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Pseudomonas aeruginosa meningitis in post neurosurgical patients

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Abstract

Background and Objective: *Pseudomonas* meningitis is a rare complication following neurosurgical procedures and is associated with high mortality and mortality. The aim of the study was to describe the clinical characteristics and risk factors associated with mortality in patients who developed nosocomial *Pseudomonas* meningitis following neurosurgical procedure. *Methods:* All patients with nosocomial post-surgical meningitis due to *Pseudomonas aeruginosa* diagnosed in the year were reviewed retrospectively. *Results:* During the period of the study, 121 cases of post surgical meningitis were diagnosed. Ten (9.9%) nosocomial *Pseudomonas* meningitis were identified. Eight patients had external ventricular drain. The antibiotic susceptibility of 10 strains was: imipenem (9/10), meropenem (7/10), amikacin (7/10), piperacillin / tazobactum (5/10), ceftrizxone (4/10), cefepime (3/10). The overall mortality was high at 80%, despite most receiving appropriate antibiotics.
Conclusion: Postoperative *Pseudomonas* meningitis is associated with high mortality.

INTRODUCTION

Primary central nervous system infections with *Pseudomonas aeruginosa* are a relative rarity. Involvement is almost always secondary to a surgical procedure or head trauma and occasionally bacteremia. The cerebrospinal fluid (CSF) profile of *P. aeruginosa* meningitis is no different from that of pyogenic meningitis. Treatment of this entity is difficult and little published information is available.[1] However, general principles involved in the treatment of meningitis apply, i.e. the need for high doses of bactericidal agents in order to attain high antibiotic levels within the CSF. Nosocomial pseudomonas meningitis is a serious complication after neurosurgery and is associated with high mortality.[2] The aim of the study was to describe the clinical features, treatment and outcome of patients of neurosurgical meningitis by *P. aeruginosa* admitted to the Neurosurgery Intensive Care Unit at Govind Ballabh Pant Hospital.

METHODS

This retrospective study was performed at the GB Pant Hospital, New Delhi. GB Pant is a tertiary care centre where 1495 neurosurgeries were performed during the study period. Medical records of 12 post neurosurgical patients who had *Pseudomonas aeruginosa* isolated from a CSF sample processed by the Microbiology laboratory between January 2008 and December 2008 were reviewed.

Samples of CSF were obtained through an intraventricular catheter (8 cases) if present and by lumber puncture in the rest (4 cases). Nosocomial meningitis was defined according to the CDC definitions.[3] The criteria for a definite diagnosis of *P. aeruginosa* meningitis included the following (i) a positive CSF culture, (ii) fever > 38^{o}C in the absence of another recognized cause and (iii) ≥ 1 of the following laboratory values: CSF WBC count of > 10 cells/ mm^{3} with > 50% polymorphonuclear leukocytes, CSF proteins > 45g/dl and/or CSF glucose level of < 40mg/dl. A positive CSF culture with normal levels of glucose and proteins and cell count in the absence of symptoms were considered as contaminant and discarded.[4] *Pseudomonas* meningitis was considered to have been acquired postoperatively if meningitis developed after neurosurgical procedure in the hospital.

Data regarding underlying diseases, CSF parameters, isolation of the microorganisms, their susceptibilities, antibiotic treatment and the outcome of all the patients were collected. Day 0 (d0) was defined as the day of neurosurgical procedure performed. Treatment was considered as appropriate if it included at least one antibiotic according to sensitivity pattern. The antibiotic susceptibility of the isolated *P. aeruginosa* strains were tested using the Kirby- Bauer diffusion

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method as described in CLSI guidelines.[5]

For comparative analysis, the 10 *P. aeruginosa* meningitis cases were divided into two groups (fatal and non-fatal). Data were analyzed by means of a Fisher's exact test.

RESULTS

Epidemiological data and predisposing factors

During the period of the study, 121 CSF samples from suspected cases of post surgical meningitis were received in the Department of Microbiology. Gram negative bacilli were isolated from 30 (29%) cases. Out of 30 cases, 12 patients had *Pseudomonas aeruginosa* isolated from ≥ 1 CSF culture performed at Microbiology Laboratory, GB Pant Hospital. Of the 12 CSF isolates recovered, 10 met the case definition of nosocomial meningitis. Two cases have been operated in other hospital were admitted in our hospital with symptoms of meningitis and hence excluded from the study.

Pseudomonas aeruginosa was the most common Gram negative isolates recovered from the CSF, representing 40% of gram negative isolates and 9.9% of all CSF isolates. All 10 cases occurred among patients who had undergone neurosurgical procedure. Of the 10 patients with *P. aeruginosa* meningitis, 7 occurred in males with a mean age of 6.5 years (range 2 months - 57 years). No clustering of cases was seen. The underlying neurosurgical conditions were detailed in Table 1. Eight patients (80%) had external CSF drainage catheters (EVD) after ventriculostomies. Four patients (40%) required mechanical ventilation. The isolation of pseudomonas occurred at a median of 11.6 days from the neurosurgical procedures.

Clinical data

Altered mental status (80%) was the most frequent symptom, followed by fever (60%) and, seizures (50%). Meningism was detected in 3 patients. The clinical and laboratory data of the *P. aeruginosa* meningitis cases are listed in Table 2.

Microbiological data

Out of 10 cases Pseudomonas meningitis, 7 had only *P. aeruginosa* as a single isolate whereas the other 3 had polymicrobial isolates. In Case 1, *Klebsiella* and *Proteus* in addition to *Pseudomonas* were isolated. Case 2 had *Citrobacter* sp. along with *Pseudomonas* as isolates. In Case 3, *Klebsiella, Esch. coli* in addition to *Pseudomonas* were isolated. Blood culture was sterile in all cases. Table 3 shows that the most active agents against *P. aeruginosa* were imipenem (90% susceptible), meropenem (70% susceptible) and amikacin (70% susceptible). Ofloxacin susceptibility was present in 40% of the isolates. Concurrent *Pseudomonas* strains were isolated from non-CSF sites in Patient no. 10 from urine as well as endotracheal tube secretions.

Treatment

All the patients had received empirical antibiotic treatments, most commonly a 3rd generation cephalosporin and an aminoglycoside (amikacin/ gentamycin) in combination and later switched to appropriate antibiotics according to the antibiogram. Initial treatment was a carbapenem (either monotherapy or combination therapy) in 40% of the patients. Overall, carbapenems were administered to 8 patients. Two patients (Patient no. 2 and 4) did not receive appropriate antibiotics. Nine patients received i.v combination therapy

Table 1: Predisposing neurosurgical conditions of the 10 *Pseudomonas aeruginosa* meningitis cases

	Number
Congenital anomaly and external ventricular drain *in situ*	3
Intracerebral tumor, post craniotomy and EVD *in situ*	3
Congenital anomaly and ventricular-peritoneal shunt *in situ*	1
Previous meningitis and external ventricular drain *in situ*	1
Arteriovenous malformation and external ventricular drain *in situ*	1
Subarachnoid hemorrhage; clipping of aneursym	1

Table 2: Characteristics of 10 *Pseudomonas aeruginosa* meningitis cases

Characteristics	Non – Fatal N = 2	Fatal N = 8	P value
Age (years)	2	14.8	1
Male Female	2 –	6 2	1
Length of hospitalization (days) Median (range)	(38-160)	33 (2-56)	0.0
Neurosurgical diagnosis Tumor Congenital malformation Previous meningitis	 0 2 0	 3 3 1	 1 0.5 1
Mechanical ventilation	0	4	0.49
External ventricular drain (EVD)	2	6	0.6
Central venous catheter	0	0	
Inappropriate therapy	1	2	1
Meningitis due to carbapenem-resistant Pseudomonas	1	1	0.4
CSF sterilization	2	2	0.5
Number of neurosurgical procedures	3 (1-5)	1.5 (1-3)	0.09
Pseudomonas isolated from non-CSF sites	0	1	1

Table 3: Results of antibiotic susceptibility of 10 *Pseudomonas aeruginosa* strains

Antibiotics	Susceptible	Resistant
Amikacin	7	3
Gentamicin	5	5
Netilmicin	4	6
Ceftriaxone	4	6
Cefepime	3	7
Ofloxacin	4	6
Levofloxacin	3	7
Piperacillin/Tazobactum	5	5
Ticarcillin/clavulanate	5	5
Meropenem	7	3
Imipenem	9	1

with carbapenem (7 cases), aminoglycoside (6 cases), and 3rd generation cephalosporin (3 cases). One patient received monotherapy with imipenem.

Evolution and mortality

Cure of the meningeal infection was reported in only 2 cases. The overall mortality was 80%. The mean time to death was 36.2 days of hospital stay. The differential characteristics between patients who died and those who survived are shown in Table 2. CSF sterilization was achieved in 5 patients with median time of 55 days. Table 4 shows the clinical isolates, their antimicrobial susceptibilities, antibiotics prescribed, duration of treatment and outcome for all patients.

DISCUSSION

Pseudomonas is responsible for a wide range of nosocomial infections including post-neurosurgical meningitis. Previous studies showed that *P. aeruginosa* was responsible for 8.3% -10.7% of meningitis in post-surgical patients.[6,7] In our study, *Pseudomonas* species were recovered from 9.9% of the post neurosurgical meningitis patients. Although *Staphylococci* is known to be a frequent pathogen in postoperative nosocomial meningitis, the risk of colonization by Gram negative bacilli is increased in hospitalized patients.[8]

Pseudomonal meningitis is severe nosocomial meningitis associated with reported mortality of 21-40% that occurs predominantly secondary to invasive procedure.[7,9] The overall mortality rate was 80% in this study. The cause of high mortality rate in the study group is complex because of the preceding neurosurgical events. High mortality in this study may be due to delay in approaching the tertiary care hospital. In a recent study evaluating the predictors of mortality in nosocomial meningitis, *Pseudomonas aeruginosa* and *A. baumannii* meningitis were significantly related to inferior outcome.[10]

Increasingly, external CSF drainage catheters are used to manage critically ill neurological patients with elevated intracranial pressure.[11] EVD provide a potential portal of entry for microorganisms and have been associated with a risk of infection of 4%-11% for ventriculostomies and 4.2% for lumbar drains.[12] In our study, eight patients (80%) had EVD placed after ventriculostomies which strongly suggests that prosthetic device were the probable route of infection. Removal of all components of the infected shunt and some component of external drainage, in combination with appropriate antimicrobial therapy, appears to be the most effective treatment for CSF shunt infections.[13]

The reported risk factors for nosocomial meningitis include CSF leakage, intraventricular shunt operations, external ventricular drainage, repeated operation, emergency surgery and, inappropriate therapy.[14,15] However, no difference in risk factors was found in our study. Similar results were reported by Ondrusova *et al*.[16]

Of the 10 patients with postoperative nosocomial meningitis, one patient who expired had concurrent nosocomial infection of the urinary tract as well as respiratory tract. Concurrent infection of other site should be treated effectively treated to reduce mortality.

Initial antibiotic selection (ceftriaxone with aminoglycoside) was based on the antibiotic policy of the hospital. Sixty percent of the *Pseudomonas* strains were multidrug resistant (MDR) and this likely contributed to the high mortality. Treatment options for the management of MDR strains were limited to carbapenems. Emerging carbapenem resistance requires the use of polymyxins and colistin intraventricularly or intrathecally. Our institute does not practice treatment with polymyxins/ colistin, but carbapenem has been delivered intraventrically to achieve high antibiotic levels at the target site in one patient without success.

Although CSF sterilization was achieved in 50% of the patients, survival rate was lower with 80% mortality. On the other hand, of the 2 patients who did not receive appropriate antibiotics, one patient was discharged after 160 days of hospital stay. The successful outcome could be related to the removal of infected EVD.

The present study has some limitations. It is a retrospective study which included all CSF received from patients with clinical symptoms of meningitis admitted to neurosurgical ICU. Also, there may be other factors which could have contributed to the risk of infection could not be assessed.

In conclusion, postoperative *Pseudomonas* meningitis is associated with high mortality. Early diagnosis of meningitis in post-operative neurosurgical patients along with appropriate choice of antibiotics is the key issue to reduce mortality. Empirical and therapeutic treatment for *Pseudomonas* meningitis requires knowledge of local resistance pattern. Continuous surveillance should be done in postoperative patients to diagnose, treat and prevent these infections

Table 4: Characteristics of Post neurosurgical pseudomonas meningitis patients

Patient	Organism(s) isolated	Day of Isolation of *Pseudomonas*	Sensitivity of *Pseudomonas*	Treatment	Day of 1st negative CSF	Hospital stay (days)
1	*Pseudomonas, Klebsiella, Proteus*	d4	Amikacin,cefepime, ofloxacin, netilmicin, gentamicin, ticarcillin / clavulanate, meropenem, imipenem	Amikacin, cefuroxime (D2) meropenem (D15); EVD removal	d16	38
2	*Pseudomonas, Citrobacter*	d17	All Resistant	Ceftriaxone, gentamicin (D4) ceftriaxone (D32)	–	49
3	*Pseudomonas, Esch. coli, Klebsiella*	d4	Amikacin, cefotaxime, ceftriaxone, ofloxacin, netilmicin, gentamicin, pipperacillin/tazobactam, ticarcillin / clavulanate, levofloxacin, tetracycline, meropenem, imipenem	Amikacin, ceftriaxone (D4) imipenem (D22)	d15	26
4	*Pseudomonas*	d36	All Resistant	Gentamicin, ceftriaxone (D36) meropenem (D20); EVD removed	d159	160
5	*Pseudomonas*	d9	Amikacin, meropenem, imipenem	Cefuroxime, gentamicin (D9) amikacin, imipenem (D23)	d32	35
6	*Pseudomonas*	d4	Imipenem, meropenem	Gentamicin, cefuroxime (D4) meropenem, amikacin (D34)	d52	54
7	*Pseudomonas*	d25	Imipenem	Amikacin, cefuroxime (D25) imipenem, gentamicin (D 31)	–	56
8	*Pseudomonas*	d5	Imipenem, meropenem	Cefuroxime, gentamicin (D5) gentamicin, ofloxacin (D14)	–	19
9	*Pseudomonas*	d4	Amikacin, netilmicin, piperacillin / tazobactum, imipenem	Imipenem (D11)	–	11
10	*Pseudomonas*	d8	Amikacin, ceftriaxone, cefepime, ofloxacin, netilmicin, gentamicin, pipperacillin/tazobactum, ticarcillin / clavulanate, levofloxacin, imipenem, meropenem	Antitubercular drugs (D42) amikacin (D34) imipenem (D16)	–	42

d= duration from the day of surgery; D= Total duration in days

which rest on careful asepsis, removal of infected prosthetic devices and judicious use of antimicrobial drugs.

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