A CASE REPORT OF SEPSIS ASSOCIATED WITH *ESCHERICHIA COLI* 0157:H7

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ABSTRACT

The reports of infections and outbreaks due to *Escherichia coli* 0157:H7 have increased in the EU for the last five years. The clinical spectrum of the infection varies from hemorrhagic colitis, hemolytic-uremic syndrome (HUS) and rarely, thrombotic thrombocytopenic purpura. This infection is new to Bulgaria, and we report a case of VT1 and VT2 positive *E. coli* O157:H7 with the presentation of this organism with the onset of haemorrhagic colitis, HUS and lethal exitus of the patient.

Keywords: *E. coli* O157:H7, hemolytic uremic syndrome, Verotoxin-producing *Escherichia coli*, antibiotics.

INTRODUCTION

Verotoxin-producing *Escherichia coli* O157: H7 is a gram-negative enterohemorrhagic bacteria that is an important food and a waterborne pathogen which causes diarrhoea, hemorrhagic colitis, hemolytic-uremic syndrome (HUS) and rarely, thrombotic thrombocytopenic purpura in humans (1). Patients usually present with acute onset of bloody diarrhoea and abdominal cramping without fever during the initial presentation. The acute watery diarrhoea initially may not be bloody. As a result of vomiting, and profuse diarrhoea, patients often note dehydration, asthenia, and decreased urine output (8). Verotoxin-producing *Escherichia coli* strains (VTEC) are characterized by their ability to produce one or more phage-encoded verocytotoxins, VT1 and VT2 (Vt1/2) which are one of the mechanisms by which the pathogen causes a range of gastrointestinal illnesses, from watery diarrhoea to hemorrhagic colitis (2). These toxins are closely related to the potent cytotoxins produced by *Shigella dysenteriae* type 1. The toxins directly damage mucosal cells and vascular endothelial cells in the gut wall. If absorbed, they exert toxic effects on other vascular (e.g. renal) endothelia (4). manifests In its most severe manifestations, *E. coli* 0157: H7 verotoxin can cause diffuse vasculitic injury that affects multiple organ systems and leads to multiple organ failures (1,5,6). Transmission of *E. coli* O157: H7 occurs via the fecal-oral route after consumption of contaminated, undercooked food of bovine origin, and sometimes fresh vegetables. It is thought to be the first source of contamination, but person-to-person transmission has also been demonstrated (3). Non-O157 STEC serotypes (particularly O26, O45, O91, O103, O111, O113, O121, O128, and O145) may also cause enterohemorrhagic illness by producing VT1/2, but serotypes O157:H7/H have been most frequently associated with HUS and outbreaks in the most parts of the USA and the EU (2, 4). HUS is characterised by acquired nonimmune hemolytic anaemia, thrombocytopenia, and acute renal failure. This syndrome can affect people of all ages but is most frequently diagnosed in children (7). All faecal samples from patients suspected of having bloody diarrhoea, HUS, or thrombotic thrombocytopenic purpura should be tested for O157:H7/H with tests demonstrating verotoxins or genes encoding these toxins= It should be kept in mind that the infection may be masquerading as gastrointestinal bleeding with a noninfectious cause, and the preceding diarrhoea may have resolved and been forgotten by the time of diagnosis of HUS or thrombotic

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thrombocytopenic purpura. Timely and accurate diagnosis can prevent secondary transmission, avert unnecessary and possibly dangerous procedures and therapies, and detect continuing outbreaks (7). This study describes a clinical case of sepsis-induced Vt1/2 positive *E.coli* 0157:H7.

CASE PRESENTING

A 78-year-old woman suffered a closed peritrochanteric fracture after a domestic fall accident. This necessitated surgery at the Traumatology Department of the hospital in Blagoevgrad, where the patient underwent endoprosthesis procedure. From the revision after the manipulation, the operator did not give any evidence of complications from the surgical process. During her post-operative stay in the Traumatology Department, the patient had several watery diarrhoea and vomiting episodes, without fever. From the epidemiological history there was no evidence of contact with patients with acute infectious diseases or consumption of risky foods and beverages. After questioning the staff of the Traumatology Department in detail, noone reported the presence of dyspeptic manifestations or disorders. There were no other patients in the ward with similar manifestations. The only food the patient consumed during the postoperative period was a banana brought from outside the facility. The patient had arterial hypertension and congestive heart failure treated with Moxogamma, Betaloc Zok, and Tritace. According to the biochemical profile, a rehydration therapy was performed in the Traumatology Department, but the patient's condition did not improve. On this occasion, on the 19th of May 2023, the woman was admitted in the Infectious Diseases Department of the hospital in Dupnitsa. Upon admission, the woman was in severe general condition. Conscious but hardly contactable. Oriented for time place and own personality. She was adynamic, with drooping eyelids and difficultly opening her eyes fully. Neurological status presented without signs of meningoradicular irritation. The skin was pale, and dry with reduced turgor, and elasticity, with the presence of swelling on the lower extremities, accompanied by oliguria with urine output up to 3450 ml in 24 hours There were clinical parameters of II to III degree dehydration. The visible mucous membranes were dry, the tongue was dry, and intensely coated with white plaque. Weakened vesicular respiration in both thoracic halves to undisturbed at the bases was documented. There was tachyarrhythmic cardiac activity, with RR 110/70 mmHg and Fr-113 beats per minute. The abdomen was soft, with violent intestinal peristalsis. There was evidence of mildly compensated metabolic acidosis: pH - 7.43; pCO2 - 44.9; pO2 - 46; HCO3 - 34.1; %SO3 - 84.5. Background, clinical parameters, biochemical profile and diagnostic test findings are presented in Tables 1 and 2.

On the day of admission, a fecal sample was sent to the NRL for Enteric Diseases, NCIPD, Sofia for examination of suspected antibiotic-associated diarrhoea due to *C. difficile*. Several hours later the laboratory diagnosis was PCR-confirmed as *E. coli* O157:H7 producing Vt1 and Vt2 toxins. Intensive rehydration therapy, reaching up to 3 L in 24 hours was started. Due to the evidence of low potassium levels-2.38 mmol/l, 4-5 ampoules of potassium salts per day were added to the infusions. A decline was also noted in total protein and albumin levels and Human albumin was administered.

On the third day (22nd May) the patient's condition improved. She was more conscious. The eyes were open. She was not adynamic. Arterial blood pressure held steady. Potassium reached a level of 4.1 mmol/l. Total protein and albumin values were normalized. in the leukocyte counts changed from leukocytosis to normocytosis. At the onset of the disease, antibiotic therapy was avoided because of the risk of HUS and acute renal failure due to the pathogenesis of VTEC according to most medicine guidelines.

Despite the strict fluid management, 4 days after presentation, the patient progressively worsened, defecations persisted, defecations were watery yellow-greenish without admixture of blood and mucus, and reached 8-9 per day. Arterial blood pressure tended to hypotension- RR 80/60mmHg. Cardiac activity became tachyarrhythmic. The urine output stopped. After consultation with the internist and anesthesiologist infusions were discontinued. Leukocytosis progressed dramatically-24.54, and total protein and albumin decreased drastically, necessitating the re-inclusion of Human albumin. The patient’s oedema became increasingly massive.

When a peripheral venous source was attempted, lymph started leaking from the skin. Throughout, the patient's urea and creatinine values remained within normal limits. Dehydration was obvious necessitating intensive intravenous rehydration. The possibility of a septic condition caused by *E.coli* 0157:H7 was also discussed, therefore Ceftriaxone 2 x 2g and Metronidazole 3 x 500 mg intravenously were successively added to the therapy. Given the unstable hemodynamics, Noradrenaline therapy was started. In the subsequent two to three days of hospitalization, the patient's condition remained critical. There was a reduction in defecations up to one per day. On 27th May the patient's condition was satisfactory. She is more alert and much more in contact. However, on the next day, she became quite flaccid, the oedema increased, and the tachydyspenia and tachyarrhythmia increased. Due to the suspicion of effusions, therapy with Furantril and Urbazone was started, decreasing the oedema At the end of that day, she became hardly contactable again and subsequently did not respond to calls, pain and touch at all. Late in the night of the same day the patient died with the picture of acute respiratory and cardiac failure

DISCUSSION

We discuss the septic condition due to colienteritis as the primary cause of death, the condition after hip surgery as well as the accompanying cardiac problems being risk factors for the lethal outcome.

Many patients with *E. coli* 0157:H7 infection require hospitalization because of dehydration, poor fluid intake, or the need for observation. The spectrum of VTEC disease varies from asymptomatic carriage to haemorrhagic colitis and HUS (5). In the present case, the main clinical manifestations were abdominal pain, myalgia, vomiting and non-bloody watery diarrhoea. Sometimes physicians do not consider enteric infection in the cases caused by *E. coli* 01 57:H7 because the patients are usually not febrile at the time of the initial medical evaluation, and may have abdominal pain as their most prominent symptom. (1,5,7). Advances in molecular detection methods contribute to the recognition of emerging pathogens and give a more accurate diagnosis. In just a few hours, the NRL of Enteric Diseases confirmed the causative agent of Vt1 and Vt2 producing O157:H7 enterocolitis, rejecting empirical therapy for CDI. Stool examinations for *Clostridium difficile* and *C. difficile* toxin were negative. The PCR assay is reliable for screening Vero toxins producing Escherichia pathogens, especially in potentially life-threatening cases associated with infection by *E. coli* 0157:H7 and application of etiotropic treatment. The mainstay of treatment for VTEC infection is supportive. Although *E. coli* is sensitive to the most commonly used antibiotics, the latter were not shown to alleviate the symptoms, reduce the microbial burdenen, or prevent HUS. Fluoroquinolones are suspected of increasing the release of enterotoxins and the risk of HUS (4). According to literature datae, there are fluctuations in antibiotic use for *Escherichia coli* O157: H7 treatment and an estimate of increased risk of HUS in association with all antibiotic classes. The strongest effect was observed for β-lactam antibiotics. According to literature data, studies on azithromycin as a main treatment for ten STEC infections reported the development of HUS in 1 up to 3 cases in which this antibiotic was administered (9). The administration of azithromycin and the consequent increased incidence of HUS in children infected with STEC were reported in other studies (10). Nonetheless, current data fail to exonerate antibiotics as a risk factor for HUS in *E. coli* O157:H7 infections. We refrained from administering antibiotic therapy because of the risk of HUS and acute renal failure associated with the pathogenesis of VTEC. Although most patients with enterohemorrhagic diarrhoea-associated HUS recover from the acute illness episode, in this particular case, the strict supportive treatment and delayed antibiotic therapy did not lead to the expected outcome. The 78-year-old female patient died.

Conclusion. The report concludes that delayed antibiotic therapy in elderly people with emergency infection contributes to poorer clinical outcomes. A greater awareness of the *E. coli* O157: H7 infection by medical personnel is required, and a nationwide surveillance system for VTEC infection is warranted.

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Table 1. Values of the main clinical laboratory parameters.

Date	Leukocytes	Granulocytes	Lymphocytes	Haemoglobin	Haematocrit	Platelets
19th	20,34	84,3	10,9	125	38,7	395
20th	17,8	82,3	11,7	111	32,6	215
22th	10,56	70,3	22	107	32	260
24th	24,54	84,3	10,8	110	33,7	252
25th	27,19	92,1	5,8	110	33,1	252
28th	12,6	81,1	11,8	90,7	30,2	189

Table 2 Dinamic biochemical profile.

Date	Glucose	Urea	Creatinine	Total protein	Albumin	K	Na	Cl	AST	ALT	CRP
19th	7,52	3,35	62	54	28,4	2,38	134	90,2	58	47	
20th		2,95	56			2,54	134	95,7			
22th		3,28	67	65	35	4,1	139	105	36	36	18,8
24th											
25th									27	28	90.2,
28th	10,0										

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