Case Report

Shiga toxin-producing Escherichia coli outbreak in a childcare facility

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Abstract

Haemolytic uremic syndrome is a rare disease typically associated with Shiga toxin-producing *Escherichia coli*.
We describe two cases of haemolytic uremic syndrome that occurred in the same childcare facility.
We collaborated with the National Reference Centre for Shiga toxin producing *Escherichia coli* to screen all 77 children and 27 adults present at the childcare facility. Shiga toxin *Escherichia coli* was detected in 7 children in the childcare facility (9%) and 1 symptomatic sibling. Only one section was touched, 8 out of 29 children from the "big" section (28%) were affected (haemolytic uremic syndrome and/or carriers).
The high prevalence of Shiga toxin *Escherichia coli* carrying in childcare facilities supports the need for early hygiene measures and information to parents.

Introduction

Haemolytic uremic syndrome (HUS) is a clinical syndrome characterized by acute renal failure (ARF) associated with anaemia and thrombocytopenia. It is the most common cause of acute kidney injury in children. Approximately 25% of STEC-HUS patients develop neurologic symptoms and is an important contributor to the morbidity of the disease (1). HUS mortality rate is 2.5-7% (2). A Belgian study reports a 2.5% lethality (3).

In 90-95% of cases, the syndrome is consecutive to an episode of diarrhoea of 2 to 14 days due to Shiga toxin-producing Escherichia coli strains (STEC) (4). STEC are classified based on their serogroup ("O"-antigen) and their serotype ("H"-antigen). Most STEC infections are caused by STEC O157:H7(1). Among STEC, some genes are correlated with an increased risk of developing HUS (*Stx2a, Stx2d*, or *Eae*) (5,6). The duration of carriage of serogroup O157 is generally ranging from 5 to 29 days but it can reach 124 days (1). It is estimated that up to 10% of patients with STEC infection may develop HUS, and up to 20% in some epidemics (4).
Human contamination occurs through consumption or handling of contaminated food. Human-to-human transmission of STEC has been described in family settings and in children's communities (7).
This mode of transmission by the fecal-oral route is important with a transmission rate of up to 20%.(4)
HUS surveillance is important to detect outbreaks, STEC strains associated with severe outcomes, and new strains emergence as well as to try to identify contamination source and remove contaminated products. HUS caused by STEC strains is a mandatory notifiable disease in our country.

We report here two cases of HUS admitted to two hospitals Brussels and our subsequent epidemiologic research in the day-care centre.

Case reports and subsequent study

The first case, a two-year-old boy, was admitted to an emergency room for seizures, diarrhoea and fever. Blood sample revealed the characteristic HUS triad. *E. Coli* O157:H7 (*Stx1+, Stx2a+, Eae+*) was detected by PCR in the stool (National Reference Centre (NRC) for STEC). The child was transferred to a paediatric intensive care unit (PICU) for status epilepticus. He required mechanical ventilation for 12 days and benefited from peritoneal dialysis followed by continuous veno-venous hemofiltration for a total of 6 days. (Peritoneal dialysis did not allow adequate fluid and metabolic control). He was hospitalized for 4 weeks and recovered completely.

The childcare facility doctor notified the case to the Infection Prevention and Control department (COCOM) and sent an information message to all parents. They were invited to contact their physician if their child presented signs of gastroenteritis and to tell him or her that a HUS has been diagnosed in the childcare facility.

Five days after admission of the first case, a 2-year-old girl was admitted to the emergency room of another hospital after 5 days of fever and vomiting but with no history of diarrhoea. Her mother brought the letter received from the childcare facility. Blood tests were characteristic for HUS. The PCR-STEC was negative in both blood and stools samples. The patient was transferred to a PICU but did not require dialysis. She was discharged and well after 2 weeks.

Because a third case of uncomplicated diarrhoea was reported by the childcare facility, it was decided to screen all children. The decision to perform systematic screening was taken by the COCOM, the childcare managers and physicians, and the NRC for STEC. The screening was initiated for the whole childcare community. All 77 children and 27 adults staff members were screened. Children were divided into three groups according to their ages and the organization of the day-nursery.

The carrying incidence was 9% in the whole childcare facility (7/77). The same STEC was indeed identified in seven children: 1 with HUS, 5 with mild gastroenteritis, 1 asymptomatic. These 7 children and the second HUS case, which was STEC negative, belonged to the same group of 29 children. The incidence of carrier status was high in this group (8/29; 28%). One sibling of a child from the day-care was also positive. No cases were identified among staff members.

To avoid further contamination, these children were banned from the nursery until two negative cultures were obtained from samples taken 24 hours apart. Appropriate hygiene measures led to a full recovery after two months (Table 2).
No antibiotic has been administered (Table 1).
Origin of the index case remained unknown despite epidemiological and field investigations.

Table 1 Comprehensive screening

Sections	Total number	Asymptomatic carrier	Symptomatic subject	HUS	Laboratory confirmed cases
Group of «small» children	22	0	0	0	0
Group of « middle » children	26	0	0	0	0
Group of « big» children	29	2	4	2	7
Staff members	27	0	0	0	0
Sibling not admitted to the day-care centre	2	0	2	0	1

HUS: Haemolytic uremic syndrome.

Discussion

Our epidemiologic study shows that a quarter of the children belonging to the same group in the childcare facility carried a STEC, sometimes for few weeks. Such incidence is rarely documented and justifies caution in high-risk groups.

Diagnosis and reporting of STEC infections are indeed of particular importance for the rapid detection of epidemics and implementation of adequate measures (6). As soon as a healthcare provider reports a HUS case, several control measures are taken by the infectious disease surveillance unit. These measures include: informing the concerned community and parents (in the form of a letter), strengthening hygiene measures, stool sampling for STEC detection, epidemiological investigation and if a source of contamination is suspected, further work-up to the Federal Agency for the Safety of the Food Chain (AFSCA) (6).

The identification of STEC carrying is made from stool sample or rectal smear. In the event of HUS or STEC outbreak, must be systematically sent to the NRC. Diagnosis is based on strain culture and serotyping, PCR amplification of virulence genes in stool, immunological tests and serologies (search for antibodies against LPS (lipopolysaccharides) of *E. coli* O-serogroups). It is not always easy to highlight STEC due to its low concentration in stool and its rapid elimination from the intestine, especially during active HUS (4). The likelihood of identifying Shiga toxin decreases dramatically over the course of the disease. Therefore stool collection should be carried out at the latest 4 to 6 days after the onset of digestive prodromes (1).

Treatment of STEC infection is usually symptomatic. Antibiotics use is controversial because in most cases bacteria lysis can release more toxins (8,9)that provided data from patients (1). In France, azithromycin is recommended, particularly in asymptomatic carriers. High quality data however are lacking (1,6).

Zhang et al suggested that in mice, azithromycin has a strong effect on Stx production by STEC and on the Stx- induced inflammatory host response and prevents death. Azithromycin may have a beneficial effect on STEC-associated disease. However further studies are required before strong recommendations (10) produces Stx from phage, and causes the development of hemolytic-uremic syndrome via Stx-induced inflammatory cytokine production. Azithromycin exhibited strong in vitro activity against STEC without inducing Stx-converting phage, in marked contrast to norfloxacin. Azithromycin decreased the tumor necrosis factor alpha (TNF-α).

Complement activation plays an important role in the pathogenesis of atypical HUS. Eculizumab is an anti-C5-convertase monoclonal antibody. It is safe and effective for the treatment of atypical HUS (11) thrombocytopenia and AKI. In ~ 90% of cases, HUS is a consequence of infection with Shiga toxin-producing E. coli (STEC. There is no controlled data investigating the use of eculizumab in STEC-HUS but many studies have shown clinical improvement in cases of STEC-HUS with neurological involvement (11,12) thrombocytopenia and AKI. In ~ 90% of cases, HUS is a consequence of infection with Shiga toxin-producing E. coli (STEC).

Two double-blind, placebo-controlled trials are underway in France and the UK to provide evidence to guide the use of this treatment in STEC-HUS(12).

Conclusion

The incidence of STEC outbreaks in childcare facilities is rarely documented. Since it could be high, particularly in children spending few hours together each day such as in our study, preventive and control measures should be implemented as soon as possible, in order to lead to rapid identification of children with HUS symptoms. Rapid and close collaborations between the public health authority, National Reference Center, childcare staff and parents insured efficient disease control.

Conflict of interest statement

The authors of this case report declare that they have no conflict of interest.

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Table 2 Temporal description of STEC and/or HUS affected children

Children	1	2	3	4	5	6	7	8	9
STEC-PCR results	10-11-19 **positive**	13-11-19 **positive**	15-11-19 negative	26-11-19 **positive**	29-11-19 **positive**	02-12-19 **positive**	02-12-19 **positive**	02-12-19 negative **06-12-19 positive**	02-12-19 **positive**
	29-11-19 **positive**	29-11-19 negative		03-12-19 positive	20-12-19 negative	07-12-19 **positive**	06-12-19 negative	12-12-19 **positive**	09-12-19 negative
	13-12-19 **positive**	10-12-19 negative		05-12-19 negative	10-01-20 negative	16-12-10 **positive**	09-12-19 negative	17-12-19 **positive**	10-12-19 negative
				12-12-19 negative		29-12-19 **negative**		20-12-19 **positive**	
						31-12-19 **negative**		07-01-20 negative	
								10-01-20 negative	
Symptoms	HUS	enteritis	HUS	enteritis	enteritis	asymptomatic	enteritis	enteritis	asymptomatic

STEC: Shiga toxin-producing *Escherichia coli*, HUS: Haemolytic uremic syndrome. Appearance in the order of positive stool cultures.