

# Nosocomial *Escherichia coli* meningitis in adults: Report of four cases and literature review

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### ABSTRACT

We report four cases of nosocomial *E. coli* meningitis, in male patients with accidental and neurosurgical trauma. The interval between accidents/neurosurgical procedures and the onset of meningitis was 2-15 days (mean 6.25 days). The most consistent clinical features were fever and deterioration of consciousness level. Emergence of extended spectrum beta lactamase *E. coli* strains had been observed in two (50%) of our cases and the mean duration of antimicrobial treatment was 16.5 days (range: 6-24 days). Two of the four patients (50%) died in the hospital.

**Key words:** *E. coli*, neurosurgical procedure, nosocomial meningitis

### Introduction

*Escherichia coli* (*E. coli*) is a Gram-negative, rod-shaped bacterium that is commonly found in the lower intestine of warm-blooded organisms (endotherms). Most of these microorganisms are harmless, but some strains can cause serious illnesses. Recent studies suggest that *E. coli* B2 strains constitute a major subgroup causing extraintestinal infections. *E. coli* is one of the most frequent causes of many common bacterial infections, including cholecystitis, bacteremia, cholangitis, urinary tract infection, traveler's diarrhea, and other clinical infections such as neonatal meningitis and pneumonia.<sup>[1,2]</sup> However, *E. coli* is uncommon as a pathogen of adult bacterial meningitis.<sup>[3]</sup> In this report, we present four cases of adult nosocomial *E. coli* meningitis, which followed different accidental and neurosurgical trauma of the head and spine. These four patients were admitted to Hamad general hospital in Qatar, during the period from 2007 to 2010. This hospital serves as a tertiary referral center with a total capacity of 600 beds. It covers all specialties except for hematology-oncology and obstetrics and includes six intensive care units, which provide a full

range of clinical services in different Departments of Surgery and Internal Medicine.

### Case Report

#### Case 1

A 44-year-old Pakistani male patient, admitted to the trauma intensive care unit after having a sustained severe head injury and forearm fracture caused by a car accident. He had immediate loss of consciousness and cranial computed tomography (CT) showed multiple skull fractures involving left frontal bone extending downward to involve the roof of orbit bone, base of the skull and anterior cranial fossa. On the following days the patient improved, he became semiconscious, but cerebrospinal fluid (CSF) leak was noted. On the fifteenth day of admission, patient developed fever with deterioration in his consciousness level. Neurological examination revealed unconscious patient, however, examination for meningeal signs was not possible due to patient's condition. CSF examination showed 6675 leucocytes/ $\mu$ l with 80% neutrophils, a protein level of 230 mg/dl and a glucose level of 34.2 mg/dl. Direct examination of CSF showed Gram-negative rods, and cultures yielded extended spectrum beta lactamase (ESBL) *Escherichia coli*, sensitive to meropenem, gentamycin and piperacillin-tazobactam. Production of ESBL was determined by disk testing in our clinical microbiology laboratory according to the Clinical and Laboratory Standards Institute performance standards M100-S20. MICs of third generation cephalosporins and

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10.4103/0976-3147.118800

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of amoxicillin–clavulanate were used as confirmatory criteria of ESBL production detected by the BD Phoenix system. Isolates recorded as possible ESBL producers by the BD Phoenix system were prospectively tested for ESBL production by using combined discs method (BD Sensi-Disc) using ceftazidime (30 µg), cefotaxime (30 µg) with and without clavulanic acid (10 µg). An increase in the inhibition zone diameter  $\geq 5$  mm in the presence of clavulanic acid was considered confirmation of ESBL production. Blood cultures were negative. Cranial CT showed parenchymal changes consistent with cerebritis. The patient was treated initially with ceftriaxone (4 g/day), which was shifted to meropenem upon receipt of culture results. The treatment continued for 3 weeks after which the patient improved and discharged from the intensive care unit without any sequela other than his primary illness.

### Case 2

A 29-year-old previously healthy Nepalese man, with no history of arterial hypertension, was admitted to our hospital complaining of headache, vomiting and left sided weakness. On examination his blood pressure was high, 220/140 mmHg. Neurological examination showed conscious, oriented patient with left sided weakness. Cranial CT showed right sided intraventricular hematoma with significant mass affect (shift of midline structure to the left). Magnetic resonance imaging (MRI) was performed and there were no vascular malformations or aneurysms. On the 7<sup>th</sup> day of admission, the intraventricular hematoma was evacuated and a right external ventricular drain (EVD) was inserted. The patient was kept in the surgical intensive unit. Two days later, the patient developed fever, headache and vomiting. Meningeal signs were absent and CSF examination revealed 190,000 leucocytes/µl predominantly neutrophils with protein of 399 mg/dl and glucose of 3.6 mg/dl. Gram stain examination of CSF showed Gram-negative rods, and cultures yielded *E. coli* sensitive to ceftazidime, ceftriaxone, cefepime, meropenem, piperacillin-tazobactam, ciprofloxacin and amoxi-clavulinate and resistance to ampicillin. Blood cultures were negative. Cranial CT showed parenchymal changes consistent with cerebritis. The patient was treated with meropenem, vancomycin and supportive treatment, but he died on the 14<sup>th</sup> day after admission most probably due to multiple unrelated complications.

### Case 3

A 52-year-old Sudanese man brought to the emergency department because of loss of consciousness. His medical history was remarkable for hypertension

and diabetes mellitus. Cranial CT showed large cerebellar hematoma with dilatation of supratentorial ventricular system associated with impending conization. An urgent craniotomy and hematoma evacuation was carried out and EVD was performed. Patient remained unconscious but with stable vitals. Four days later, the patient developed fever. CSF examination revealed the following values; leucocytes 6083/µl with 97% neutrophils, glucose 32.4 mg/dl and protein 250 mg/dl. CSF and blood cultures yielded *E. coli* resistant to ampicillin, ceftazidime, ceftriaxone, cefepime, piperacillin-tazobactam, ciprofloxacin and amoxi-clavulinate and sensitive to meropenem. Despite antibiotic treatment with meropenem and supportive therapy, the patient deteriorated and died 4 weeks after admission probably due to overwhelming sepsis in addition to his primary illness.

### Case 4

A 40-year-old Egyptian man was admitted to the neurosurgery service at Hamad general hospital. He had lower back pain of sudden onset and the straight-leg-raising test on 30° was positive. A central disc herniation was documented at L4-L5 by MRI of the lumbar spine. Lumbar discectomy was performed with drain insertion. Four days later, the patients developed severe headache, vomiting and fever and there was obvious neck stiffness. Examination of CSF showed a leucocyte count of 56250/µl with 87% neutrophils, protein level of 298 mg/dl, and glucose level of <1.8 mg/dl. Gram staining of CSF demonstrated the presence of Gram-negative bacilli. CSF yielded ESBL *E. coli* sensitive to meropenem, piperacillin-tazobactam and gentamycin, but blood culture was negative. The patient was treated with meropenem and supportive treatment. After 15 days of treatment the patient's condition improved, allowing his discharge without any sequela other than his primary illness.

## Discussion

*E. coli* meningitis is rare in adults, developing mainly as a complication variety of accidental and neurosurgical trauma, such as craniotomy, placement of internal or external ventricular catheters, lumbar puncture, intrathecal infusions, or spinal anesthesia; head injury.<sup>[4,5]</sup> Similarly, all patients in this series developed meningitis after accidental or neurosurgical trauma. The interval between neurosurgical or accidental trauma and the onset of meningitis in our patients was short (2-15 days [mean 6.25 days]) compared with what have mentioned in other reports.<sup>[3,5]</sup> On the other hand,

community-acquired meningitis in adults due to *E. coli* usually develops secondary to metastatic infection in patients with bacteremia of intestinal origin. The main risk factors are alcoholism, liver cirrhosis, neoplastic diseases, diabetes mellitus, and treatment with immunosuppressive agents.<sup>[6,7]</sup>

As noted in this and other reports, the most consistent clinical features of nosocomial *E. coli* meningitis are fever and deterioration of consciousness level.<sup>[3,5]</sup> Although these findings are non-specific, they can provide a clue to the diagnosis of nosocomial meningitis.

In Gram-negative bacillary meningitis, the choice of an empiric therapy depends on the knowledge of the most common causative bacteria and the reported efficacy of different antimicrobials, which should be modified after bacteriological culture results. In our series, emergence of ESBL *E. coli* strains had been observed in two (50%) of our cases. The emergence of ESBL *E. coli* strains has become a therapeutic challenge in many centers as well as in ours, raising doubt about the efficacy of third generation cephalosporins in the empiric treatment of Gram negative meningitis.

It is difficult to establish how the infection affects the mortality in patients with neurosurgical procedures, in the presence of concurrent medical problems. Many factors had been identified as risk factors for mortality associated to *E. coli* meningitis; in the multiple logistic regression analysis, only appropriate antimicrobial therapy and septic shock were strongly associated with mortality even after adjusting for other potentially confounding factors.<sup>[7]</sup> In our series, the mortality was high, but the real causes of death had been unidentified as autopsy was not performed.

## Conclusions

It should be emphasized that during hospitalization of patients with a variety of accidental and neurosurgical trauma, fever should warrant special attention to possibility of nosocomial infection, and if this is also accompanied with change in mental status, central nervous system (CNS) infection should be strongly suspected followed with MRI or Lumbar puncture. Regular CSF studies should be performed, especially on patients with EVD for early diagnosis and effective treatment of CNS infections. Meropenem seems to be the drug of choice, while the third generation cephalosporins are the next best choice.

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**How to cite this article:** Khan FY, Abukhattab M, Anand D. Nosocomial *Escherichia coli* meningitis in adults: Report of four cases and literature review. *J Neurosci Rural Pract* 2013;4:349-51.

**Source of Support:** Nil. **Conflict of Interest:** None declared.