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Two cases of urinary tract infection caused by Shiga toxin-producing *Escherichia coli* O157:H7 strains

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ABSTRACT

STEC strains can infect extra-intestinal sites such as the human urinary tract and sometimes cause severe complications. We report two cases of urinary tract infection caused by STEC in two elderly women with comorbidities. Although both strains belonged to the O157:H7 serotype and carried genes associated with severe illness, none of the patients developed hemolytic uremic syndrome (HUS). These findings provide additional evidence for the presence of these agents in our country and in the region, and highlight the need to maintain an active surveillance system of HUS cases, placing special emphasis on the study of other sites of infection in patients with non-diarrheal HUS.

Key words: *E. coli* O157:H7, STEC, urinary tract infection

RESUMEN

Dos casos de infección del tracto urinario causados por cepas de *Escherichia coli* O157:H7 productoras de toxina Shiga. En los seres humanos, las cepas STEC pueden producir infección en sitios extraintestinales, como el tracto urinario, y causar complicaciones graves. Comunicamos dos casos de infección urinaria por STEC en dos mujeres ancianas con comorbilidades. Aunque ambas cepas correspondieron al serotipo O157:H7 y portaban los genes asociados con enfermedad grave, ninguna de las pacientes desarrolló síndrome urémico hemolítico (SUH). Estos hallazgos constituyen una evidencia adicional de la presencia de estos agentes en nuestro país y en la región, y destacan la necesidad de mantener un sistema activo de vigilancia, con especial énfasis en el estudio de otros sitios de infección en pacientes que presentan SUH no asociado a diarrea.

Palabras clave: *E. coli* O157:H7, STEC, infección del tracto urinario

Shiga toxin (Stx)-producing *Escherichia coli* (STEC) can cause diarrhea, hemorrhagic colitis and hemolytic uremic syndrome (HUS). Post-enteric HUS, a life-threatening complication, is characterized by thrombocytopenia, microangiopathic hemolytic anemia and acute renal failure. Moreover, STEC strains can infect the human urinary tract and also cause non-diarrheal HUS (1, 6).

The ability of STEC strains to cause severe disease in humans is related to the capacity to secrete Stx1, Stx2, and/or variant toxins (1), encoded by lysogenic bacteriophages. Another virulence factor of STEC strains is a 94-kDa outer membrane protein, called intimin. It is encoded by an *eae* gene located within a 34-kb chromosomal pathogenicity island termed locus of enterocyte effacement (LEE). This locus is associated with intimate adherence to epithelial cells, initiation of host signal transduction pathways and formation of attaching-and-effacing intestinal lesions (1). Some STEC strains also produce an enterohemorraghic hemolysin (EHEC-Hly), encoded by a large plasmid-borne (90-kb) *ehxA* gene, which has been associated with severe clinical disease in humans (1).

In the present report we describe two cases of urinary tract infection (UTI) caused by STEC O157:H7 in adults who did not develop HUS.

M.P.G., N.D. and M.I.M. contributed equally to this work.

First case. An 84-year-old woman with a medical history of hypertension, vaginal prolapse and a stage 3 chronic kidney disease was admitted to hospital on July 5, 2010 with fever and anorexia. She had watery diarrhea during 48 hours prior to admission, without fever, nausea or vomiting. Diuresis was maintained.

Laboratory tests yielded the following results: serum potassium 8.5 mEq/l (normal range 3.5-5.5 mEq/l), azotemia 1.65 g/l (normal range 0.2-0.6 g/l), creatinine 1.78 mg/dl (normal range 0.2-0.6) mg/dl, and hemoglobin 9.6 mg/dl (normal range 12-16 mg/dl). The blood cell count, peripheral blood smear and liver function tests were normal.

The urine analysis showed some polymorphonuclear leukocytes. The clean-catch midstream urine specimen yielded a pure culture with a count of 10^5 CFU/ml. The patient received 3 g of ceftriaxone i/v per day, with good clinical outcome. The isolate (IH1) was identified as *E. coli* O157 (99 % probability) using the Vitek 2 Compact System (bioMérieux, Inc., Marcy l'Etoile, France) and was then sent to the Bacteriology and Virology Department-Institute of Hygiene, Universidad de la República, and to the National Reference Laboratory of Argentina, to complete its characterization.

Second case. A 72-year-old woman with a medical history of urinary incontinence and repeated urinary infections, living in an elderly long term care facility located in the same town as that of the first patient, was admitted to hospital with symptoms of acute cystitis on October 25, 2010.

In 2002, she had undergone total hysterectomy and bilateral anexectomy due to an ovarian mucinous cystadenoma.

The urine analysis showed leukocytes, erythrocytes and 0.3 g/l proteinuria. The clean-catch midstream urine specimen yielded a pure culture with a count higher than 10^5 CFU/ml and the isolate (IH2) was identified as *E. coli* O157 (99 % probability) using the Vitek 2 Compact System. The patient received 15 mg/kg of cefuroxime axetil orally every 24 hours, with good clinical outcome. The strain was also submitted to the abovementioned laboratories to complete its characterization.

Confirmation of isolates as *E. coli* was performed through biochemical tests and the serotyping was conducted using antisera provided by the Instituto Nacional de Producción de Biológicos - ANLIS "Dr. Carlos G. Malbrán".

Antimicrobial susceptibility to amikacin, ampicillin, ceftriaxone, cefuroxime, ciprofloxacin, cloramphenicol, colistin, gentamicin, nalidixic acid, nitrofurantoin, streptomycin, tetracycline, and trimethoprim-sulfamethoxazole was established according to Clinical Laboratory Standards Institute (CLSI) guidelines (2).

The stx_1, stx_2, and rfb_{O157} genes were detected by multiplex PCR as described by Leotta *et al.* (4), while the *ehxA, eae*, and $fliC_{H7}$ genes were investigated according to previously described procedures (5).

In order to determine Stx production, bacterial supernatant and periplasmic cell extracts were used on Vero cells for cytotoxicity assays (5).

The orientation of the invertible DNA element containing the *fimA* promoter was determined using a PCR-RFLP assay (7).

Phage typing was performed by the method described by Khakhria *et al.* (3).

Strain IH1 was characterized as *E. coli* O157:H7 harboring the stx_1, *eae*-γ1, *ehxA,* $flic_{H7}$ and *fimA* (phase off) genes of phage type (PT) 39. Meanwhile, the strain IH2 was characterized as *E. coli* O157:H7 harboring the stx_1/stx_2, *eae*-γ1, $flic_{H7}$ and *fimA* (phase off) genes of PT40. The expression of toxicity in Vero cell assays, and of flagellar antigens by slide agglutination were demonstrated in both isolates.

Both strains were susceptible to all antibiotics tested.

Unusual cases of HUS involving patients presenting with UTI have been previously reported. The O-groups of the STEC strains involved were OX3, O5, O103, O138, O145, and O157 (6).

However, this is the first report in Uruguay and in the region of extra intestinal STEC infections. It provides evidence of two episodes of UTI occurring in two elderly women with previous gynecologic and urinary disease, which are known predisposing factors favoring access and settlement of bacteria in the urinary tract. The first patient also had a previous watery diarrhea episode; however, no studies were conducted for detection of enteropathogens.

Although both strains belonged to the O157:H7 serotype and carried genes associated with severe illness, neither patient developed HUS.

Neither the origin and the reservoir of the recovered O157:H7 STEC strains, nor the epidemiologic link between both UTI cases could be established. Furthermore, both strains showed different *stx*-genotypes and PTs.

We can assume that the STEC O157:H7 strains reached the urinary tract by the ascending route from the gastrointestinal tract. Both patients had known predisposing factors that favored it.

Between 2002 and 2008, we studied 36 children with clinical diagnoses of post-enteric HUS; in three cases we recovered STEC strains of serotypes O157:H7, O111:NM, and O26:H11, and in a fourth case a STEC O26:H11/O145:HNT co-infection was detected (8). However, there have been no previous local or regional reports of non-diarrheal HUS caused by STEC or UTI episodes due to this pathogen.

The detection of STEC O157:H7 in urine infections provides additional evidence about the presence of this serotype in the region, reinforcing the importance of conducting active surveillance of gastrointestinal and urinary infections caused by STEC.

Written consent: both patients have given their informed consent for the case reports to be published.

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