



Case Report

Protracted course of chemical meningitis following posterior fossa epidermoid cyst excision – A case report

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ABSTRACT

Background: Chemical meningitis, a subtype of aseptic meningitis, as a complication of posterior fossa surgery is not a rare complication. However, the description of a severe protracted course following the surgical resection of an epidermoid cyst has not been described in the current literature. Chemical meningitis is thought to be associated with a hyperreactive inflammatory response, mediated in part by interleukin (IL)-10, IL-1 β , and tumor necrosis factor- α , to the postoperative keratin debris from the spontaneous leakage or surgical release of epidermoid contents into subarachnoid spaces, which ultimately can result in patient symptoms of meningitis and hydrocephalus. Often, this remains mild and the recommended management includes a short course administration of corticosteroids.

Case Description: The authors report such a case in a patient who underwent a redo-resection for a fourth ventricular epidermoid cyst. Postoperatively, the patient returned several times with symptoms of meningitis and hydrocephalus requiring multiple hospitalizations in the ensuing months. The patient required emergent cerebrospinal fluid diversion, further posterior fossa exploration and an extended high-dose corticosteroid treatment regimen.

Conclusion: The authors summarize the current understanding of the biochemical processes involved for the rare presentation of postoperative chemical meningitis.

Keywords: Aseptic meningitis, Chemical meningitis, Epidermoid cyst, Neurosurgery, Posterior fossa

INTRODUCTION

Epidermoid cysts are benign lesions that occur due to a disorder in neural tube closure during development, in which epithelial remnants are trapped inside neural tissue.^[16,20] These tumors are lined with a capsule made of keratinized squamous epithelium and have a central core of keratin, desquamated cells, water, and cholesterol.^[2,16,20] The cysts grow due to a continual process of desquamation of epithelium and account for approximately 0.2–1.8% of all intracranial tumors, making cysts in the posterior fossa relatively rare.^[2,16,20] Complications of posterior fossa surgery can include the manifestation of meningitis, hydrocephalus, cerebrospinal fluid (CSF) leakage, and/or pseudomeningoceles which can indicate any or all the above.^[8,13] Chemical

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meningitis is a form of aseptic meningitis, not caused by a virus, and presents with similar symptoms as infectious meningitis, but is differentiated by a negative spinal fluid Gram stain, negative results of spinal fluid cultures, and failure of antibiotics to improve the patient's condition.^[9,22] Chemical meningitis as a complication of posterior fossa surgery is not a rare complication; however, development of such a severely protracted course following the surgical removal of a posterior fossa epidermoid cyst has not been described.^[10,22] Here, we present a patient case following the resection of a fourth ventricular epidermoid cyst and resultant protracted course of aseptic meningitis that was further complicated by hydrocephalus requiring CSF diversion, a posterior fossa wound revision, a prolonged comatose state, and a need for extended duration of supraphysiologic steroid administration followed by a long course of neurorehabilitation.

Illustrative case

A 33-year-old woman underwent a redo-resection for a fourth ventricular epidermoid cyst which had previously been operated on 4 years prior [Figure 1]. The patient presented 1 week after surgery with scant drainage from the surgical site, superficial dehiscence, and headache. The wound was superficially reapproximated and treated for a superficial wound infection with oral antibiotics. The patient was also treated with a short course of dexamethasone for a presumed chemical meningitis.

One month later, the patient returned with nausea, vomiting, and intermittent fevers of up to 101°F. Computed tomography (CT) of the brain demonstrated the formation of a suboccipital pseudomeningocele. There was no wound dehiscence and following an additional short course steroid taper administration that the patient's headache and nausea improved.

Two weeks later, she once again presented with worsening headache, nausea, but this time with episodes of confusion, fever, and chills. A repeat CT showed development of moderate hydrocephalus and the progressive enlargement of the suboccipital pseudomeningocele [Figure 2]. An magnetic resonance imaging (MRI) brain with contrast was also obtained and demonstrated leptomeningeal enhancement concerning for meningitis [Figure 3]. CSF was obtained from a lumbar puncture which showed a neutrophilic pleocytosis (66%) with elevated protein (458 mg/dL), hypoglycorrhachia (4 mg/dL), and elevated white blood cell count (WBC) (101/mm²), and CSF cultures were negative. Aspiration of the pseudomeningocele was obtained for additional CSF analysis which, similar to the lumbar cistern obtained CSF, demonstrated continued neutrophilic pleocytosis (79%), elevated protein (393 mg/dL), hypoglycorrhachia (21 mg/dL), and elevated

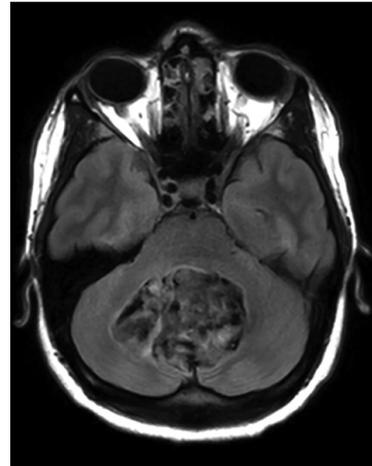


Figure 1: T2 FLAIR Axial MRI – Preoperative image of a fourth ventricular epidermoid cyst.

WBC (528/mm²). CSF cultures were negative. The patient continued to have intermittent fevers without leukocytosis, tachycardia, or worsening of presenting symptoms. Following a course of broad-spectrum antibiotics for the treatment of a possible occult bacterial meningitis, the patient continued to endorse symptoms of hydrocephalus. As a result, with continued clinical symptoms of hydrocephalus and low concern for infectious etiology, the patient underwent the placement of a ventriculoperitoneal shunt (VPS).

Afterward, the patient remained in the hospital and continued to exhibit intermittent fevers. Several days postoperatively, she developed an acute onset right facial droop and double vision. A repeat MRI showed further progression of the leptomeningeal enhancement concerning for worsening meningitis; however, repeat CSF Gram stain and culture remained negative. Over the coming days, the patient's symptoms improved and she was again started on a course of steroids for chemical meningitis and discharged home following a 3-week admission.

Two days later, the patient returned to the emergency department with acute onset symptoms of VPS failure and underwent an emergent revision of the VPS. She quickly improved following shunt revision and was again discharged home when appropriate.

One-month later, the patient returned with a complaint of persistent postoperative pain, and a new area of swelling underlying the prior suboccipital incision for the past 4 days. She also endorsed progressive diplopia, blurry vision, and headaches while bending forward. On physical exam, there was a 1-cm erythematous fluctuant granulomatous nodule without frank discharge or CSF leak. The patient had a deconjugated gaze and inability to abduct the right eye and

bilateral horizontal nystagmus without any additional lower cranial nerve dysfunction. MRI brain with contrast showed increased nodular leptomeningeal enhancement, and the interval development of multiple peripherally enhancing

lesions throughout the brain parenchyma, the largest of which measured 1.4 cm within the left caudate [Figure 4].

The patient was again admitted, and while the CSF profile continued to raise suspicions for an occult infectious process

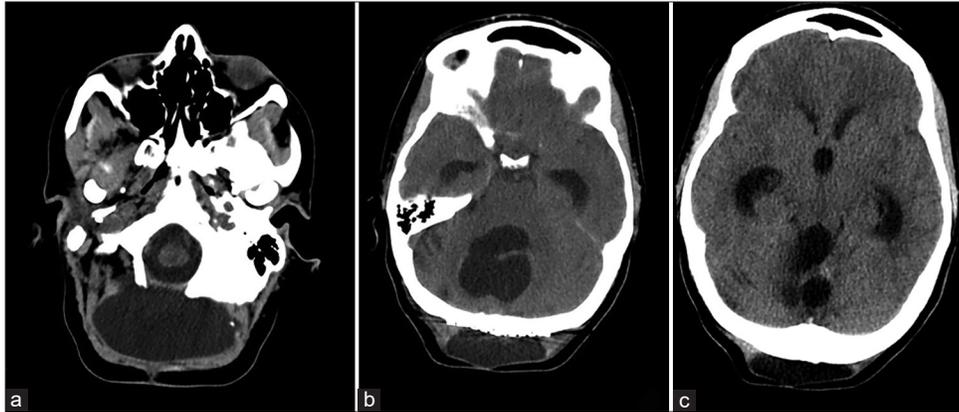


Figure 2: Postoperative computed tomography head 2-months after resection – (a) enlarging pseudomeningocele and (b and c) development of ventriculomegaly.

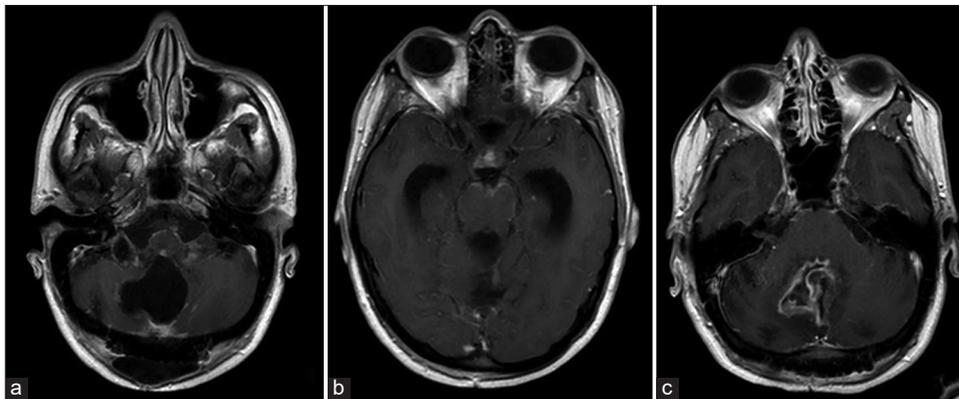


Figure 3: Magnetic resonance imaging brain w/o contrast – (a and b) leptomeningeal enhancement concerning for meningitis and (c) progression of enhancement.

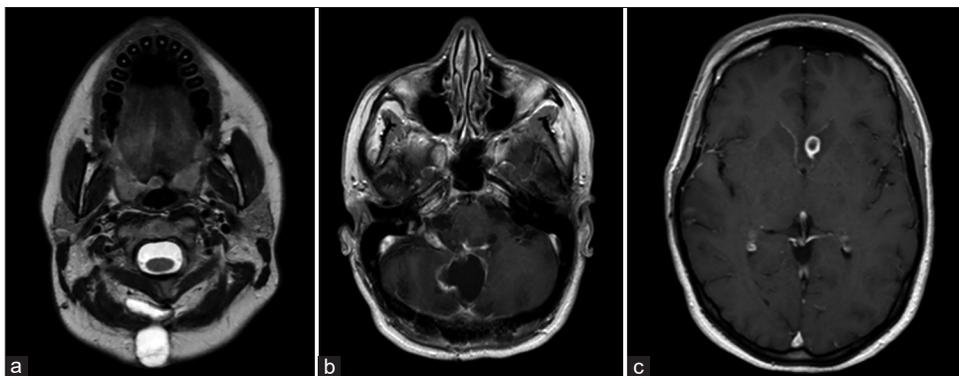


Figure 4: Magnetic resonance imaging (MRI) brain w/o contrast – images obtained at time of most recent admission (a) axial T2 MRI w/o contrast, (b) axial T1 MRI w/contrast, and (c) axial T1 MRI w/contrast. Demonstrate a persistent pseudomeningocele with new parenchymal involvement and progression of leptomeningeal enhancement.

(WBC [101/mm²], lymphocytes [94%], protein [842 mg/dL], glucose [14 mg/mL], and normal neutrophils [3%]) that the Gram stain remained negative.

Several hours into her admission, the patient developed symptoms of acute hydrocephalus, having projectile emesis, and became obtunded. An emergent CT-head was obtained which confirmed acute hydrocephalus, and the patient was transferred to the neurological intensive care unit (ICU), where the VPS was explanted at bedside and a ventriculostomy catheter was soft passed through the prior right frontal burr hole until CSF egress was obtained. Despite the drain placement and adequate CSF drainage overnight, the following morning her clinical status continued to decline necessitating emergent intubation. Afterward, the patient was taken emergently to the operating room for suboccipital craniotomy and posterior fossa exploration.

Intraoperatively, there was no gross purulence encountered. Tissue obtained shows cerebellar parenchyma with epidermoid cyst, chronic inflammation, necrosis, granulation tissue, and foreign body reaction with degenerating keratin debris [Figure 5]. A postoperative MRI brain was obtained which demonstrated worsening vasogenic edema within the posterior fossa and brainstem [Figure 6]. The patient required persistent ICU level care with continued decline into a comatose state.

Ultimately, following multidisciplinary discussions between infectious disease, immunology, rheumatology, and neurology for atypical clinical course, the patient was started on high-dose prednisone (60 mg) for severe chemical meningitis.

The patient's clinical examination slowly improved to the point of being able to follow simple one-step commands. Subsequent CSF analysis began showing improvement in profile (WBC 4/mm², 45% neutrophils, 25% lymphocytes, 88 mg/dL glucose, and 9 mg/dL protein) and the leptomeningeal enhancement was no longer identified on further follow-up imaging. Throughout the remainder of her hospitalization, her mentation continued to improve. The VPS was replaced before her discharge to a neurorehabilitation facility, where she completed a long course of therapy. The patient is now 24 months postoperative from her second resection, with ataxic gait and partial 6th and 7th nerve palsies bilaterally.

DISCUSSION

Aseptic meningitis

Typically following epidermoid resection, resultant postoperative aseptic meningitis is thought to arise from the release of breakdown products, mainly keratin and

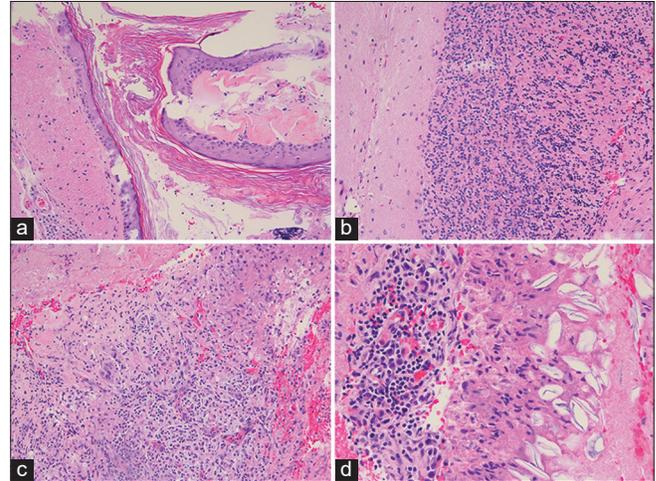


Figure 5: Histopathological findings – (a) cyst lined by squamous epithelium with granular layer containing laminated keratin, consistent with epidermoid cyst. (b) Adjacent relatively uninvolved cerebellar parenchyma. (c) Necrosis with inflammation, granulation tissue, and giant cells. (d) Degenerating keratinocytes with inflammation and histiocytic reaction.

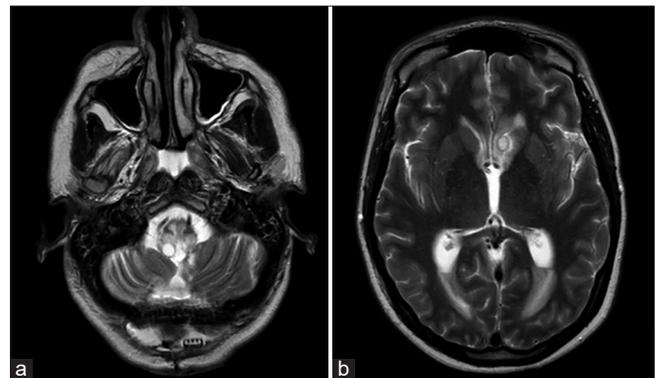


Figure 6: Postoperative magnetic resonance imaging brain axial T2 – (a and b) vasogenic edema throughout posterior fossa and brainstem. Decreased ventricular caliber.

cholesterol, from either the spontaneous leakage or surgical release of epidermoid contents into subarachnoid spaces leading to the inflammatory reaction.^[2,16,19,20] Due to this risk, care must be taken during surgical excision to avoid rupture to prevent leakage of cyst contents with the goal of safe and complete resection without damage to surrounding neurovascular structures.^[16,18,20,23,24] The risk of aseptic meningitis is high and thought to be related to the amount of residual cyst postoperatively.^[20,24]

Characteristic symptoms of aseptic meningitis include headaches, vomiting, fevers, meningismus, and cognitive impairment.^[9,10,22] Diagnostic signs are obtained through lumbar puncture which often demonstrates an elevated CSF white cell count, protein, reduced glucose, negative Gram stain and culture results (diagnosis can be confirmed after three consecutive

negative results), as well as CT and MRI imaging with associated hydrocephalus and meningeal enhancement.^[4,10,19,22] Complications of posterior fossa surgery, other than aseptic meningitis, include a CSF leak, hydrocephalus, and the formation of a pseudomeningocele.^[8,13,20]

Hydrocephalus can often be associated with aseptic meningitis. The occurrence of aseptic meningitis is the result of epidermoid cyst contents entering the subarachnoid space which results in a cascade of inflammatory changes.^[3,11,19,24] These inflammatory changes can contribute to decreased CSF absorption. In addition, the occurrence of hydrocephalus as a surgical complication is commonly seen in 10–30% of patients undergoing posterior fossa surgery. It is often associated with either a CSF infection and/or a CSF leak occurring more frequently in patients with larger tumors and in those with a prior history of cranial surgery.^[8] Furthermore, the presence of a postoperative pseudomeningocele may be a sign of early hydrocephalus.^[12-14,17]

The treatment for patients with aseptic meningitis, with or without hydrocephalus, involves the initial use of antibiotic therapy until infectious meningitis etiologies are ruled out, at which point they should be discontinued and systemic steroid treatment initiated, along with CSF diversion if clinical signs and symptoms of hydrocephalus are present.^[22] One case, similar to the above-described report, highlights a patient who was diagnosed with chemical meningitis and underwent treatment with 40mg of intramuscular prednisolone for 5 days and then slowly tapered over the course of next 10 weeks.^[5]

Inflammatory mediators

The specific biochemical inflammatory cascade driven by the breakdown products such as keratin in epidermoid cysts that result in aseptic meningitis has not been thoroughly investigated. However, a study by Cuff *et al.* found interleukin-6 (IL-6) to be elevated in patients with either an infectious or noninfectious cause of meningitis and lower levels of IL-17 in noninfectious meningitis patients.^[6] IL-6 has been known to provide a variety of central nervous system (CNS) functions including neuroprotection and pathological inflammatory responses.^[21] A study performed on pediatric patients found that in aseptic meningitis, the pro-inflammatory cytokines, IL-1 β and tumor necrosis factor (TNF)- α , as well as the anti-inflammatory IL-10 are all upregulated. However, high initial levels of IL-10, which marks inhibition of both innate and T-cell dependent immune responses, was noted to decline over time, thus, prolonging the disease course and recovery.^[15] TNF- α is itself a pro-inflammatory cytokine with important CNS functions that initiate a major cascade of other inflammatory cytokines, including IL-6.^[21] This mechanism functions by causing the phosphorylation of nuclear factor kappa B which enters

the cell nucleus and induces the transcription of responsive genes including the pro-inflammatory cytokines IL-6 and more TNF- α .^[21]

Steroids are known to be responsible for the alteration of inflammatory gene transcription. In animal models, it has been shown that dexamethasone reduces concentrations of IL-1 β and TNF- α , especially in bacterial meningitis.^[7] Steroids have also been demonstrated to activate gene expression of IL-10, which function as an anti-inflammatory cytokine.^[1] Supratherapeutic steroid administration was paramount to the recovery in the above-presented case and we suspect its effects specifically in decreasing TNF- α and prolonging IL-10 contributed to the patient's recovery. However, further investigation into the optimal steroid dosing, duration, versus need for empiric treatment or prophylactic use is needed to better identify difficult/protracted episodes of aseptic and chemical meningitis to provide better diagnosis and treatment regimens for this rare presentation of postoperative aseptic meningitis.

CONCLUSION

To the author's knowledge, this is the first reported case of such a protracted course of aseptic meningitis requiring a lengthy critical care period in the months following the resection of a posterior fossa epidermoid cyst. While aseptic meningitis following resection of epidermoid cysts is not a rare phenomenon, the clinical course and severity of the inflammatory reaction in this patient is quite unique. The patient's clinical course was presumed to be associated with the above-described hyperreactive inflammatory response to residual postoperative keratin debris that resulted in this delayed episode of acute hydrocephalus and severe inflammatory changes throughout the brain. No infectious etiology was ever identified during the patient's extensive clinical course. The authors report the above-illustrated case in the hopes of increasing the neurosurgeon's awareness to the possibility of this rare but severe presentation as there are currently no criteria to identify those patients at risk. Today, the patient lives independently.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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