Acute meningitis and emphysematous pyelonephritis due to extended-spectrum beta-lactamase-producing E. coli

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September 25, 2021

Abstract

We present a case of acute meningitis due to extended-spectrum beta-lactamase-producing E. coli in a patient with immune thrombocytopenic purpura and diabetes mellitus. This challenging entity is uncommon but has a high mortality rate. The exact mechanism for the pathogenesis is not obvious and needs further studies

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Key words: *Escherichia coli,* enterobacteriaceae, meningitis, mortality

Key messages:

Escherichia coli represents a rare cause of community-acquired acute meningitis in adults with high mortality rate. The exact mechanism for the pathogenesis is not obvious and needs further studies.

Introduction

Acute bacterial meningitis is a potentially life-threatening condition and in adults is most often caused by *Streptococcus pneumoniae*and *Neisseria meningitidis* . Among other pathogens that cause bacterial meningitis, gram-negative bacilli (GNB) are an uncommon cause, ranging from 0.7 to 7% across the world [1].

Escherichia coli (*E. coli*) is a commensal bacteria within the human gut. However certain strains are associated with infections that urinary tract infection is the most presentation. Other manifestations are nosocomial pneumonia, cholecystitis, peritonitis, cellulitis, osteomyelitis and septic arthritis [2]. *E. coli*represents a rare cause of community-acquired meningitis in adults comprising about 1 % of meningitis cases and occur almost always in cases with an underlying risk factor, such as diabetes mellitus, alcoholism, cirrhosis, HIV infection and malignancies. This is usually secondary to a distant or contiguous focus of infection, such as urinary tract or gastrointestinal infection [3, 4]. Here we report a case of acute community-acquired meningitis which resulted from the hematogenous spread of *E. coli* emphysematous pyelonephritis in a 53-year-old diabetic woman with immune thrombocytopenic purpura (ITP).

Case presentation

A 53-year-old diabetic woman, was admitted to the emergency department with a three days history of fever and altered consciousness. One week before hospitalization, the patient had left flank pain. She was a known case of ITP and had been receiving prednisolone 5mg/d. Upon admission, the patient was febrile (38.5 °C) and hemody- namic status was stable. She showed no localized motor or sensory deficits, but was aphasic and opens the eyes just with painful stimulation. No other physical abnormality was found.

Initial laboratory evaluation are shown in table 1. Brain computed tomography scan was normal and lumbar puncture was performed. Cerebrospinal fluid (CSF) examination showed white blood cells of 9600 cells/mm^3 (80% neutrophil), glucose level of 20 mg/dl with corresponding blood sugar of 130 mg/dl and elevated protein of 80 mg/dl. Blood, CSF and urine cultures were sent. The patient was started on Meropenem 2gr IV every 8 hr and Vancomycin 1gr IV every 12 hr as empiric therapy for acute meningitis. Dexamethasone 8 mg IV every 6 hr for 4 days was started before the initiation of antibiotics.

According to the previous history of flank pain and the pyuria in urine analysis, initial kidneys ultrasound was performed and it revealed air focus in the parenchyma of the left kidney, which confirmed in abdominopelvic CT scan and was consistent with emphysematous pyelonephritis. In consultation with urologist, surgery was not recommended and antibiotic therapy was continued with close monitoring. After three days of treatment, the patient became afebrile. The results of cultures of urine, blood and CSF yielded Extended Spectrum β-Lactamase (ESBL) *E. coli* . Hence she was diagnosed as acute meningitis and emphysematous pyelonephritis due to *E. coli* . ELISA test for HIV antibody reported a negative result. Brain magnetic resonance imaging was performed and revealed no brain abscess. Transthoracic echocardiography was normal and no evidence of endocarditis was reported. Despite antimicrobial therapy, the neurological condition of the patient only minimally improved. Repeated blood cultures and also urine culture were sterile after initiation of antibiotic therapy. On day 20 of hospitalization, the patient died from sudden decrease in O2 saturation and respiratory failure followed by cardiopulmonary arrest.

Discussion

Community-acquired *E. coli* meningitis in adults is a severe disease, often with poor outcome and high case fatality rate even with appropriate antimicrobial treatment. In addition to systemic complications that are an important cause of death in these patients, multi-organ failure and sepsis appear to be a major cause**.**Compared to general population with bacterial meningitis due to other pathogens, patients with GNB meningitis like *E. coli* , more often had comorbid conditions [5].

Microbiological studies indicated a majority of wild-type *E. coli*and other items included quinolone resistant or trimethoprim–sulfamethoxazole resistant, ESBLs and penicillinase producer [1].

Enterobacteriaceae are not a frequent cause of meningitis in adults and*E. coli* is a rare etiology in community-acquired adult meningitis and recent reports of this entity is a challenging issue. In a study by Bodilsen et al. one of the most differences in clinical presentation of patients with *E. coli* meningitis was a low incidence (41%) of fever and classic meningitis triad including fever, neck stiffness and altered mental status. Also this study showed that patients with GNB meningitis were older and more often had comorbid conditions with a mortality rate of 36% [2]. Zafar et al. described a case of meningitis due to *E. coli* , presented with complaints of vomiting, severe headache, altered level of consciousness and fever. In this case urine and blood culture came out to be negative and no distant source of origin was identified [6]. Pomar et al. reported that the overall mortality rate for patients with spontaneous GNB meningitis was high (53%). The authors found that advanced age, positive blood cultures, inappropriate initial antibiotic therapy, and complications were associated with greater mortality in these patients [7]. In the study by Yang et al. 15 cases of adults with the diagnosis of *E. coli*meningitis were evaluated. Six cases were community acquired and diabetes mellitus was an important risk factor. The overall mortality reported in this study was 47% [8].

Cromlin et al. reported a case of O117:K52: H *E. coli* meningitis and multiple brain abscesses with the demonstration of acute pyelonephritis as the primary source. The patient died from complications [9]. Common risk factors for GNB meningitis include cirrhosis, alcoholism, malignancy, diabetes mellitus, immunosuppressive drugs and HIV infection [10]. The presented case was a known case of ITP, and was on

prednisolone 5mg/d. Hence the patient was not an immunocompromised case according to the corticosteroid duration of use and doses, but she was a diabetic patient as the important risk factor.

In our 53-year-old patient acute meningitis was accompanied by an emphysematous pyelonephritis as the primary focus of infection in which the same organism was isolated from the blood, CSF and urine.

Emphysematous pyelonephritis is a life-threatening infection of the kidney that is characterized by an accumulation of gas in the renal parenchyma. The most common predisposing factor is diabetes mellitus. The management include antibiotic therapy alone, percutaneous drainage in addition to antibiotics or nephrectomy, if the patient has progressive disease or has unstable hemodynamic status. The most common pathogen is *E. coli* cultured from urine and blood [11]. In serial imaging our patient showed improvement for emphysematous pyelonephritis with antibiotic therapy.

According to the study by Bichon et al. up to 7% of community acquired infections with *E. coli* are ESBL producer and 9% are broad spectrum betalactamase producer with resistance to penicillin group [1]. Diabetes mellitus, previous hospital admission and older age in male patients have been described as risk factors for infection of ESBL producing *E. coli* [12].

It is important to say that the majority of *E. coli* meningitis develop as a result of hematogenous spread, but the underlying mechanism for *E. coli* penetration of the blood brain barrier (BBB) is not clear and is a challenging entity. In-vivo and in-vitro studies indicates that meningitic *E. coli* strains have the ability to invade the brain, and lead to BBB disruption [13]. Some studies revealed that crossing of the BBB by this bacteria requires a high degree of bacteremia for brain penetration but it is not enough for the pathogenesis. The important prerequisite for penetration of *E. coli* into the brain is binding and invasion of human brain microvascular endothelial cells. Traversal of the BBB as live bacteria is another critical factor for the development of meningitis by this organism [14].

Conclusion

E. coli is described as a rare cause of community-acquired meningitis in adults and occur almost always in cases with an underlying risk factor, such as diabetes mellitus, alcoholism, cirrhosis, HIV infection or malignancies. This challenging entity is often secondary to a distant or contiguous focus of infection. The exact mechanism for the pathogenesis is not obvious and needs further studies.

Author contributions

M.S; S.S; A.H; F.M and M.T acquired data, analyzed and interpreted the data. A.H and F.M wrote the first draft of the manuscript. All authors have read, revised and approved the final manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

Ethical statement:

This research was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and written informed consent was obtained from the patient.

Data availability statement:

Data sharing is not applicable to this case report type article as no new data were created or analyzed in this study.

Acknowledgments

None.

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Table 1. Laboratory data at admission.

Laboratory test										
WBC(/µl)	Neutrophil (/µl)	PLT(/µl)	Hb (g/dl)	BUN (mg/dl)	Cr (mg/dl)	AST (IU/L)	ALT (IU/L)	PT (seconds)	INR	CI

WBC, White blood cells; CRP, C-reactive protein; PLT, Platelets; Hb, Hemoglobin; BUN, Blood Urea Nitrogen; Cr, Creatinine; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; ESR, Erythrocyte Sedimentation Rate; PT, Prothrombin Time; INR, International Normalized Ratio; Na, Sodium; K,

Potassium