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Article begins on page three of this document.

Title	Locally acquired extended spectrum β -lactamase <i>Shigella</i> infection
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Locally acquired extended-spectrum β -lactamase *Shigella* infection

Clinical record

A 32-year-old Australian-born, human immunodeficiency virus (HIV) negative man presented to hospital with 3 days of cramping abdominal pain, diarrhoea and fevers, 5 days after having unprotected receptive anal intercourse. Regular medications were tenofovir disoproxil fumarate and emtricitabine for pre-exposure prophylaxis (PrEP), with complete adherence. On examination, he had left lower quadrant abdominal tenderness. White cell count was $7.3 \times 10^9/L$ (reference range [RR], $3.9\text{--}12.7 \times 10^9$ cells/L) and C-reactive protein (CRP) 164 mg/L (RR, 0–5 mg/L). A presumptive diagnosis of infective colitis was made, and he was empirically commenced on intravenous ceftriaxone 2 g daily. He initially improved with resolution of fever and abdominal pain. A sexually transmissible infection screen was performed, which was negative, including HIV serology. Faecal cultures returned positive for *Shigella flexneri* serotype 3a. The patient completed 5 days of ceftriaxone therapy and was discharged home improved, with a CRP of 28 mg/L.

Four days later, he was re-admitted to hospital with recurrent symptoms and recommenced on intravenous ceftriaxone. CRP was 111 mg/L and an abdominal computed tomography scan with contrast demonstrated inflammatory changes in his sigmoid colon, but no evidence of bowel perforation or intra-abdominal collection. His diarrhoea and abdominal pain persisted and a repeat stool culture was again positive for *S. flexneri* serotype 3a. Antimicrobial susceptibility testing revealed resistance to azithromycin, trimethoprim–sulfamethoxazole and ceftriaxone. Subsequent genomic analysis demonstrated the presence of a CTX-M-27 extended-spectrum β -lactamase. Antimicrobial susceptibility testing on the first isolate was indeterminate, possibly due to loss of the plasmid encoding resistance genes during incubation, a known characteristic of *Shigella* spp. The organism retained fluoroquinolone susceptibility and our patient was successfully treated with oral ciprofloxacin 500 mg twice a day for 14 days. After this treatment, he remained well with no recurrence of his symptoms.

Discussion

In Australia, shigellosis is an increasingly common cause of diarrhoeal disease, particularly in returned travellers and men who have sex with men (MSM). While most healthy individuals will recover without treatment, antibiotics are typically recommended to reduce the duration of symptoms and prevent transmission of this highly infectious pathogen. Rates of antimicrobial resistance have been rising in *Shigella* spp, with resistance to ciprofloxacin now widespread and azithromycin resistance being particularly common in the MSM population.¹ In the Australian setting, resistance to ceftriaxone is thought to be rare and this drug is increasingly relied upon for empiric therapy.² Worldwide, however, resistance to third-generation cephalosporins is increasing, particularly in areas of high endemicity.³

We have described the first reported case of locally acquired shigellosis in Australia with treatment failure due to underlying ceftriaxone resistance. Our patient had not travelled overseas in over a year. This apparent local acquisition is concerning, particularly in light of recent data demonstrating extensive local transmission of drug-resistant *Shigella*.¹ If multidrug-resistant *Shigella* becomes widespread in the Australian community, it may lead to the loss of standard therapeutic options, which may have significant clinical and public health implications. While our patient may have acquired the infection directly from someone recently arrived from overseas, it is also possible this case heralds a warning about the possibility of ceftriaxone-resistant *Shigella* circulating within the Australian population.

Over the past 20 years, *Shigella* spp have been increasingly recognised as sexually transmitted pathogens, and the MSM population is a significant reservoir of multidrug-resistant *Shigella* strains worldwide. There has been clonal spread of *S. flexneri* serotype 3a among MSM globally,⁴ and acquisition and transmission of azithromycin resistance is well reported, with rates of about 50%.^{1,2} High rates of transmission of resistant organisms within the MSM population are hypothesised to be multifactorial, driven by oro-anal and other sexual practices, HIV co-infection, and selective pressure from the empirical use of antibiotics such as azithromycin to treat other sexually transmitted infections.⁴ The role of other factors including online dating and widespread PrEP uptake remains to be defined. Strategies such as safe sex practices, effective hand hygiene and abstinence while recovering from infection are important ways to reduce transmission among MSM.⁵

The inexorable progression of multidrug resistance in gram-negative bacilli including *Shigella*, as illustrated by our case, highlights the importance of culture-based stool testing for cases of presumed infectious gastroenteritis. The increasing failure of standard empiric oral therapy for shigellosis is foreseeable, meaning that antimicrobial susceptibility testing is crucially important, not only for individualised patient management but also for broader epidemiologic surveillance to inform guideline recommendations. Strategies such as preserving currently available antibiotics by judicious use, implementation of comprehensive antimicrobial stewardship programs and stringent infection control practices in both hospitals and the community may help reduce resistance while we await the development of new antimicrobials with novel mechanisms of action in the future.

Lessons from practice

- The prevalence of multidrug-resistant *Shigella* infection with resistance to first-line agents ciprofloxacin and azithromycin is increasing, particularly among men who have sex with men (MSM).
- Culture-based stool diagnostics with antimicrobial susceptibility testing is critically important to inform both individual patient treatment as well as future guideline recommendations.
- While *Shigella* isolates in Australia generally retain susceptibility to ceftriaxone, clinicians should be aware of the possibility of resistance, which could lead to treatment failure.
- While sporadic cases of ceftriaxone-resistant *Shigella* within Australia are generally thought to be imported from overseas, there is a high risk of local transmission and dissemination, particularly within the high risk MSM population.

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