Salmonella gastrointestinal infections result in bacteraemia and generally this is more common in infants, the elderly or the immunocompromised. Bacteraemia is associated with a secondary focal infection, especially endovascular infection, with up to 25% of patients over the age of 50 developing this complication. S. bredeney is a rare, non-typhoidal Salmonella that has only occasionally been reported in outbreaks (Jahraus & Philips, 1999; Moore et al., 2003).

In suspected or documented EHEC infections, decisions to treat with an antibiotic should be weighed up carefully due to the perceived risk of developing HUS (Wong et al., 2000). Guidance from the Infectious Diseases Society of America states that management of cases should be purely supportive and that antibiotics should be avoided (Guerrant et al., 2001). In a recent review of the issue, the authors concluded that more randomized controlled trials are necessary in order to answer this question more fully.

A recent study that utilized real-time PCR on samples from patients with diarrhoea in Kolkata indicated that polymicrobial infections were present in 63% of stool samples (Sinha et al., 2012). This is, however, from a setting in which cholera and dysentery are endemic. They go on to question the ‘one pathogen one disease’ concept.

In our case, it is difficult to judge whether both organisms were active pathogens. The Salmonella isolate could have caused bloody diarrhoea and finding it in the bloodstream and growth after 16 h of incubation certainly makes it highly significant. The significance of the EHEC is then in question – was it also an active pathogen and contributing to this patient’s symptoms or did its presence reflect colonization only? It did, however, grow directly on the primary plates suggesting at least 10\(^4\) c.f.u. (ml faeces)\(^{-1}\). It is plausible that both played a role as their pathogenic mechanisms differ. Salmonella adheres to and invades intestinal epithelial cells thereby creating inflammation, which leads to fluid secretion and diarrhoea, whereas EHEC releases Shiga toxin, which blocks cell protein synthesis and causes cell death. This isolate was positive for stx2 and eae, indicating that it was a true EHEC. The mild renal failure and slow fall in haemoglobin in our patient made us concerned about development of HUS, so we initially withheld antibiotics and only started them after signs of colitis had resolved. In the absence of any further evidence, we therefore treated this patient as if she had an active infection with both pathogens.

In conclusion, in this very unusual case of dual infection with non-typhoidal Salmonella and EHEC, we decided, given current knowledge and national guidance, to delay antibiotic therapy for Salmonella while carefully observing any signs of deterioration. This may not be possible in patients with significant underlying immunosuppression. The issue of concurrent infection with multiple bowel pathogens merits further research.

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References


