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## CASE REPORT

# An adult case with shigellosis-associated encephalopathy

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**SUMMARY**

A 45-year-old man was presented at the emergency department with altered neurological status and a 1-day history of diarrhoea and fever. The patient's sexual history revealed multiple male partners. As bacterial meningitis or viral encephalitis was suspected, treatment was started accordingly. Cerebrospinal fluid investigations only showed a slight increase of leucocytes, and microbiological studies remained negative. Stool culture revealed *Shigella flexneri*, after which *Shigella*-associated encephalopathy was suspected. The patient recovered quickly with antibiotic treatment. The incidence of *Shigella* infections in the Western world is rising due to sexual transmission among men who have sex with men. *Shigella*-induced encephalopathy is a notorious complication among children with a severe form known as the Ekiri syndrome, though rarely seen in adults. This is the second report of encephalopathy in an adult with *S. flexneri* enteric infection.

**BACKGROUND**

Shigellosis is a common disease worldwide. It causes bloody stool with mucus, together with fever and abdominal cramps. The *Shigella* bacillus was discovered by the Japanese doctor Kiyoshi Shiga in the early 20th century (figure 1).<sup>1</sup> *Shigella* spp cause almost 200 million infections per year in children under the age of 5 years.<sup>2</sup> In the Netherlands, with a population of almost 17 million, there are between 300 and 500 infections with *Shigella* spp annually, of which 60% after recent travel.<sup>3</sup>

A known complication among children is *Shigella* encephalopathy. It can present with altered consciousness, seizures and coma.<sup>4 5</sup> All the known *Shigella* spp (*Shigella sonnei*, *Shigella flexneri*, *Shigella dysenteriae* and *Shigella boydii*) can cause this complication, with a prevalence of 12%–45% in children.<sup>6</sup> A lethal toxic encephalopathy with rapid onset of neurological abnormalities and only a mild colitis is known as the Ekiri syndrome.<sup>7</sup>

Humans are the only host for *Shigella* spp. It is mostly contracted via the faecal–oral route with a low infectious dose. *Shigella* infections in the Western world are usually associated with travel to endemic countries. Recently, there are increasing reports of cases in men who have sex with men (MSM) without reported history of travel.<sup>8 9</sup> The rising incidence in this population has the potential to cause outbreaks of *Shigella* infections in low-risk regions.<sup>10 11</sup>

Here, we present a case of an adult with *Shigella*-associated encephalopathy in an MSM.

**CASE PRESENTATION**

A 45-year-old man was presented at the emergency department of our hospital with altered neurological status and a 1-day history of diarrhoea and fever. He had no relevant medical history. His male partner had found him earlier that day with fever, diarrhoea and diminished ability to speak. Heteroanamnesis revealed recent unprotected sexual contact with multiple men and no history of travel. Physical examination showed a lethargic patient with a temperature of 39.5°C, blood pressure of 100/50 mm Hg and a pulse of 104/min. He was confused and disorientated, unable to speak nor to perform any assignments. His abdomen was soft and non-tender with normal bowel sounds. Other physical examination revealed no abnormalities. Bacterial meningitis or viral encephalitis were suspected and antibiotic and antiviral therapy was started according to our local protocol; ceftriaxone, amoxicillin and acyclovir intravenously.

**INVESTIGATIONS**

A CT brain scan and lumbar puncture were performed. The CT scan showed no sign of cerebral bleeding or hydrocephalus. The cerebrospinal fluid (CSF) revealed mild pleiocytosis of  $8 \times 10^6$  cells/L with normal glucose and protein levels. Bacterial culture and PCR for enterovirus, herpes simplex virus type 1 and 2 and varicella zoster virus were negative. C reactive protein in serum was 210 mg/L with decreased leucocyte count of  $2.4 \times 10^9$  cells/L. Serum creatinine levels were elevated with 136 µmol/L. Stool culture showed *S. flexneri*, sensitive to ceftriaxone, though resistant to ciprofloxacin and trimethoprim/sulfamethoxazole. The patient tested negative for HIV.

**DIFFERENTIAL DIAGNOSIS**

The differential diagnosis of adult with altered mental status and fever is extensive. *Shigella* encephalopathy was considered based on the absence of other causes and presence of *S. flexneri* in a stool sample.

Although the patient was hypovolaemic, this was considered unlikely as a cause for his confusion. Also, his confusion remained after volume resuscitation. Further blood investigation revealed a normal calcium, thyroid-stimulating hormone and only a slight hyponatraemia and hypokalaemia of



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**Figure 1** Dr Kiyoshi Shiga. Source: [https://en.wikipedia.org/wiki/Kiyoshi\\_Shiga#/media/File:Kiyoshi\\_Shiga.jpg](https://en.wikipedia.org/wiki/Kiyoshi_Shiga#/media/File:Kiyoshi_Shiga.jpg).<sup>28</sup>

respectively 130 mmol/L and 3.4 mmol/L, all of which could not explain his neurological status. Sepsis was considered unlikely, since blood cultures remained negative, blood pressure was within normal limits and serum lactate levels were normal. The patient had no history of substance abuse or intoxications. A delirium at time of an infection is usually seen in the elderly but can occasionally occur in younger patients with risk factors, like underlying neurological disease or the use of multiple medications. However, this was not the case in our patient.

### TREATMENT

After the negative PCR results of the CSF acyclovir was stopped. The disturbances in fluid and electrolyte balance were treated with fluid resuscitation and potassium supplementation. Volume repletion was achieved quickly. The patient's neurological status recovered within 36 hours after the start of ceftriaxone intravenously. Normalisation of sodium levels occurred within 24 hours and potassium levels normalised within 48 hours, after which fluid resuscitation was stopped.

### OUTCOME AND FOLLOW-UP

Three days after admittance to the hospital and the start of intravenous antibiotic treatment, the patient had recovered so far that he could be discharged. The stool consistency returned to normal over time. Because of subsiding symptoms in a non-immunocompromised patient, no further antibiotic treatment was found necessary. At a follow-up visit several weeks later, he had recovered fully, except for some memory problems.

### DISCUSSION

Shigellosis is a common gastrointestinal infection, which can cause severe neurological symptoms. Although fairly common in children, this clinical presentation is rarely seen in adults. Only one article from Spain reported on a similar case with *S. flexneri* enteritis.<sup>12</sup> A second case of shigellosis-associated encephalopathy is described in a patient with *S. sonnei* gastrointestinal infection.<sup>13</sup> Like our case, both previous patients were suspected of having bacterial meningitis or viral encephalitis and treated accordingly.

Central nervous system manifestations of shigellosis are common, especially in children. Convulsions are present in 5%–45% of children with *Shigella* infection and are associated with younger age.<sup>14–17</sup> Lethargy, disorientation and coma can also occur, most often referred to as encephalopathy.<sup>16 18</sup> A potential lethal form of encephalopathy in children with shigellosis is known as Ekiri syndrome. It is characterised by a distinctive rapid onset of neurological symptoms with a mild colitis and was first described in Japanese patients in the first half of the previous century.<sup>7</sup> A more recent study found 5 cases of lethal encephalopathy among 1295 children (0.4%) presented to the hospital with shigellosis.<sup>6</sup> However, it is unknown whether the Ekiri syndrome is the same as more recently reports on lethal toxic encephalopathy in children. It is possible that the high death rate among these Japanese children with *Shigella* enteric infection was a result of the standard of living in those times.<sup>19</sup>

Despite much speculation, the pathogenesis of this encephalopathic syndrome is still unknown. For long, it was reasoned that the Shiga toxin 1 or 2 were involved. However, it is shown that these toxins do not play a role in the pathogenesis of shigellosis-associated encephalopathy.<sup>20</sup> Besides this, they are only produced by *S. dysenteriae* serotype 1, while the encephalopathy is seen with infections with all *Shigella* spp. Other *Shigella*-specific toxins enterotoxin 1 and 2 may contribute to the high volume and watery diarrhoea, though are not associated with neurological symptoms.<sup>18</sup> Although a relationship with a still unknown enterotoxin is likely, further research is necessary to further explore the exact pathogenesis.<sup>20</sup>

Several extraintestinal complications other than encephalopathy can follow a *Shigella* infection, such as haemolytic uraemic syndrome (HUS) and reactive arthritis.<sup>21 22</sup> Antimicrobial therapy can lower the overall mortality rate and shortens the duration of gastrointestinal complaints, but the effect on complications is unclear. A Cochrane review from 2010 concluded that there is no difference between treatment with fluoroquinolones and beta-lactams on the development of severe complications, but the follow-up time was too short to measure the long-term effects.<sup>23</sup> However, early administration of effective antimicrobial therapy is associated with reduced risk on HUS after infection with *S. dysenteriae* serotype 1. This in contrast to the Shiga toxin-producing *Escherichia coli* O157:H7.<sup>24</sup> There are no studies on the effect of (prolonged) antimicrobial treatment on the functional outcome of *Shigella* encephalopathy.

This patient was most likely infected by faeco–oral transmission through sexual contact with other MSM. This is a cause of rising incidence and outbreaks of shigellosis in low-prevalence countries.<sup>11 25–27</sup> Rare complications like presented in this case report may become more common as this trend continues. There should be raised awareness among clinicians for this kind of transmittable diseases among MSM, and it presses the importance of identifying risk factors by taking a thorough (sexual) history.

## Learning points

- ▶ Although *Shigella* encephalopathy is a well-known entity in children, it can also affect adults.
- ▶ There is a rising incidence of shigellosis among adult men in the developed world due to sexual transmission among men who have sex with men.
- ▶ *Shigella* encephalopathy can present with symptoms similar to meningitis or encephalitis.
- ▶ The pathophysiology of shigellosis-associated encephalopathy remains unclear.

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