OLGU SUNUMU / *CASE REPORT*

Meningitis Due to Multiple Gram-negative Bacilli: A Report of Two Cases and the Literature Review

Çoklu Gram Negatif Basillere Bağlı Menenjit: İki Olgu Sunumu ve Literatür Taraması

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ABSTRACT

Meningitis due to multiple Gram-negative bacilli is a rare condition. It has been reported that meningitis is often associated with an infection of the paravertebral space, a nosocomial infection that becomes complicated following complex neurosurgical procedures or colorectal diseases. The aim of this study is to report two Syrian refugee patients with multiple Gram negative bacterial growth in cerebrospinal fluid cultures after neurosurgical interventions.

Key words: *gram-negative bacteria; meningitis; nosocomial*

ÖZET

Çoklu Gram negatif bakteri üremesine bağlı görülen menenjit, nadir görülen bir durumdur. Menenjitin sıklıkla paravertebral alan enfeksiyonu, karmaşık nöroşirürji prosedürleri veya kolorektal hastalıkları takiben karmaşıklaşan bir nozokomiyal enfeksiyon ile ilişkili olduğu bildirilmiştir. Bu çalışmanın amacı nöroşirurjik müdahalelerden sonra beyin omurilik sıvısı kültürlerinde çoklu Gram negatif bakteriyel büyüme gösteren iki hastayı bildirmektir. Polimikrobiyal menenjit, omurga cerrahisinden sonra nadir görülen bir komplikasyon olmasına rağmen, genel önlemler ile büyük ölçüde önlenebilir.

Anahtar kelimeler: *gram negatif bakteri; menenjit; nozokomiyal*

Introduction

Complex neurosurgical procedures like craniotomy, placement of internal or external ventricular catheters, lumbar puncture, intrathecal infusions of medications, or an infection of the paravertebral area during spinal anesthesia, complicated head trauma, or in rare cases, metastatic infection in patients with hospital-acquired bacteremia can cause nosocomial bacterial meningitis. Infection rates after neurosurgical procedure vary with the type of surgery and the anatomical site.

Ventriculo-peritoneal shunt (VP shunt) is a suitable procedure, that primarily treats hydocephalus and has a low mortality rate[1]. However nosocomial meningitis has been estimated to occur in 4–9% of all patients with hydrocephalus after internal catheter insertion. The complications appear within the first three months after surgery; an infection, however, may occur at all times. Statistically, about 3–12% of patients will develop an infection[2,3].

The incidence of surgical site infection after decompressive laminectomy and fusion has been estimated to be 3% or even lower, but the incidence may increase to as high as 12% with the additional instrumentation[4].

Nosocomial meningitis is caused by a spectrum of microorganisms that differs from community settings. Diagnosis of meningitis consists of cerebrospinal fluid analysis (cell counts, Gram's staining, biochemical tests for glucose and protein, and cultures), blood cultures and neuroimaging. Neuroimaging can help for the

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examination of ventricular size and provides information about possible malfunction of the shunt or potentially contaminated catheters, that are present from previous surgical procedures[5].

We describe two cases of multiple Gram-negative bacteria isolation in cerebrospinal fluid (CSF) cultures after neurosurgical procedures as nosocomial meningitis.

Case Presentations

First Case

A 5-month old Syrian patient underwent a VP shunt operation in a private hospital due to hydrocephalus. The patient only had complaints of fatigue, nausea, vomiting and decreased oral intake when he was brought to the pediatric clinic about 1 month ago.

Electrolyte imbalance due to prerenal renal failure was detected. The patient was consulted to infectious diseases without sampling any CSF. According to their routine protocols, prophylactic ceftriaxone treatment (2×350 mg/day) was started due to C-reactive protein (CRP) elevation and clinical condition.

The patient was referred to the university hospital on the 1st week of hospitalization, considering the dysfunction of the VP shunt. The patient was hospitalized in the Neurosurgery Intensive Care Unit. Computerized tomography (CT) revealed hydrocephalus which might be due to infection or dysfunction of the shunt. External ventricular drainage system applied to relieve hydrocephalus. CSF sample was taken during this protocol. Empiric antibiotic therapy was started as colistin + gentamicin, according to the recommendations of the Pediatric Clinic. The biochemical results were consistent with meningitis (protein: 345.3 mg/dL, glucose: 8 mg/dL and chlorine: 90 mEq/L). Microscopic investigation of CSF revealed Gram negative bacilii and white blood cell (WBC) infiltration. CSF specimen was cultured on, % 5 Sheep blood agar, McConkey agar and anaerob cultivation was performed with BacT-ALERT 3D system in identification of the Gram-negative bacilli. The identification and antimicrobial susceptibility testing of strains were determined by the Phoenix automated system (BD Diagnostic Systems, Sparks, MD) according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations. After centrifugation at 1500 revolutions per minute (rpm) for 15 min, the precipitate was stained and Gram− negative bacilli was detected. In neurosurgery practice, lumboperitoneal shunt is contraindicated in the presence of bacteria in CSF. However, CSF drainage is essential for both managements of increased intracranial pressure and treatment of meningitis. For this reason, CSF drainage was continued by the use of external drainage system. According to culture results taken from CSF, the antibiotic regimen changed to colistin and tigecycline. The case has been followed with the possible difference in life functions and he was referred to the pediatric hospital again.

Second Case

A 72-year-old male patient complained of pain in the waist and both legs. The complaints have existed for 5 years and have increased in the last 6 months. The neurogenic claudication started at 150 meters. According to the sagittal magnetic resonance (MR) examination; spondylosis, foraminal stenosis and degenerative scoliosis in the L1-S1 vertebrae segment was detected. Both patellar reflexes decreased and 1/5 force loss was detected in right dorsal flexion. Surgery was planned for the patient. L3-L4-L5-S1 vertebrae were stabilized with transpedicular screw rod system under general anesthesia and total laminectomy and bilateral foraminotomies were performed at L3-L4-L5 levels. During the operation, at the level of L5, midline dural laceration was occurred and cerebrospinal fluid leakage was seen. This defect was repaired by primary suture and using a tissue adhesive. CSF flow was stopped. The patient was followed up for 2 days in the Intensive Care Unit after the operation, and then was taken to the Neurosurgery Clinic. A clear neurological examination could not be performed because the patient had both a language problem and excessive pain. After 5 days, the patient's right ankle was found to have lost 4/5 in dorsal flexion strength. On the CT examination, it was seen that the right L4 screw was inappropriately positioned during the operation resulting in the compression of the relevant nerve root causing radicular pain and loss of muscle strength. The patient was re-operated on the ninth day and CSF collection encountered in operation field. The right L4 screw, which had made nerve pressure, removed. No dura or nerve damage was observed. Tissue adhesive was applied again to the dural defect. The loss of dorsal flexion of the right foot was improved to 1/5 level found in the preop period. In following days; fever, drowsiness and neck rigidity was detected. Culture sample was taken from CSF, which was accumulated under the skin. A lumbosacral MR scan showed air values in the operation log.

Hematoma and abscess were observed. The mental state of the patient worsened and referred to intensive care unit. Vancomycin (4×150 mg), colistin (2×25 mg) and meropenem (3×150 mg) were initiated according to the culture results. But the general condition of the patient has not improved and died due to meningitis.

CSF specimen was cultured on, %5 Sheep blood agar, chocolate agar and McConkey agar and anaerobic bottle cultivation was performed with BacT-ALERT 3D System (Biomerieux, France). After centrifugation at 1500 rpm for 15 min, the sediment was Gram stained and Gram-negative bacilli was detected. *E.coli* (susceptible only to imipenem, amikacin and colistin), *Acinetobacter baumannii* (susceptible to ciprofloxacin, co-trimoxasole, imipenem, meropenem, gentamicin and amikacin) and *Stenotrophomonas maltophilia* was identified in the first case CSF culture. In the second case report, *A.baumannii* (only sensitive to colistin and co-trimoxazole) and *E.coli* were isolated in the CSF culture (Table 1). On the same day *E.coli* and *Enterococcus faecalis* were isolated from the wound culture. Blood and CSF analysis are shown in Table 2. The identification and antimicrobial susceptibility testing of strains were determined by the BD Phoenix 100 automated system (BD Diagnostic Systems, Sparks, MD) according to the EUCAST recommendations.

Table 1. *Cerebral fluid culture results of two case reports*

	First case resistance			Second case resistance	
Antibiotic	*A.baumannii*	*E.coli*	*S.maltophilia*	*A.baumannii*	*E.coli*
Ampicillin	R	R	R	R	R
Piperacillin		R	R	R	R
Amoxicillin/klavulunate	R	R	R	R	R
Aztreonam	R	R	R	R	IM
Imipenem	S	S	R	R	S
Meropenem	S	IM	R	R	R
Gentamycin	S	R	R	R	R
Amicacin	S	S	R	R	S
Netilmicin		R	R	R	R
Ciprofloxacin	S	R	R	R	
Ceftriaxone	R	R	R	R	R
Cefuroxime	R		R	R	
Piperacilline/tazobactam	R	R	R	R	S
Tigeciklin	IM		IM		
Colictin		IM	S	S	S
Ertapenem	R	R	R	R	R
Ceftazidime	R	R	R	R	R
Co-trimoxasol		S	S	S	R

R, resistant; S, susceptible; IM, intermediate.
Interpretation, identification and susceptibility testing was performed with automated identification and susceptibility system.

Table 2. *CSF (cerebrospinal fluid) and blood biochemical values*

First Case			Second Case	
CSF protein	345.3 mg/dL	285.7 mg/dL	426.9 mg/dL	
CSF sugar	8 mg/dL	47 mg/dL	6 mg/dL	
CSF chlorine	90 mEq/L	109 mEq/L	126 mEq/L	
Blood sugar	136 mg/dL	106 mg/dL	120 mg/dL	
CRP	297 mg/dL		349 mg/dL	127 mg/dL
Procalsitonin	1.47 ng/L		2.48 ng/L	1.02 ng/L
WBC	11.70×10^9/L	27.16×10^9/L	13.02×10^9/L	11.85×10^9/L

CRP, C-reactive protein; WBC, white blood cells.

Discussion

To the best of our knowledge and literature, the two cases are the first reported multiple Gram-negative bacterial meningitis.

It has been reported that meningitis develops 2–8.9% after neurosurgery[6,7]. The incidence of post-surgical meningitis in which patients received prophylactic antibiotics has been reported to 5%, and up to 10%, in cases who didn't receive any prophylaxis[8]. It was reported that postoperative CSF leak, high APACHE II Score and the duration of external ventricular drainage are independent risk factors for the development of post-neurosurgical meningitis[9].

The most common bacterial species in hospitalized patients for a long period after penetrating trauma, basilar skull fracture or neurosurgical operations are flora bacteria such as coagulase-negative *staphylococci* or *Propionibacterium acnes.* They are also common etiologies in patients with interventions such as internal ventricular drainage[10].

Enterobacterales are frequently isolated as a Gram negative organism in nosocomial meningitis[11]. In a retrospective study, *Klebsiella* spp. (26%) and *Acinetobacter* spp. (10.3%) were the most common pathogens causing postraumatic meningitis[12]. According to a study done by Sipahi and his colleagues[13], 899 nosocomial meningitis cases were obtained from 858 patients, and mostly isolated pathogens were *Acinetobacter* spp. (30.7%), coagulase-negative staphylococci (21.2%) and *Staphylococcus aureus* (19%). 18 of 48 (37.5%) *Acinetobacter* spp. were resistant to carbapenem. The mortality rate was 160/593 (27%).

At the first case, both *A.baumannii*, *E.coli* and *S.maltophilia*; and at the second case, *A.baumannii* and *E.coli* were isolated in the same CSF culture.

Pantoea calida was recently identified as the cause of post surgical meningitis after a pituitary adenoma resection[14]. Nosocomial meningitis due to *Acinetobacter* species have been reported more recently, that was resistant to third-generation and fourth-generation cephalosporins[15].

Kim and co-workers[15] treated 14 patients with multi-drug-resistant *Acinetobacter baumannii* meningitis or ventriculitis, administering colistin trough different routes and were able to cure 13 patients. In a retrospective study, it all 8 patients with *Acinetobacter meningitis*, who received intravenous and intrathecal colistin survived[16]. Several studies have shown favorable results in the treatment of *A.baumannii* meningitis with intrathecal colistin[17–19]. Mellon et al.[20] suggested that, multiresistant *A.baumannii* meningitis could be treated successfully with high doses of ampicillin/sulbactam combined with rifampicin and fosfomycin.

In diagnosis of bacterial meningitis additional tests have been evaluated. The lactate concentration of 4 mmol per liter or more in the CSF is shown to have a sensitivity of 88%, a specificity of 98%, a positive predictive value of 96%, and a negative predictive value of 94% and CSF/blood glucose ratio for the identification of bacterial meningitis following neurosurgery[21]. According to Lozier et al.[22], inoculation of pathogens during external ventricular device (EVD) placement, contamination and colonization of the EVD system during the postoperative period leads to EVD-related infections. Causes of postoperative colonization are the endogenous organisms present on the skin, which spread along the intracutaneous tract or by health-care workers during manipulation at the EVD system. Antimicrobial coated EVD catheters can prevent endogenous infections decreasing bacterial colonization[23]. Removing all components of the infected shunt and some component of external drainage with a combination of appropriate antimicrobial therapy is the most effective treatment for CSF shunt infections. The drainage catheter is able to clear the shunt infection of ventriculitis very rapidly and allows continued treatment of the hydrocephalus[24].

Some precautions should be taken to reduce the likelihood of infection, such as adoption of aseptic techniques, optimization of patient status pre-operatively and intra-operatively, appropriate use of pre-operative antibiotics, and good postoperative follow-up.

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