Shigella spp. are transmitted directly from person to person or indirectly by low-inoculum infection (1). Among men who have sex with men (MSM), Shigella spp. are mostly transmitted sexually; clusters of such cases have been documented in Montreal and surrounding neighborhoods (2,3). Azithromycin is an alternative treatment for multidrug-resistant Shigella spp. infections in adults and children, but routine testing for azithromycin susceptibility is not yet standardized and recommended (1,4–6). In the United States, azithromycin MICs for 392 wild-type Shigella strains isolated in 2005–2006 were estimated to be 4–16 mg/L; the azithromycin MIC for 90% of the isolates was 8 mg/L (7).

The Study

In December 2012, the microbiology laboratory of the Centre Hospitalier de l’Université de Montréal–Hôpital Saint-Luc identified Shigella spp. with reduced susceptibility to azithromycin from 2 patients who had received this agent as treatment for shigellosis. The Montréal Public Health Department and Laboratoire de Santé Publique du Québec (LSPQ) were alerted. Retrospective and prospective laboratory surveillance was initiated to cover the period January 2011–April 2013. Laboratories routinely report shigellosis to the Montreal Public Health Department (Quebec, Canada).

Phenotypic identification of all Shigella spp. at the genus and species levels (8) was confirmed at LSPQ as described (9), after which serologic identification by slide agglutination (Denka Seiken Co., Ltd, Coventry, UK) was performed. Pulsed-field gel electrophoresis (PFGE) was performed at LSPQ according to international standards set by the US Centers for Disease Control and Prevention (10). Pulse types were determined by Shigella species, serotypes, and PFGE patterns. All Shigella spp. isolated during 2011–2013 underwent susceptibility testing for ampicillin, trimethoprim/sulfamethoxazole, and ceftriaxone by use of Vitek 2 (bioMérieux, Marcy l’Étoile, France) and for azithromycin and ciprofloxacin by use of Etest (AB Biодиск, Solna, Sweden). Shigella spp. with elevated MICs for azithromycin were also tested by disk diffusion for 30 μg nalidixic acid and by Etest for tetracycline and chloramphenicol. Vitek 2 and Etest susceptibility testing was performed as recommended by the manufacturers, and quality control strains gave expected results. The mph(A) gene, which codes for the macrolide 2′-phosphotransferase, was detected by PCR, as described (11).

After receiving ethics approval from the Centre Hospitalier de l’Université de Montréal–Hôpital Saint-Luc, we reviewed hospital charts and public health investigation files of patients who were harboring Shigella spp. with decreased susceptibility to azithromycin. Differences were analyzed by using the Fisher exact 2-tailed test with Epi Info software, version 6.0 (Centers for Disease Control and Prevention, Atlanta, GA, USA). Statistical significance was set at p<0.05.

From January 1, 2011, through April 30, 2013, a total of 45 patients were infected by 46 Shigella spp. strains isolated from fecal samples, including 2 also isolated from blood. A total of 33 Shigella spp. isolates were acquired locally by 33 men, and 13 Shigella spp. isolates

Table 1. Azithromycin susceptibility of 26 Shigella spp. isolates from 25 patients, Centre Hospitalier de l’Université de Montréal–Hôpital Saint-Luc, Montreal, Quebec, Canada, January 2012–April 2013

| Azithromycin susceptibility | No. infections acquired locally | No. infections acquired abroad |
|----------------------------|-------------------------------|-------------------------------|
| Reduced                    | 10                            | 0                             |
| Susceptible                | 9                             | 0                             |

*p = 0.0039. All patients with locally-acquired Shigella and 3 patients with Shigella infections acquired abroad were men. One patient was infected successively with 2 Shigella species with reduced azithromycin susceptibility. For all patients infected with Shigella spp. with decreased azithromycin susceptibility, the strains were isolated from feces and none from blood.
were acquired abroad, outside Canada, in the week before symptom onset, by 6 men and 7 women (p = 0.00003).

From January 2012 through April 2013, infection with 4 *Shigella* spp. pulse types with decreased azithromycin susceptibility was locally acquired by 9 patients (mean age 45 years, range 29–55 years) (Tables 1, 2). Among these patients, 1 HIV-positive man was infected successively with 2 *Shigella* species with reduced azithromycin susceptibility, 11 months apart, resulting in a total of 10 infections (Figure). All 9 men reported having had sex exclusively with 2 species with reduced azithromycin susceptibility, 1 originated from outbreaks among MSM (Figure), which are being investigated by Quebec public health departments and LSPQ.

During the 2011–2013 surveillance period, azithromycin MICs for 35 of 36 *Shigella* spp. isolates with no reduced azithromycin susceptibility were 2–8 mg/L, and the MIC for 1 isolate was 16 mg/L; this latter isolate was negative by PCR for *mph*(A), and the other 35 isolates were not tested. The 10 *Shigella* spp. isolates with reduced azithromycin susceptibility had azithromycin MICs ≥64 mg/L and were positive for the *mph*(A) gene by PCR. The 3 *S. flexneri* and 1 *S. sonnei* pulse types were susceptible to nalidixic acid, ciprofloxacin, and ceftriaxone (Table 2); 3 pulse types were resistant to ampicillin, trimethoprim/sulfamethoxazole, or chloramphenicol; and 4 pulse types were resistant to tetracycline (Table 2). During 2012–2013, *Shigella* spp. with reduced azithromycin susceptibility represented 57.1% of 7 locally acquired pulse types (data not shown). Pulse-Net Canada *XbaI* and *BlnI* pattern designations were SFXXAI.0205/SFXBNI.0092 and SFXXAI.0204/SFXBNI.0093 for *S. flexneri* serotype 2a pulsvars 15 and 16, respectively; SFXXAI.0193/SFXBNI.0084 for *S. flexneri* serotype 3a pulsvar 6; SSOXAI.0395/SSOBNI.0020 for *S. sonnei* pulsvar 101; and SSOXAI.0174/SSOBNI.0176...
Dispatches

for S. sonnei pulsivar 105. No PFGE matches were identified in isolates from other Canada provinces.

Conclusions

During 2012–2013, at the Centre Hospitalier de l’Université de Montréal–Hôpital Saint-Luc, 10 infections with 1 of the 4 Shigella spp. pulse types with reduced azithromycin susceptibility were documented for 9 MSM, 7 of whom were HIV positive. These 4 locally acquired Shigella pulse types had increased azithromycin MICs of ≥64 mg/L and were positive by PCR for mph(A).

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