Fatal Outcome of Alimentar Escherichia Coli O157: H7 Toxiinfection

Abstract
Medical records showed that in two young tourists, different gender from Macedonia developed at the same time symptoms of acute alimentary toxinfection. In male person, there was regression of symptoms after completion of home treatment (oral rehydration and diet).

In the female case (18 years) home treatment conducted under the same conditions, did not yield satisfactory results. Disease progression was monitored clinically from the appearance of sub febrile temperature, with vomiting, watery diarrhea and abdominal pain to development of hemorrhagic colitis (spasmodic pain in the lower abdomen, then bloody diarrhea), which forced her to search medical help. The dramatic course of the development of clinical disease, occur 7-8 days after onset. Coincides with the early development of hemolytic uremic syndrome (HUS), and later development of acute renal failure. Those 18-th days from the onset of the disease ended in death. In the last stage of hospital treatment and analyzing, at the Nephrology Clinic in Skopje, swab of the mucous membrane proved verotoxin of E. coli O157.

Introduction
In the late XIX and early XX century, the progress of science and technology has enabled a revolutionary discovery. In medicine it is visualization of microorganisms, the discovery of antibiotics, vaccines and others. This contributed to preoptimistic predictions that infectious diseases become history, recalled by the history and heroes of antic times. In the twenty-first century, this prediction has not been realized. Infectious diseases continue to take place in the spotlight of world medical and scientific community, they are the major cause of morbidity and mortality of the population worldwide. Predictions for the future in relation to these diseases are not optimistic. There are many contributing factors, ranging from those that natural evolution provided to microcosm, to those which are caused by human activities.

Antibiotics that entered in a big way in medicine have been a powerful weapon in the fight against a number of bacterial infections for a long time. Modern aspects of their use are warning in relation to their growing powerlessness in the overcoming some bacterial infections. In some infections, their use is contraindicated, for which a typical example is toxic infection caused by enterohemorrhagic Escherichia coli (E. coli) (EHEC) [1], also known as Shiga toxin – producing E. coli (STEC) [2,3], or verocytotoxigenic E.coli (VTG). This pathogen is a food and waterborne pathogen [4] that spreads also by zoo-notic or person-to-person transmission rut causing severe enteric infection [5].

The toxin of E. coli, which similar to Shiga toxin, causes acute hemorrhagic colitis, which represent ¼ of all cases of hemorrhagic colitis. Complications that can occur involve bleeding or perforation of the intestinal wall. The most serious complication that occurs in 5 - 10% of people is hemolytic uremic syndrome (HUS). In 3-5% of cases of HUS, the prognosis is poor and leads to death. Use of antibiotics may accelerate the development of HUS or even introduced in HUS patients [6]. Although a relatively small percentage of HUS causes death, such an outcome of a bacterial infection in the modern world is difficult to accept. Quick and exact diagnosis and appropriate treatment is crucial for the prognosis of disease [7,8]. A case of fatal alimentary toxinfection by Enterohaemorrhagic E. coli O157: H7 is presented.

The Medical Documentation

Victim of fatal infection caused by Enterohaemorrhagic E. coli O157: H7 is a young female tourist (19 years old) from Macedonia, who was staying in Montenegrin coast, July 2007.

The disease started 2-3 days before the first medical examination, with sub febrile fever, watery diarrhea and abdominal pain. Her friend, with whom she was on vacation, also had similar symptoms. After completion of home treatment (diet and intestinal symptomatic therapy), a man had regression of symptoms, and conversely, girl had progression of disease.

On the third day of illness, in the evening, the patient visited emergency unit of Primary Health Care Center in Budva due to severe pain in the lower abdomen and with the data that they occurred after two days of frequent water stools. The protocol of this institution registered diagnosis colica abdominals. She received symptomatic infusion rehydration therapy: salt glucose 500 cc intravenous (intravenous) with vitamin cocktails, amp. Ranisan, eubiotics with the recommendation to continue per oral rehydration, diet regimen, eubiotic, she was send home.
The next day (fort day of illness) at noonture, she again visited this institution due to worsen condition, intensifying the pain in her lower abdomen. Patient registered macroscopic presence of blood in the stool during examining she was conscious, oriented, hypotensive. Under the diagnosis hemorrhaga gastrointestinal is, she was sent to Urgent ambulance vehicle to surges in General Hospital (GH) in Kotor. In the report of specialist surgeon it is stated: subfebrility 37,5 °C, palpatory belly soft, painfully sensitive, especially in the left hypogastrium. Rectal tuse present the signs of diarrhea stool with an admixture of blood and mucus. The basic laboratory - biochemical findings were done which were normal. Additional diagnostic (abdominal ultrasound, X-ray image native abdominal, gynecological examination), exclude acute surgical and gynecological disease. The patient was admitted to the Department for infectious Diseases of the institution with the diagnosis obs. Enterocolitis acute haemorrhagica. Physical examination on admission to the department that the registered adynamic, exhausted, sub febrile 37,5 °C, conscious oriented. In neurological status, meningial signs has negative. Of the skin and visible mucus, no present jaundice, and rash of infectious origin. The belly of the plane of the chest, soft, palpatory sensitive in the lower part, audible peristalsis, organomegalyti not registered, as confirmed by ultrasound (US) examination of the abdomen. Moving limbs without edema. He denies previous illnesses. Anamnesis without menstrual cycle is correct. He denies the pregnancy.

After admission the rehidratation infusion and antibiotic treatment initiated: salt 500 cc. Ringer –iv., 5% salt dextrose 2 x 500 cc. iv, 20 cc. iv of Kalium Chlorid (KCl iv.), cefuroxime 750 mgr. per 8 hour, eubiotic Flonivin 4 x 2 caps. Planned and performed basic biochemical laboratory findings, electrocardiogram (EKG), and ultrasound examination of the abdomen. Kidneys of appropriate size and width of parenchyma, with discreet ultrasound signs microlytiasis on the right ren. Urinary bladder less distended. Uterus in the AVF. In Douglas ileocecaly, free fluid. In Morrison there was not free liquid. Distinguished cyst, the left adnexa 37 cm. The Douglas is still differentiating ultrasound of the abdomen was normal. Right adnexal follicular cyst, the left adnexa 37 cm. The Douglas is still differentiating free fluid. In Morrison there was not free liquid. Distinguished mesometrium. During stay in the Department for Infectious Disease – Kotor, consultative examinations by surgery where conducted daily since the persistent pain in the lower part of stomach. Abdomen below the level of the chest, painfully sensitive, left and right inguinal. No signs of acute surgical diseases, with would require emergency surgery. The native image of the stomach subfreniums were free, no aeroxydratic level, meteoriom found.

The seventy day of illness she was discharged at the request of her mother, to return to Macedonia. The laboratory on discharge: sedimentation (Se)- 8/, leucocytes (le) -9,2 (granulocytes-82,5%,lymphocytes-14,4%), erythrocytes (er) -4,42, hemoglobin (hb)- 133, platelets (PLT) -180, sodium -142,9 , potassium -3,70, fibrinogen -2,2, alkal phosphatase (AF) - 105, urea -3,6, glucose- 4,1, serum proteins - total -67,3, AST-16, ALT-19, total bilirubin (TB) / 18,9, CRP- 16.

She was with dradrawn from the Department for Infectious Disease, General Hospital – Kotor, with a diagnosis: gastroenterocolitis ac hemmorhagica, colic abdominals, cystitis, folliculitis s. l. dex.

On the eighth day of illness she was hospitalized on Department for Infectious Diseases, General Hospital, Stip, Macedonia.

Laboratory findings were done : le-6,0 / 6,1: Er-3,28/3,20 : hb: 97 / 98 : PLT – 53 / 108, TB-54,4, conjugated bilirurin-4,4, AST-125/ 116, ALT- 42/45, urea -18,8 / 20,8, kreatinin-136 / 194, hémoglobina-7,7 / 6,3, Liver markers-negative. Tension 130 / 80, diuresis 400 ml. The X-ray native image of the abdomen shown: free both diaphragmatic domes, aeroxydratic levels were not registered. On gynecological ultrasound (US), cyst on both ovaries were monitored and effusion in Duglas.

Treated with amp. Ceftriaksone 2 x 2 gr., salt Ringer, salt Physiological, salt Dextrose, total 2500, amp. Lasix 10 mgr. On the ninth day of illness about 20,00 h., she had convulsions. Under the diagnosis Syndrome hepatorenale, status post enterocolitis acuta, cyst ovarii l. dex, she was referred to the Clinic for Infectious Disease in Skopje, Macedonia. From the discharge list of Department for Infectious Disease General Hospital in Stip, obvious deterioration of health condition of the patient was obvious. With clinically manifested jaundice, diuresis was decreased. In laboratory findings: decrease in the number of red blood cells, platelets, increasing the value of urea, creatinine, and serum aminotransferase activities. Native X-ray of the abdomen was normal, consulted surgeon and gynecologist. US of abdomen showed enlargement of both kidneys. Stool formed, with an admixture of blood.

From the tenth to the thirteenth day of disease she was staying at the Clinic for Infectious Disease and obscure febrile conditions in Skopje. The diagnostic procedure involved: infectious disease specialist, surgeon, hematologist, transfuziologist. In the clinical picture the dominant was abdominal colic. Stools are described as formed with the presence of blood. Progression of jaundice was registered, with a further decline in red blood cells and platelets.

Fourteenths day of illness with the diagnosis: anemia hemolytica (Coombs negative), thrombocytopenia, HUS in obs, Acute renal failure (ARF), gastroenterocolitis acuta, she was moved to the Hematology Clinic in Skopje, where she stayed 4 days (until the eighteen day of illness). In this institution with rehydration infusion and antibiotics (ceftriaxone and trimetoprim-sulfamethoxasole), she also received supportive therapy.

Eighteenth day of illness the patient has been moved to the Clinic of Nephrology in Skopje, due to the development acute renal fallore (ARF) and the need to join the haemodialysis program.

In the Nephrology Clinic the following microbiological
findings were made: blood cultures, urine culture (negative). Enterohaemorrhagic bacteria were not isolated with rectal swab, but it proved verotoxin in E. coli O157. Pneumoslide was negative.

Death outcome occurred at this Clinic on the eighteenth day of the disease.

**Discussion**

The case of fatal gastrointestinal infection with E. Enterohaemorrhagica coli O157: H7, is an illustrative example of how the health service is sometime unable to fight with the micro - world [6,7].

Post diarrhoeal hemolytic - uremic syndrome (D + HUS) is a severe, life – threatening complication, occurring in 10% patients infected by E. coli O157: H7, or other members of the E. coli Enterohaemorrhagic species, which produce Schiga toxin (Stx).

D+HUS caused by E. coli, was first described in the 1955, but it was not identified as a secondary consequence of infection with E. coli until 1982. Later E.coli is recognized as a frequent cause of acute renal disorders in children and young people.

Occurrence of epidemic diseases caused by Enterohaemorrhagic E. coli occur by eating contaminated food. Out of many Enterohaemorrhagic serotypes E. coli is the most important O157: H7, as among Enterohaemorrhagic strains the most frequent cause of diarrhea in humans in developed countries. Enterohaemorrhagic E. coli is a highly infections bacteria. Infectious dose required for the occurrence of manifest disease in only 100 bacteria [8,9].

The clinical picture of disease is very varied, ranging from mild diarrhea to severe hemorrhagic colitis with haemolytic uremic syndrome – which can be fatal, as in the case described in two patients: a male transient digestive disorder, and in female with haemorrhagic colitis with HUS infection and death.

HUS is manifested by acute renal failure, thrombocytopenia and microangiopathic hemolytic anemia. Manifestation by the central nervous system (CNS) include disorders of awareness, from lethargy to coma, and hemiparesis. Lesions in the course of HUS as result of action of toxins (Stx), produced by E. coli O157: H7. [6].

The presence of appropriate receptors on enterocytes, facilitates absorption of toxin in the intestinal capillaries, from which it goes to systemic circulation, where attacking the corresponding receptors on the cells of white blood cells. The toxin then reaches the kidneys, where there are plenty of appropriate receptors designated GB3, on which it is bind. Organic damage primarily depends on the functions of the GB3 receptor that bind the toxin, the localization and density of these receptors. Receptors are heterogeneously distributed in the vital organs of human body (kidneys, pancreas etc.). After adherence of toxins to receptors on the cell surface, it reaches the cell cytoplasm, where disrupts the entire protein machinery, which results in cell deterioration and / or cell death. Damage in cells activates blood platelets and coagulation cascade with subsequent formation of thrombus in microcirculation system of kidney, and development of acute renal failure [10].

Erythrocytes are exposed to hemolytic destruction by Stx and / or due to disoder of microcirculation. Platelets are destroyed in the spleen.

Factors that lead to the development of HUS are not well defined. Potential factors include: age (the youngest and oldest age), females, presence on antigens on the surface of bacteria, which are responsible for the adhesion of erythrocytes, bloody diarrhea, fever, increasing the total number of white blood cells, antibiotic treatment. In many cases these risk factors have not been confirmed. There are published cases of incomplete HUS [8,10,11]. In the case described in this paper, out of the risk factors the following were present: yang person, female sex, bloody diarrhea and antibiotic treatment.

Recent studies have also pointed out that in typical cases of HUS, virulence factor – cytotoxin (Sub AB) was included, which is sometimes present in E. coli O157: H7 and in other members of the Shiga toxigenic E. coli [2,12,13].

Antibiotic therapy is reserved for severe cases and is usually applied ex juxvanitus or before isolation of pathogens. It consists mainly of one – day or three – day application of trimethoprim and ciprofloxacín -sulfometoxasol [14,15]. In our case patients received cephalosporin therapy first, and after development of HUS trimetoprin- sulfomethoksazole [16].

**Conclusion**

We present the case of severe acute enterocolitic - hemorrhagic disease, causing by Enterohaemorrhagic E.coli (O157: H7), developing of the hemolytic – uremic syndrome (HUS) as complication that ended in death. Etiologic agent was discovered only after the emergence of complications at the Clinic for Infectious Disease in Skopje. It remains an open question whether the timely detection of pathogens has led to a different outcome.

There is a need that small diagnostic laboratory have a minimum of diagnostics for Enterorhagic E. coli. In conditions of insufficient competence of laboratories to diagnose Enterohaemorrhagic E. coli, clinicians must thinks of them as a possible cause of hemorrhagic diarrhea due to complications that can develop in the course of infection and even lead to death.

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