Post-traumatic Meningitis: Risk Factors, Clinical Features, Bacteriology, and Outcome
B Plaisier, C Yowler, W Fallon, M Likavec, J Anderson, M Malangoni

Abstract
Patients with post-traumatic meningitis (PTM) at two trauma centers from January 1992-December 1999 were retrospectively analyzed. Twenty-seven of 4,788 (0.56%) patients with head injury developed meningitis. Twenty-one (78%) patients were male. Mean age was 31.3 years. Twenty-three (85%) patients sustained blunt trauma and four (15%) had penetrating injuries. Median initial Glasgow coma scale (GCS) was 6. Twenty-one (78%) patients had pneumocephalus. Twelve (44%) patients had a cerebrospinal fluid (CSF) leak. Fever was seen in all patients and 23 (85%) displayed a decrease (greater than 2 points) in GCS. Twelve (44%) patients had an intracranial pressure (ICP) monitor, eight (30%) a ventriculostomy, and 12 (44%) underwent craniotomy prior to developing meningitis. Median interval between injury and diagnosis was 10 days. Pathogens were isolated from the CSF in 15 patients and brain tissue in one. Treatment in the remainder was based on elevated CSF white blood cell count, elevated CSF protein concentration, and low CSF glucose concentration. Measured functional outcome was good in 10 (37%) patients while 8 (30%) had a residual disability requiring dependent care and 5 (19%) remained in a vegetative state. Four (15%) patients died. Admission GCS was predictive of a good functional outcome (p < 0.01), but did not predict death from infection.

INTRODUCTION
Meningitis after head injury is uncommon with a reported incidence of 0.38-2.03%. Post-traumatic meningitis (PTM) can lead to devastating results and mortality rates up to 65% have been reported. A wide variety of gram-positive and gram-negative microorganisms may be responsible for this infection. While the time between injury and infection may be brief, there are numerous cases where PTM has been diagnosed years after injury. Because PTM often occurs in critically ill patients, it can be obscured by the patient’s condition and coexisting neurological problems. We analyzed patients with PTM in order to determine the associated risk factors, clinical characteristics, microorganisms involved, and the impact of this infection on outcome.

MATERIALS AND METHODS
Patients who developed meningitis following head injury at two American College of Surgeons-verified Level 1 Trauma Centers, from January 1992-December 1999, were retrospectively analyzed. The diagnosis of meningitis was based on compatible clinical signs and one of the following: positive CSF culture or a negative CSF culture in the presence of elevated neutrophil count, elevated protein concentration, and decreased (or less than two-thirds serum) glucose concentration. Two patients were treated based upon a clinical diagnosis alone, since lumbar puncture was believed to place them at unacceptable risk for transtentorial herniation.

Data were obtained from the hospital charts and trauma registries (TraumaBase version 5.2, Clinical Data Management, Inc., Conifer, Colorado and Trauma! version 4.3.15, Cales and Associates, LLC, Louisville, Kentucky). For intubated patients, admission GCS was determined by assigning one point for the verbal component. Clinical outcome was measured using the Glasgow outcome scale (GOS) which defines five categories: 1) death, 2) vegetative (unresponsive), 3) severe disability (unable to live independently), 4) moderate disability (independent but unable to return to work or school), and 5) good recovery (able to return to work or school). Chi-square was used for statistical analysis where appropriate and differences were considered significant at p < 0.05.
RESULTS

Twenty-seven of 4,788 (0.56%) patients with blunt or penetrating head injury developed meningitis. Clinical and demographic data are displayed in Table 1.

Figure 1

Table 1: Clinical Data in Patients with Post-traumatic Meningitis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Gender</th>
<th>ISS</th>
<th>GCS</th>
<th>AIS</th>
<th>Duration</th>
<th>Fever</th>
<th>Headache</th>
<th>Photophobia</th>
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Twenty-one (78%) patients were male. Mean age was 31.3 ± 14.4 years (median = 27 years). Twenty-three (85%) patients sustained blunt trauma and four (15%) had penetrating injuries. Motor vehicle crashes were the most common mechanism of injury, accounting for 14 (51.9%) patients. Four (14.8%) patients were injured in falls, five (18.5%) from blunt assault, and four (14.8%) by gunshot wounds. Injury severity and length of stay data are displayed in Table 2.

Figure 4

Table 2: Injury Severity and Length of Stay

<table>
<thead>
<tr>
<th>Case</th>
<th>ISS</th>
<th>GCS</th>
<th>AIS</th>
<th>Duration</th>
<th>Fever</th>
<th>Headache</th>
<th>Photophobia</th>
<th>Vomiting</th>
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The majority of these patients were severely injured as indicated by ISS, GCS, and AIS (Abbreviated Injury Score). Only four patients were not cared for in an intensive care unit. Associated craniofacial injuries and the use of ICP monitors and ventriculostomy catheters are outlined in Table 3.
Basilar skull fractures and pneumocephalus were each seen in 21 (78%) patients. Clinical CSF leaks were seen in 13 (48%) patients (eight with rhinorrhea, four with otorrhea, and 1 with persistent leakage at a ventriculostomy site). Seventeen (63%) patients underwent placement of an ICP monitor and/or ventriculostomy catheter during their course. The mean duration of ICP monitoring and ventriculostomy use was 4.1 ± 3.1 days and 9.7 ± 4.6 days, respectively. Twelve patients (44%) underwent craniotomy prior to developing meningitis.

While individual patients showed variation in the severity of PTM, most showed evidence of central nervous system involvement. Fever was a universal finding. A decrease in GCS from admission (greater than two points) occurred in 23 (85%) cases. Neck stiffness was seen in 13 (48%) cases, not observed in 7, but was not recorded in 7 patients. Rhinorrhea was seen in eight (30%) and otorrhea in four (25%). We were not able to accurately record the frequency of headache as many patients had a low level of consciousness.

Twenty-four patients had CSF sampling either through lumbar puncture (n = 17), ventriculostomy (n = 4) or lumbar drain (n = 3). In one patient, CSF was assayed via both lumbar puncture and ventriculostomy. The CSF was not sampled in two patients for fear of precipitating transtentorial herniation. Results of CSF assays are displayed in Table 4.

Streptococcus pneumoniae was the most common (n = 6) organism isolated. A single patient’s CSF culture was positive for both Staphylococcus aureus and Pseudomonas aeruginosa. Fourteen patients had received prior antibiotic prophylaxis and seven (50%) of these had positive cultures. Of the 13 patients who did not receive prophylaxis, nine (69%) had positive culture results.

Mean injury-infection interval was 97.7 ± 320 days (range = 1-1643 days) and median injury-infection interval was 10 days. The diagnosis of PTM was made within 15 days of injury in 21 (78%) cases (Figure 2). Streptococcus pneumoniae occurred in cases of both the shortest and longest injury-infection intervals (range 1-1643 days). Gram-negative PTM typically occurred about one week post-injury.
Figure 8
Figure 2: Injury – Infection Interval by Organism

Associated infections occurred in 19 (70%) patients. Pneumonia was seen in 17, urinary tract infection in six, and bacteremia was detected in eight patients. The organism grown from CSF was cultured from the blood in four. Ten (37%) patients had two or more associated infections.

Four (14.8%) patients died. Three deaths were attributed directly to PTM, while the fourth had intentional withdrawal of support after markedly brain function from PTM. One patient had a worsened GCS at discharge due to PTM. Among survivors, mean time of follow-up was 2.3 months. Five (18.5%) patients were functioning normally at discharge and five other patients were discharged to a rehabilitation facility with only mild to moderate disability. Eight (29.6%) patients had severe disabilities, but nearly all (n = 7) were discharged to rehabilitation. Five (18.5%) patients remained in a persistent vegetative state. Admission GCS was predictive of a good functional outcome (9.9 vs. 4.7, p < 0.01), but did not predict death due to PTM (Figure 3).

Figure 9
Figure 3: Admitting GCS and Follow-Up GCS

DISCUSSION
Post-traumatic meningitis in head injured patients is uncommon, with a reported incidence ranging from 0.38-2.03%. Typically, a skull fracture with accompanying dural tear results in a CSF fistula. This allows the subsequent passage of microorganisms into the cranial compartment. A CSF fistula is seen in 16.5-80% of cases and when present, is an important finding since this may serve as a portal of infection. Careful questioning and examination are crucial, since CSF leakage may be low volume, intermittent or obscured by blood.

PTM has also been reported with fractures across infected paranasal sinuses, middle ear structures, and mastoid air cells even without a dural tear. In rare cases, PTM is seen after spinal column fracture or blunt pelvic trauma. Cases following animal bites or burns to the face are believed to occur as a result of retrograde passage of infected venous thrombi into the cranial compartment.

Skull fractures are noted on radiologic imaging studies in 33-89% of cases. Many of the series in our review were published before the advent of computed tomography (CT), and since skull radiographs or tomograms were used exclusively, the number of fractures is probably underestimated. Unsuspected fractures have been found at craniotomy or autopsy in numerous patients with normal skull radiographs. Using coronal CT, Farrell evaluated 30 patients with non-meningococcal meningitis following head injury and found a fracture in all cases, which corresponded to the site of the dural tear when surgery was carried out.

Pneumocephalus was seen in 78% of our patients and in 86% of those with a skull base fracture. This finding is indicative of a dural tear with passage of air into the cranial cavity from an adjacent structure (paranasal sinuses or mastoid) or a foreign body such as a bullet. Pneumocephalus was not seen in other series. This may due to insufficient sensitivity from skull radiographs compared with our series where CT was used exclusively.

Signs and symptoms in PTM are variable, but most patients are critically ill and display evidence of central nervous system involvement. Fever is seen in 86-100% of cases. Deterioration in consciousness has
been reported in 97-100% of cases and was noted in 85% of our patients. This change in mental status may be extremely rapid and progressive. Clinicians should be alert for PTM if patients display increased drowsiness with no sign of transtentorial herniation. In a study of recurrent PTM, Hosoglu found that a triad of fever, stiff neck, and change in mental status occurred in all ten patients. Headache is also common and has been noted in 57-86% of patients. We were unable, like many authors, to determine the frequency of headache since underlying mental status often precluded its assessment.

The time between injury and diagnosis of PTM ranges from less than 24 hours to many years. Concomitantly, mean injury-infection intervals range from 8.4 days to 3.4 years. The median injury-infection interval, which may give a truer representation of the disease process, ranges from 5-13 days. In series where the median injury-infection interval is not explicitly stated, most patients are diagnosed within two weeks following injury. Our series is consistent with others as the median injury-infection interval was 10 days and the diagnosis of PTM was made within 15 days of injury in most (78%) cases.

Causative agents for PTM include a wide range of both gram-positive and gram-negative organisms. Streptococcus pneumoniae is the most common agent found in most series and is isolated in 52-100% of cases. Other often reported gram-positive organisms include Staphylococcus aureus and streptococcal species. Rates of gram-negative PTM range from 17-100% and are most often noted in series with a preponderance of open cranial wounds or lengthy hospitalizations. Commonly isolated gram-negative bacteria include Escherichia coli, Klebsiella pneumoniae, Neisseria meningitidis, Haemophilus influenzae, and Pseudomonas aeruginosa.

The diagnosis of PTM is usually made by CSF cultures with positive results seen in 73-100% of patients. Cultures of CSF may fail to yield an isolate, however and negative cultures have been reported in up to 27% of cases. Eleven (41%) patients in our series had negative CSF cultures. This may be due in part to the fact that eight patients were receiving prophylactic antibiotics. Interestingly, blood cultures may be positive in up to 86% of patients and are particularly useful for documenting the presence of pneumococcus.

Antibiotics should be chosen in accordance with the clinical situation and ability to penetrate the blood-brain barrier. Jones found that PTM onset within 3 days in patients with non-penetrating, non-depressed injuries was uniformly pneumococcal and recommend empiric therapy against this organism. While the infecting organism is likely to be from the nasopharynx or external auditory canal, nosocomial bacteria cannot be excluded until culture results are known. In patients with penetrating injuries, prolonged hospitalizations, delayed PTM onset, or antibiotic prophylaxis, definitive therapy should include broad spectrum drugs since the risk of infection with gram-negative or resistant microorganisms is higher.

As with other aspects of this disease process, outcome is widely variable. Mortality rates range from 0-65%. In serially ill adult patients, our mortality rate of 15% is comparable with other series which specifically address functional outcome. In a study of 116 patients who talked after sustaining head injury and later died, 86 were judged to have avoidable factors which contributed to death. Of these 86, PTM caused 7 deaths and four of these cases were completely unsuspected, underscoring the diagnostic difficulty. A patient who dies with PTM should have a post-mortem examination as the case may have significant forensic implications. In series which specifically address functional outcome, 47-75% of survivors, were independent at discharge. In our series, 37% reached functional independence by hospital discharge.

Our study has certain limitations. Retrospective analysis did not allow us to evaluate specific risk factors for PTM, but rather simply to note associations with other injuries and findings. Patients were followed to a maximum of 6 months, so we may have underdiagnosed delayed cases. The study was not designed to assess the impact of antibiotics used for prophylaxis. Our sample size did not allow for detailed statistical analysis. The number of patients (second largest series in the English literature) and functional outcome assessment are strengths of this study.

In conclusion, although uncommon, PTM may be associated with devastating results. While basilar skull fracture and pneumocephalus are common, PTM may occur in the absence of clinical CSF fistula. Fever and decreased mental status are usually seen. Streptococcus pneumoniae is the most common causative organism in most series. The injury-
infection interval is highly variable, but most cases occur within the first two weeks following injury. Neurologic outcome is usually related to the underlying brain injury, however many patients have a poor outcome (death or worsened GCS) attributable to PTM.

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