

Case Report

Post-Traumatic Meningitis: Case-Based Review of Literature from Internists' Perspective

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Abstract

Most cases of post-traumatic meningitis (PTM) occur following immediate head trauma or neurosurgical procedures. Hence, internists do not often come across these patients. However, closed-head trauma can be associated with community-acquired meningitis (CAM), and this history can often be missed especially if it is remote or trivial in nature. Therefore, meticulous clinical assessment is necessary to identify cases of community-acquired PTM. Knowledge about pathophysiological, anatomical, and microbiological context of community-acquired PTM is required in order to manage these patients. The role of internist is to provide holistic management in these patients which includes not only antimicrobial treatment but also timely referral to surgical specialties if required as well as vaccination to prevent further episodes. Here, we present a case of CAM with remote history of close head trauma and cerebrospinal fluid rhinorrhea for years who was found to have base of skull (BOS) defect on imaging of skull. He was treated with antibiotics and referred to surgical specialties for repair of BOS defect as well as given pneumococcal vaccine to prevent further episodes of meningitis.

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Introduction

In this era of widespread vaccination, the incidence and mortality from community-acquired meningitis (CAM) have declined significantly. However, owing to the potential intrinsic risk factors of head trauma and traumatic brain injury on the rise [1], post-traumatic meningitis (PTM) is an important entity. Meningitis is an emergency condition which has high incidence of mortality and neurological sequelae in the absence of treatment. The basic principles of meningitis management remain the same irrespective of the predisposing factors and cause. However, identification of PTM could be challenging especially if this happened years back following a trivial closed-head trauma. There are some differences in the anti-

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crobial management of PTM as compared to CAM. We report a case of meningitis who was found to have a base of skull (BOS) defect and cerebral spinal fluid (CSF) leakage as a result of a trivial head trauma years back. We also review the literature about PTM emphasizing on the epidemiology, anatomical and pathophysiological basis, and management principles.

Case Report

A 33 years old otherwise healthy male with no apparent comorbidities presented with new-onset refractory status epilepticus. On admission, his vital signs were pulse-110 bpm (regular), blood pressure 160/100 mm Hg, temperature 101° Fahrenheit, respiratory rate 18/min, SpO₂ 98% at room air. There was no evidence of lymphadenopathy, organomegaly, or any external scar mark. On initial neurological examination, he was obtunded with only movements on painful stimulation and had Glasgow coma score-8 (E1M5V2), pupils 3 mm bilaterally/reacting to light, no gaze deviation, fundoscopy revealed bilateral optic disc edema. He had neck rigidity with positive Kernig's and Brudzinski signs. He was able to move all 4 limbs spontaneously on painful stimulus, deep tendon jerks were brisk, and extensor plantar response bilaterally.

Given his decreased level of consciousness (LOC), for airway protection, he was intubated and placed on mechanical ventilation. He was started on injection levetiracetam (40 mg/kg intravenous [IV] loading dose followed by 20 mg/kg BID). Given his presentation of fever, meningeal signs and decreased LOC with high suspicion of meningitis, lumbar puncture was performed for cerebrospinal fluid study. Empirically for meningitis, he was started on ceftriaxone 2 g IV 12 hourly, vancomycin 1 g IV 8 h, and acyclovir 500 mg IV 8 h. He was also given dexamethasone 10 mg with first dose of antibiotics and thereafter every 6 h.

CSF study revealed: cell count-1,900/cmm (polymorphonuclear leukocytes-60%, lymphocytes 40%), protein-425 mg/dL, glucose-31 mg/dL (blood glucose-104 mg/dL), gram/Ziehl-Neelsen/India ink stains – all negative. Rapid PCR test of CSF (CSF Biofire: 94.2% sensitivity and 99.8% specificity) came positive for *Streptococcus pneumoniae* [2]. Given findings of bacterial meningitis, Acyclovir was stopped. Magnetic resonance imaging (MRI) of brain done revealed features of old blood products and gliotic changes in basi-frontal lobe (Fig. 1), which can be expected in head trauma.

After initial stabilization of the patient, his family members were interviewed about his clinical history. Although they denied any usual risk factors for meningitis [3–5], they mentioned about a fall from height with minor head trauma after binge drinking dated about 10 years back. This was followed by 1-day history of LOC which was not investigated further as it was thought to be attributed to alcohol intake. With presentation of pneumococcal meningitis and previous history of head trauma and having high suspicion of bony defect, we performed computed tomography (CT) scan of his BOS. CT scan of BOS revealed defects in the roof of right frontal sinus and right ethmoid sinuses with fluid collection (mucosal thickening) in the same sinuses (Fig. 2), and this could explain route of entry for microorganisms responsible for meningitis.

The patient gradually regained consciousness on the Day 2 without any further seizure episodes or fever. In response to treatment, he was extubated on Day 4. After regaining consciousness, he further confirmed of intermittent clear thick nasal secretion since the head injury possibly suggestive of CSF rhinorrhea. His IV antibiotics were continued for 10 days while dexamethasone and levetiracetam were continued for 4 days. He was discharged on Day 11. Before discharge, he was given pneumococcal vaccine and follow-up appointment with neurosurgery and otorhinolaryngology were arranged.

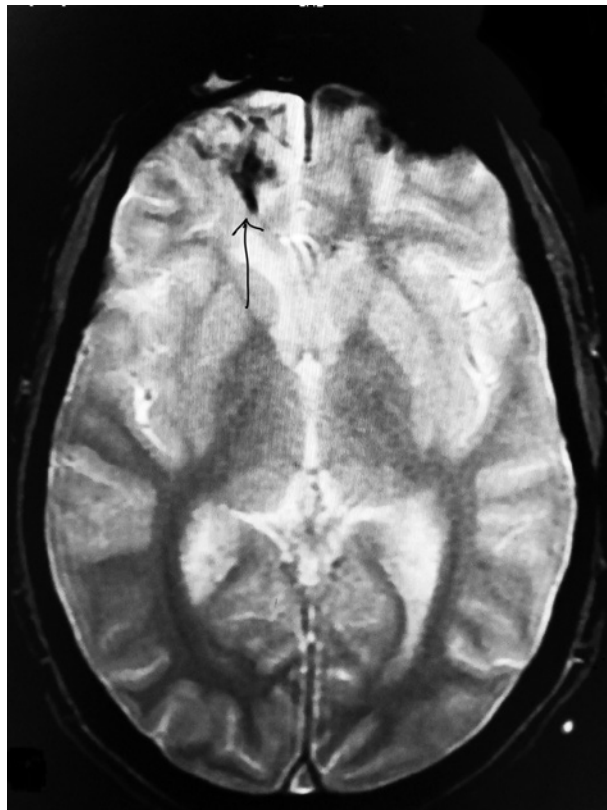


Fig. 1. MRI brain GRE sequence showing old blood products and gliotic changes in the frontal lobe (arrow). MRI, magnetic resonance imaging.

Discussion and Review of Literature

In this following discussion, we review the literature about PTM from internists' perspective focusing on dilemmas about case definition, epidemiology, anatomical and pathophysiological basis, and holistic management plan.

Dilemma about Case Definition

From epidemiological aspect, PTM is included under healthcare-associated meningitis (HCM). The basis of this epidemiological distinction is prevalence of different spectrums of microorganisms in HCM than CAM [6]. Moreover, HCM occurs more often during hospitalization after head injury/for neurosurgical intervention or after hospital discharge. However, the pathophysiological basis of PTM after closed-head injury (discussed later) is different from those following open head traumas. Therefore, not all cases of PTM should be included under broad classification of HCM. Furthermore, PTM after closed-head injury often bears similar risk factors and microbiological profile as CAM [7, 8]. Hence, history of head trauma even if trivial in nature should be enquired in all cases of CAM.

Epidemiology and Anatomical Context

Blunt head trauma is very common and most frequently associated with traffic accidents, fall from heights, sports, or workplace injury, etc. [9]. According to current evidence, 30–40% of blunt head injuries are associated with skull fractures [10, 11]. Basilar skull fractures (BSFs) are one of the most common skull fractures [12]. Given anatomical proximity of meninges and brain to the inner surface of skull, BSF can produce dural tear leading to CSF leak. Ethmoid and frontal bone are very commonly involved in BSF [13]. The degree of deformation and extent of



Fig. 2. CT of base of skull showing bony defect on the roof of ethmoid labyrinth and cribriform plate (arrow). CT, computed tomography.

fracture/defect following skull fracture are dependent on many factors, one of the most important among which is the physical properties of the skull-bones including their thickness and elasticity. The cribriform plate of the ethmoid bone is a horizontal plate that is connected to the ethmoid notch of the frontal bone and forms a thick and strong bone complex. However, the junction between the cribriform plate and relatively thinner ethmoid labyrinth containing ethmoidal air cells is particularly vulnerable to traumatic injuries as a result of change in the bone density between these structures. Furthermore, involvement of frontal sinus is also common in BSF and even considered high risk given association with contusions to the anterior portion of the frontal lobes and with dural tears with possibility of CSF leak (Fig. 3).

Pathophysiology

Generally, major pathophysiological mechanisms for developing any meningitis include: spread from colonization in the nasopharynx to bloodstream and subsequently central nervous system (CNS) invasion, CNS invasion following bacteremia from localized source or, direct entry of organisms into the CNS from a contiguous infection (e.g., sinusitis and mastoiditis)/trauma (e.g., BOS fracture)/neurosurgery/medical devices (e.g., CSF shunts) [3–5].

PTM in closed-head injury generally results from BSF with dural tear and more frequently with CSF leak [15]. However, PTM can also result from contagious spread of infection from brain or ventricles to meninges. This is reported in autopsy finding in a case of PTM where there was more chronic inflammation in brain tissue-proper close to contusion/skull fracture than further away meningeal infiltration of inflammatory cells suggesting spread of infection from brain proper to meninges. The authors coined this as *indirect meningitis* [16].

Another proposed hypothesis for PTM pathophysiology is spread of infected microthrombi to the intracranial (IC) compartment through diploic vein with opening of scalp vessels which can happen in closed traumatic injury of head even without destruction of bone and dura as reported by Schurmann [17].

Common Causes

Mostly gram-positive bacteria (GPB) like *S. pneumoniae* followed by Neisseria spp., Staphylococcus spp., etc., have been reported to be associated with PTM as they were retrieved from CSF culture in cases of community-acquired PTM or, meningeal swab assay in autopsy

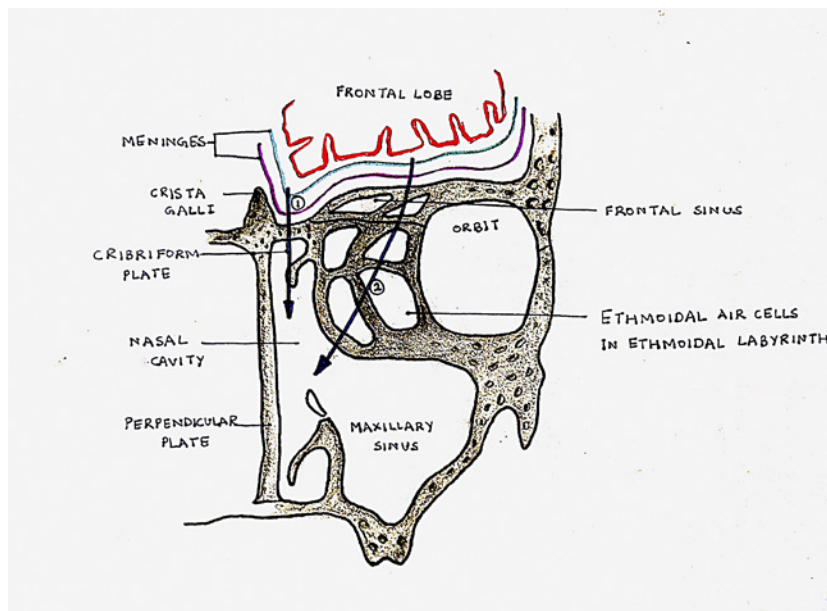


Fig. 3. It represents skeletal framework of BOS and nasal cavity. Arrows indicate common areas of traumatic bony defect and CSF leakage. 1: cribriform plate, 2: along ethmoid and frontal sinuses (Modified from Drake et al. [14], by permission from the publishers). BOS, base of skull; CSF, cerebral spinal fluid.

studies [7, 8, 15, 16, 18–20]. These GPB are common nasal/nasopharyngeal colonizer [21]. With breach in nasopharyngeal barrier as a result of fronto-basal skull injury, these GPB can gain access to the IC milieu. However, there are also reports of gram-negative bacteria or fastidious organisms causing PTM [7, 16, 22, 23]. Some authors have suggested emergence of these multiresistant organism with use of prophylactic antibiotics [16]. Hence, use of prophylactic antibiotics in isolated basilar fracture or CSF leak of <7 days duration following BSF has been controversial and probably not recommended [24, 25].

Basis of Diagnostic Dilemma

A high index of suspicion is required while investigating PTM cases as the clinical presentation, demographics, predisposing risk factors vary widely. PTM has been reported in all age-groups ranging from pediatric population to adult patients in their 90s [15, 16]. This is reflective of the fact that traumatic injury of head is very common in all age-groups [9]. In a prospective cohort study in adults, PTM was accounted for in 53% cases of recurrent bacterial meningitis where the mean age of the study population was 43 years [7]. Males were affected more than female in the reported studies which are obvious as males are affected more than females in traumatic events.

The history of head trauma, rhino-otoliquorrhea, or recurrent/past history of meningitis or anosmia should be enquired thoroughly as well as careful clinical examination should be done thoroughly with identifications of Battle's signs, Raccoon eyes, etc., indicating BSF. The presentation of meningitis could vary from days to years after the index head trauma. Meningitis as late as 30 years following head injury has been reported, hence, even a history of trivial head trauma should not be missed during clinical assessment [15, 16]. Majority of recurrent meningitis is thought to be as a result of PTM. One should be highly suspicious of PTM in cases of recurrent meningitis. In observational studies, the cause of 50–75% of acute recurrent bacterial meningitis was due to PTM [7, 8].

History of traumatic CSF leakage should be enquired as this could be the route of entry for microorganism and can be acute or delayed following the incident head trauma. About 12–30%

of BSF is associated with CSF leakage whereas as high as 20% in those with post-traumatic rhinoliquorrhea have been associated with developing meningitis [26, 27]. While meningitis with history of CSF leakage in a patient with recent head injury is easy to diagnose, delayed CSF rhinorrhea or recurrence of previously ceased CSF leakage can be missed, especially in cases of trivial injuries. CSF rhinorrhea as late as 1 year after the head injury has been reported [15]. Delayed or recurrence of CSF leakage could be as a result of re-fistulization of osteomeningeal defect that developed following index injury of BOS. As the dural layer is closely apposed with the inner surface of skull base, with increase in IC tension brain tissue may herniate down this osteomeningeal defect obliterating this deficiency. Hence, as reported in few operated cases, it was not unusual to find adhesions and scars on adjacent tissues including brain, meningeal layers with CSF spaces, bone, and mucosal layer of ethmoid sinus. The brain tissue can also become necrotic as a result of this which is often seen as encephalocele. This encephalocele or the herniated brain tissue in 1 hand closes the communication between IC space and ethmoid/frontal sinus, however, more importantly can prevent natural healing of damaged dural layer thereby creating a permanent fistula between IC cavity and external environment. This communication between IC and extracranial environment can open up with sudden changes in the pressure gradient (e.g., during coughing, sneezing, or straining) disrupting the healing wound site leading to delayed or, recurrence of previous spontaneous closure of CSF leakage [15]. Talamonti et al. [15] further proposed the “growing fracture” phenomenon for delayed complications of BSF. Although this phenomenon is mainly seen in children, according to the authors, the herniated brain or encephalocele not only shape or cover the osteomeningeal defect but may possibly enlarge it leading to fistulous communication between IC space and external environment. Furthermore, there has been reported of intradiploic leptomeningeal cysts following head trauma which may enlarge the skull fracture with CSF leakage in the intradiploic space creating permanent dehiscence or fistulous tract for delayed complications.

CSF rhinorrhea/otorrhea is not always easy to diagnose as it might be blood tinged and not always clear. “Halo sign” or “ring sign” or “target” sign have been mentioned to be useful for determining presence of CSF [28]. As halo sign test is not always specific, CSF can be distinguished from local nasal secretions more accurately by the presence of beta-trace protein (which is found in high concentrations in CSF) [29] or beta-2 transferrin (found only in CSF, perilymph, and aqueous humor) [30]. As these laboratory tests could be limited in clinical settings, CT cisternography could also be performed if there is high degree of suspicion. In a retrospective study of acute recurrent traumatic bacterial meningitis, 11 out of 15 patients with PTM who underwent CT cisternography were found to have CSF leakage [8]. Brain imaging can provide clue about traumatic injury to brain as was seen in our patient with findings of old blood products and gliotic changes in the frontal lobe (Fig. 1).

Management of PTM

The dimensions of management include empiric antimicrobial management in a suspected case of PTM, whether there is any role of prophylactic antimicrobial therapy in BOS fracture without any evidence of meningitis, management of traumatic CSF leakage, vaccination, etc. An approach to the management of PTM is presented in Table 1.

Conclusion

The above case report and review focus on the salient features of PTM necessary from an internist’s perspective. History of trivial or remote closed-head injury can be easily overlooked in a case of CAM. Hence, the role of an internist is to have thorough clinical assessment with a very low threshold of suspicion for diagnosing community-acquired PTM. BOS imaging

Table 1. An approach to the management of PTM

Empiric antimicrobial management in suspected PTM	<ol style="list-style-type: none"> 2004 IDSA practice guidelines [31] for bacterial meningitis management (secondary to head trauma) <ul style="list-style-type: none"> Secondary to BSF: vancomycin plus a third-generation cephalosporin Secondary to penetrating head trauma: vancomycin plus an antipseudomonal beta-lactam* 2017 IDSA practice guidelines [25] for healthcare-associated meningitis management (including meningitis following head trauma): Vancomycin plus an antipseudomonal beta-lactam
Role of prophylactic antimicrobial management in BSF	Routine antibiotic prophylaxis in isolated BSF should not be used unless there are complications (e.g., CSF leakage) predisposing to bacterial meningitis. This recommendation is based on current evidence including a meta-analysis which showed no significant differences in the frequency of meningitis, all-cause, and meningitis-related mortality and, need for surgical correction in patients with CSF leakage when compared between antibiotic prophylaxis and control group [24, 32, 33]
Management of traumatic CSF leakage	<ol style="list-style-type: none"> Generally, there is spontaneous closure of CSF leakage in most patients and CSF fistulae persisting for >7 days had a significantly increased risk of developing meningitis [34] For CSF leakage persisting >7 days or recurrent CSF leakage or leakage after spontaneous closure <ul style="list-style-type: none"> Immediate consultation with neurosurgery or otorhinolaryngology for the need for expedited repair of CSF leakage Consultation with infectious disease to determine about necessity of antibiotic management/prophylaxis as current evidence is sparse Surgical repair of CSF leakage indicated where the risk of complicating meningitis is high [15]: <ul style="list-style-type: none"> Post-traumatic fistulae associated with pneumocephalus Severe craniofacial destruction Entrapment of the facial nerve Disruption of the ossicles Acute fistulae which do not stop within 1–2 weeks CSF leakage recurring after resolution Intermittent or delayed CSF fistulae
Vaccination in pneumococcal PTM and those at risk of PTM [35]	<ol style="list-style-type: none"> Previous vaccination with pneumococcal vaccine <ul style="list-style-type: none"> With both PCV13 and PPSV23: revaccinate with PPSV23 every 5–7 years (if PCV13 given recently, delay vaccination until ≥8 weeks have passed) With only PPSV23: vaccinate with PCV13 ≥1 year after PPSV23 followed by revaccination with PPSV23 every 5–7 years With only PCV 13: vaccinate with PPSV23 ≥8 weeks after PCV13 followed by revaccination with PPSV23 every 5–7 years No previous vaccination with pneumococcal vaccine <ul style="list-style-type: none"> Single dose of PCV13 followed by PPSV23 ≥8 weeks Revaccinate with PPSV23 every 5–7 years

BSF, basilar skull fracture; CSF, cerebrospinal fluid; IDSA, Infectious Diseases Society of America; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine; PTM, post-traumatic meningitis.

*Antipseudomonal beta-lactam: cefepime, ceftazidime, or meropenem.

to identify any defect/fracture or CSF cisternography to detect CSF leakage can be helpful diagnostic modality for establishing the pathway of entry for microorganisms. Generally, management of PTM includes initiation of broad-spectrum antibiotics based on epidemiology and type of head trauma (closed vs. open). The antibiotic should be narrowed down later depending upon the final organism retrieved in microbiological assay. The duration of antibiotic

management is generally 10–14 days. Neurosurgical or otorhinolaryngology assessment of surgical repair is required for CSF leakage >7 days duration. Furthermore, pneumococcal PTM or those CSF leakages following head trauma needs to be assessed for pneumococcal vaccination.

Statement of Ethics

Written informed consent was obtained from the patient presented in the manuscript, for publication in this journal.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contribution

S.D. was responsible for design, literature search, and first draft of the manuscript. T.P. was responsible for acquisition of case details, design, and revision of the draft of the manuscript. Ultimately, the final version of the manuscript was approved by S.D. and T.P. before submission to the journal.

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