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Keratitis Due to Shigella flexneri

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Multiresistant Shigella flexneri isolates were cultured from the cornea and stool of a girl. Genetic analysis showed the isolates were identical. Shigella spp. are rare causes of ulcerative keratitis; there have only been 14 published cases since 1943. Although prognosis after local treatment is good, shigellosis is a systemic infection, possibly leading to dehydration.

CASE REPORT

An 8-year-old girl, whose father was born in Ghana, presented to the emergency department with a 5-day history of a painful red left eye and severe photophobia after her cornea was damaged by a fingernail of a girl in Ghana 5 days before. The patient had been otherwise well, except for a 2-day episode of slight diarrhea during her stay in Ghana. No additional information about the girl who caused the trauma was available. Physical examination disclosed a deep stromal tear with two infiltrates in the central part of the left cornea as well as a hypopyon. The conjunctiva was markedly injected. Visual acuity of the eye was limited to light perception. The iris, lens, and fundus were normal, and the pupil reaction was intact. The right eye was normal in every aspect. The girl had no fever, and the remainder of the physical examination was unremarkable. After admission to the hospital, corneal scrapings were obtained for culture, and empirical topical therapy using cefazolin (3.3%) and gentamicin (2.25%) eye drops every hour was started. Shigella flexneri was obtained in pure culture from the corneal scrapings. The isolate was susceptible to cefazolin, gentamicin, nalidixic acid, and ciprofloxacin; intermediate susceptible to chloramphenicol; and resistant to amoxicillin, tetracycline, and trimethoprim-sulfamethoxazole. After the results of the culture were known, a fresh specimen of the stool was taken. Shigella flexneri and a swab from the last digit of each finger were cultured: the remainder of the physical examination was unremarkable. After the acute infection has subsided.

Other ocular manifestations of shigellosis include conjunctivitis (during or after the acute infection) and iridocyclitis. The age range of published cases of Shigella keratitis (from 3 months to 8 years) is in accordance with this high incidence of shigellosis in children (1–3, 5, 6, 9, 12, 13, 15, 17, 19, 20, 22). Little is known about the incidence of this complication in adults: corneal ulceration in a patient with dysentery (Shigella species unknown) during World War I was noted, although the association was not clear (22). It is possible that more hygienic behavior (better handwashing after defecation and/or less hand-eye contact) or the lower incidence of Shigella in adults diminishes the risk of contamination of the eye in that age group. Other ocular manifestations of shigellosis include conjunctivitis (during or after the acute infection) and iridocyclitis (20). Conjunctivitis can be associated with either urethritis or arthritis after the acute infection has subsided.

Shigella is a rare cause of infection of the cornea: no Shigella was cultured from 494 culture-proven corneal ulcers in New York (1950 to 1979) and from 238 such ulcers in Florida (1969 to 1977) (1) or identified among 1,558 isolates (from 1,303

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Cultured (4, 11, 25, 27). From the blood of four patients with keratitis, whose blood was S. sonnei during that time (18), although another possibility is that the same species was present under the nails of the other girl as well and contaminated the cornea of the patient at the time of the trauma in Ghana. No microbiological data for the latter were available, and the incubation period (1 to 7 days, usually 1 to 3 days) did not discriminate between these two possibilities. The isolate was resistant to amoxicillin, tetracycline, and trimethoprim-sulfamethoxazole. This multiresistance has appeared in most areas of the world, but is more common in African and Asian than in industrialized countries and is probably related to widespread use of antibiotic agents.

A great number of organisms may cause keratitis if there is a corneal defect, but only a limited number, including Shigella spp., Neisseria gonorrhoeae, and Corynebacterium diphtheriae, have the ability to penetrate an intact cornea by the release of toxins or enzymes: unlike with our patient, the cornea in 7 out of 12 published cases was intact (Table 1). So, although the damage to the cornea of our patient could have facilitated the entry of the microorganisms, it was possibly not essential for the emergence of the infection. Virulent strains of Shigella spp. can, in contrast to, for example, Salmonella and other gram-negative species, penetrate the intact cornea of rabbits and guinea pigs. In rabbits, the cornea became necrotic and opaque about 5 days later, but corneal transparency was regained spontaneously without scar formation within 3 weeks after inoculation (6). In the cornea of contaminated guinea pigs, ulceration was noted by the third day. Unless the infection became chronic, which might last for 6 months or longer, healing was completed without treatment within 3 weeks to 6 months with slight residual scarring (19). Recovered eyes of rabbits and guinea pigs were immune to reinfection.

In most of the published patients, only minor scars remained (7/11) or even full resolution (2/11) was observed; but in 2 patients there was still heavy scarring 4 months later or a diffusely cloudy cornea on day 30 (Table 1).

Topical antimicrobial therapy is indicated in bacterial keratitis, because of the dangers of perforation and visual loss due to central scarring. As long as the organism and the results of the susceptibility testing are not yet known, a broad-spectrum antibiotic regimen, including gentamicin or one of the fluoroquinolones, like ofloxacin, is indicated, because it is unlikely that even multiresistant Shigella spp. are resistant to these drugs. Cycloplegics are indicated if there is a severe anterior chamber reaction to relieve ciliar spasm and prevent the formation of synchiae. Mydriatics were given to 8 of 12 patients. In one patient, both S. sonnei and Staphylococcus aureus were isolated from the cornea from two separate cultures. Little is known about the association between keratitis and, respectively, Shigella dysenteriae and Shigella boydii. These species are both less frequent (together 3% in industrialized and 12% in developing countries) (14), although S. dysenteriae was the predominant species in the world until World War I, and this species has been documented as a reemerging pathogen in Latin America, central Africa, Asia, and the Indian subcontinent since the 1970s (12). It has been mentioned that keratoconjunctivitis associated with S. dysenteriae has been reported in the past (18), and keratitis in a case of dysentery (variety not stated) had been briefly reported in 1913 (5).

The recovery of the same genotype of S. flexneri from the cornea and the stool of our patient suggests autoinoculation of the damaged cornea via the fingers, after the trauma had happened, although another possibility is that the same species was present under the nails of the other girl as well and contaminated the cornea of the patient at the time of the trauma in Ghana. No microbiological data for the latter were available, and the incubation period (1 to 7 days, usually 1 to 3 days) did not discriminate between these two possibilities. The isolate was resistant to amoxicillin, tetracycline, and trimethoprim-sulfamethoxazole. This multiresistance has appeared in most areas of the world, but is more common in African and Asian than in industrialized countries and is probably related to widespread use of antibiotic agents.

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It is not clear if the use of topical corticosteroids to minimize the inflammatory sequelae can adversely affect the results of the antimicrobial therapy. Experiments in animals with Staphylococcus aureus and Pseudomonas aeruginosa suggest that ste-
TABLE 1. Clinical data and outcome of keratitis by *Shigella* spp.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Preceding event/defect</th>
<th>Cornea presentation</th>
<th>Culture</th>
<th>Source</th>
<th>Systemic signs</th>
<th>Effective treatment</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>9 mo</td>
<td>No</td>
<td>Small ulcer (right) just below center of pupil, anterior uveitis</td>
<td><em>S. sonnei</em></td>
<td>Eye, stool</td>
<td>Dysesthesia, fever</td>
<td>Sulfonamide orally, atropine</td>
<td>Very small scar, restored pupil reaction after 50 days</td>
<td>26</td>
</tr>
<tr>
<td>Male</td>
<td>6 yr</td>
<td>Trauma (pair of scissors) 7 days before</td>
<td>Ulcer (right), lower one-half</td>
<td><em>S. flexneri</em></td>
<td>Eye</td>
<td>Diarrhea</td>
<td>Chloramphenicol, neomycin, polymyxin B, gramicidin, atropine</td>
<td>Heavy scar formation (4 mo)</td>
<td>18</td>
</tr>
<tr>
<td>Male</td>
<td>2 yr</td>
<td>No Ulcer (left) with large opacity</td>
<td><em>S. flexneri</em></td>
<td>Eye, stool</td>
<td>Diarrhea, fever, moderate dehydration</td>
<td>Rehydration, oral gentamicin, neomycin, polymyxin B, sulfonamide, oral corticosteroids</td>
<td>Cornea diffusely cloudy (day 30)</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1 yr</td>
<td>Blunt trauma 5 days before</td>
<td>Ulcer (right), anterior uveitis</td>
<td><em>S. sonnei</em> and <em>S. aureus</em></td>
<td>Eye</td>
<td>Fever (38°C)</td>
<td>Neomycin, polymyxin B, sulfonamide, phenylephrine/scopolamine</td>
<td>Residual paracentral nubula</td>
<td>10</td>
</tr>
<tr>
<td>Male</td>
<td>2 yr</td>
<td>Herpes keratitis? Large ulcer (left) involving lower third</td>
<td><em>S. sonnei</em></td>
<td>Eye, stool</td>
<td>Diarrhea until 3 days before onset</td>
<td>Gentamicin, neomycin, polymyxin B, gramicidin, oral cephalaxin, debridement</td>
<td>Faint stromal scar, vision 6/9 (6 wk)</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3 yr</td>
<td>No Ulcer (left), lower one-half, mild anterior uveitis</td>
<td><em>S. flexneri</em></td>
<td>Eye, stool</td>
<td>Diarrhea, fever, and seizures 10 days before</td>
<td>Gentamicin, chloramphenicol, atropine</td>
<td>Superficial scar (4 mo)</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 yr</td>
<td>No Several ulcers (left)</td>
<td><em>S. sonnei</em></td>
<td>Eye, stool</td>
<td>Diarrhea 10 days before</td>
<td>Gentamicin (also parenteral), atropine</td>
<td>Full resolution</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1 yr</td>
<td>No 3 ulcerations (left)</td>
<td><em>S. sonnei</em></td>
<td>Eye</td>
<td>Diarrhea 4–6 days before</td>
<td>Ceftazolin, gentamicin, homatropine</td>
<td>Small peripheral scars (day 20)</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1 yr</td>
<td>Red eyes last week before</td>
<td>Large ulcer (right) inferior lateral, 2 ulcers superior medial</td>
<td><em>S. sonnei</em></td>
<td>Eye</td>
<td>No diarrrhea</td>
<td>Ceftazolin, gentamicin, atropine</td>
<td>Minimal scar (day 26)</td>
<td>27</td>
</tr>
<tr>
<td>Female</td>
<td>3 mo</td>
<td>No Ulcer (1 by 2 mm) (left) hypopyon</td>
<td><em>S. flexneri</em></td>
<td>Eye, stool</td>
<td>Diarrhea, fever, severely dehydrated</td>
<td>Gentamicin, chloramphenicol, ampicillin i.v.</td>
<td>Died (day 6)</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5 yr</td>
<td>Herpes keratitis Ulcer (2 mm), hypopyon</td>
<td><em>S. sonnei</em></td>
<td>Eye, stool</td>
<td>Diarrhea until 2 days before</td>
<td>Tobramycin, ceftazolin (1/2), atropine</td>
<td>Recovered</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8 yr</td>
<td>Nail Trauma by fingernail (left), 2 central ulcers, hypopyon</td>
<td><em>S. flexneri</em></td>
<td>Eye, stool</td>
<td>Diarrhea recently</td>
<td>Ceftazolin, gentamicin, steroids</td>
<td>Hypopyon vanished in 4 days, slight scarring; visual acuity 20/25 (5 mo)</td>
<td>Present case</td>
<td></td>
</tr>
</tbody>
</table>

*Antimicrobial agents associated with clinical improvement or in vitro susceptibility; local therapy unless stated otherwise. i.v., intravenous.

Associated with progression.

roids in combination with bactericidal antibiotics do not have this effect (2). Whether the early addition of corticosteroids to the antibiotic treatment has contributed to the favorable outcome of the patient is unknown.

It is important that the ophthalmologist realize that shigellosis can be a serious systemic disease, especially in the very young: 2 out of 14 patients with keratitis were dehydrated (respectively, 2 years and 3 months old), and the 3-month-old girl died. If *Shigella* is isolated from the eye, culture of the stool is indicated. Antimicrobial treatment was restricted to the eye in 7 out of 12 patients, including our patient. In five patients, antimicrobial agents active outside the eye were also prescribed to treat the systemic infection (four patients) or to treat the gastroenteritis locally (one patient). Although shigellosis is normally self-limited, lasting an average of 4 to 7 days, and carriage usually ceases within 4 weeks, systemic antimicrobial therapy is indicated in all cases, including mild, nondsenteric infections, to prevent spread of the organism (8). A short course (3 to 5 days) of systemic antibiotics, to which the organism is susceptible, will cure the infection and interrupt fecal excretion. It has even been advised to treat carriers, because person-to-person transmission is common (8).

The large-scale use of antibiotics has led to considerable resistance of shigellae to ampicillin and tetracycline and in developing countries (including Africa, south-east Asia, and South America) to trimethoprim-sulfamethoxazole as well. A
fluoroquinolone is suitable for empirical systemic treatment, because resistance is rare, although routine use of fluoroquinolones in children is not approved. The combination of trimethoprim with sulfamethoxazole (co-trimoxazole) is considered a second-best choice. Infection prevention precautions (“enteric precautions”), with strict attention to hand disinfection, are indicated if the patient is admitted to the hospital, because the organism is easily transmitted, and these precautions are advised until three stool cultures after cessation of antimicrobial therapy are negative.

REFERENCES