Recurrence meningitis associated with frontal sinus tuber encephalocele in a patient with tuberous sclerosis

Case report

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Tuberous sclerosis complex (TSC) is a genetic neurocutaneous disorder that commonly affects the CNS. The most commonly associated brain tumors include cortical tubers, subependymal nodules, and subependymal giant cell astrocytomas (SEGAs). The authors report an unusual case of recurrent meningitis due to a tuber-containing encephalocele via the posterior wall of the frontal sinus.

An 11-year-old girl presented with a history of TSC and previous SEG A resection via interhemispheric approach. She presented twice within 4 months with classic bacterial meningitis. Cerebrospinal fluid cultures revealed Streptococcus pneumoniae. Computed tomography and MR imaging of the brain showed a right frontal sinus encephalocele via a posterior frontal sinus wall defect. Both episodes of meningitis were treated successfully with standard regimens of intravenous antibiotics. The neurosurgical service was consulted to discuss surgical options.

Via a bicoronal incision, a right basal frontal craniotomy was performed. A large frontal encephalocele was encountered in the frontal sinus. The encephalocele was herniating through a bony defect of the posterior sinus wall. The encephalocele was ligated and resected followed by removing frontal sinus mucosa and complete cranialization of frontal sinus. Repair of the sinus floor was conducted with fat and pericranial grafts followed by CSF diversion via lumbar drain. Histopathology of the resected encephalocele showed a TSC tuber covered with respiratory (frontal sinus) mucosa. Tuber cells were diffusely positive for GFAP. The patient underwent follow-up for 2 years without evidence of recurrent meningitis or CSF rhinorrhea.

This report demonstrates that frontal tubers of TSC can protrude into the frontal sinus as acquired encephaloceles and present with recurrent meningitis. To the authors’ knowledge, recurrent meningitis is not known to coincide with TSC. Careful clinical and radiographic follow-up for frontal tubers in patients with TSC is recommended.

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Tuberous sclerosis complex is a neurocutaneous disorder affecting multiple organ systems, including the CNS, heart, kidneys, and skin. Although TSC is transmitted in an autosomal dominant fashion, two-thirds of cases are sporadic, resulting from spontaneous mutations or mosaicism. Two major disease-causing genes have been identified, TSC1 and TSC2, which code for their respective gene products, hamartin and tuberin.

Clinical criteria, usually described as the Vogt triad, are used for the diagnosis of TSC. The triad includes seizures, mental retardation, and facial angiofibromas. However, this triad is seen in fewer than 50% of patients with TSC, and the current diagnosis of TSC requires the presence of major and minor clinical features agreed on at the Tuberous Sclerosis Complex Consensus Conference in 1998. These include ash leaf spots, facial angiofibromas in a malar pattern, retinal hamartomas, cardiac rhabdomyoma, and renal angiomylipoma. The CNS is affected by cortical heterotopias and cortical tubers, subependymal nodules or “candle guttering,” and SEGAs. Approximately 90% of patients with TSC suffer from seizures, and epilepsy is the leading cause of morbidity.

Despite modern antibiotics, bacterial meningitis is still associated with high rates of morbidity and mortality. The mortality rate ranges from 10% to 25% in infants, 3% to 7% in small children, and 10% to 25% in adults. Even if the meningitis is not fatal, sequelae such as epilepsy, cranial nerve palsies, and hydrocephalus may occur.

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skull base defects or spinal dural defects, gains entrance into the CNS and should be taken into consideration when children face recurrent bacterial meningitis. However, symptoms and signs of CSF rhinorrhea or otorrhea are rare in such patients.13

A literature search was conducted and did not reveal any prior cases of reported encephaloceles in children with TSC. We report a rare case of TSC presenting with recurrent meningitis due to tuber-containing encephalocele in the frontal sinus.

**Case Report**

**History and Examination.** This 11-year-old girl with a known history of TSC, seizure disorder, and previous SEGA tumor resection via interhemispheric transcallosal approach, presented to the emergency department with a 1-week history of intermittent fever, neck pain, headaches, and more frequent complex partial seizures. She had presented with *Streptococcus pneumoniae* meningitis 4 months earlier that was successfully treated by intravenous ceftriaxone. There was no history of CSF rhinorrhea. According to immunization records, the child had not received the pneumococcal conjugate vaccine as an infant.

At the current presentation, laboratory workup revealed leukocytosis. Lumbar puncture confirmed bacterial meningitis. The CSF culture was again consistent with *S. pneumoniae*. The patient was admitted to the hospital and received intravenous antibiotics. Because of the recurrent nature of her bacterial meningitis, CT scanning followed by MR imaging of the brain and entire spine were performed. The MR images showed stable subependymal nodules and cortical tubers with no evidence of SEGA tumor recurrence. There was a right frontal sinus encephalocele, measuring $0.9 \times 1.2 \times 1.3$ cm, via a posterior sinus wall defect (1 cm) (Figs. 1 and 2). The neurosurgical service was consulted to discuss surgical options.

A careful inspection of all previous CT and MR images did not show the sinus wall defect or the encephalocele, except for the most recent MR imaging study obtained prior to the first meningitis episode that showed an early development of small encephalocele via a small frontal sinus wall defect. The extension of a previous frontal craniotomy used for the interhemispheric transcallosal resection of SEGA was not adjacent to or violated the frontal sinus.

**Operation.** After successful treatment of the acute bacterial meningitis episode, the patient was taken to the operating room for a planned resection of the encephalocele and cranialization of frontal sinus. Via a bicoronal incision, a right basal frontal craniotomy was performed. A frontal encephalocele, measuring $0.9 \times 1.2 \times 1.3$ cm, was encountered in the right frontal sinus. The encephalocele was herniating through a bony defect of the posterior sinus wall. Intraoperatively, the dural coverage of the encephalocele was ulcerated anteriorly and inferiorly. The content of the encephalocele was firm and calcified. The encephalocele was ligated and resected followed by surgical stripping of frontal sinus mucosa and complete cranialization of frontal sinus. Repair of the sinus floor was performed using abdominal fat and pericranial grafts followed by CSF diversion via a lumbar drain.

**Postoperative Course.** The patient recovered well without any new neurological deficits. Cerebrospinal fluid was drained from a lumbar drain.
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diversion via a lumbar drain was continued for 3 days. No postoperative CSF rhinorrhea was noted. The patient returned for follow-up at 3, 12, and 24 months postoperatively. Follow-up MR and CT imaging revealed complete cranialization of the right frontal sinus with no new abnormalities. Pneumococcal vaccine polyvalent (Pneumovax 23, Merck & Co., Inc.) was administered after the surgical procedure. No episodes of recurrent meningitis occurred during the 2-year follow-up period.

**Histological Examination.** Examination of the encephalocele showed clusters of large astrocytes displaying eosinophilic cytoplasm with foci of calcifications consistent with a tuber of TSC. Large (cytomegalic) neurons were seen. No atypia or pleomorphism was noted. Mitosis and tumor necrosis were not seen. The entire lesion was covered with respiratory-type epithelium corresponding to the frontal sinus mucosa. Tuber cells were diffusely positive for GFAP and S100 protein. Multiple foci of hemosiderin-laden macrophages and calcifications were noted (Figs. 3 and 4). The histopathological findings are different from the gliosis expected in chronically strangulated encephaloceles due to the presence of large (cytomegalic) neurons.

**Discussion**

Anterior encephalocele is a rare condition, and only a few large series have been published in the literature. The incidence is highest in Southeast Asia. Frontoethmoidal encephaloceles are the most common type, followed by the nasopharyngeal and orbital types. Among the frontoethmoidal encephaloceles, nasoethmoid is the most common type, and patients with this type present with swelling over the bridge of the nose with significant hypertelorism and orbital deformities. The nasopharyngeal type remains occult and presents with nasal obstruction or CSF rhinorrhea. Rarely, the patient may present with meningitis. Recurrence of bacterial meningitis is not only potentially life-threatening, but also involves or induces psycho-

![Fig. 3. Representative photomicrograph displaying frontal sinus respiratory-type mucosa covering clusters of astrocytes (tuber). H & E, original magnification ×200.](image)

![Fig. 4. Photomicrograph showing diffuse positivity of the tuber for GFAP. Original magnification ×200.](image)

logical trauma in patients through repeated hospitalization and multiple invasive investigations if the underlying cause remains undetected. Bacterial migration, along congenital or acquired skull base defects or spinal dural defects, gains entrance into the CNS and should be taken into consideration when children face recurrent bacterial meningitis. However, symptoms and signs of CSF rhinorrhea or otorrhea are rare in such patients. Recurrent meningitis is a rare event and should always prompt a thorough search for an underlying cause of the infection. Several case reports have demonstrated nasal meningoencephaloceles as a possible, though rare, cause of recurrent meningitis. Two main forms have been described: congenital malformation and posttraumatic meningoencephalocele. Diagnosis can be complicated by the fact that meningitis might occur long after the underlying trauma or even without a history of trauma in cases of congenital malformation. Elaborate imaging is needed because routine axial CT scanning might not detect the encephalocele and the nasal or sinus mass might be misdiagnosed as severe sinusitis, leading to wrong and potentially disastrous surgical therapy. Magnetic resonance imaging allows detection of the composition of the encephalocele and thereby facilitates planning of the operative treatment. Besides the regular treatment using antibiotics, surgical repair of the defect is needed in these patients to prevent further episodes of meningitis. With correct diagnosis and early treatment, the prognosis in these patients is usually good.

To our knowledge, recurrent meningitis is not known to coincide with TSC. Although the radiographic evidence suggested a right frontal sinus encephalocele herniating via a posterior sinus wall, we had a very low suspicion of a tuber-containing encephalocele. We believe that this is an acquired form of encephalocele because we were unable to visualize the sinus wall defect or the encephalocele on previous radiographic images, except for the most recent MR imaging prior to the first meningitis episode, which showed early development of a small encephalocele via a small frontal sinus wall defect.

We hypothesize that the inhomogeneous nature of the pulsatile frontal lobe and the physical (firm and calcified)
consistency of the frontal tuber may have promoted a focal erosion of the thin posterior sinus wall. This is a unique case of recurrent meningitis in a patient with TSC due to an acquired tuber-containing encephalocele. Whether the presence of a firm and calcified tuber just posterior to the thin posterior sinus wall promoted the development of this acquired encephalocele is difficult to determine.

Reconstruction of the anterior skull base following extensive trauma or tumor resection is challenging and controversial. Dural and sinus wall defects are usually covered with different autograft, allograft, or synthetic materials. Free bone graft or allograft reconstruction of anterior skull defects exposed to the sinonasal or pharyngeal cavity is vulnerable to infection or necrosis. Therefore, covering the grafts with vascularized tissue, such as pedicled pericranium or harvested fat, should reduce these complications.9,14

The management of nontraumatic spontaneous or iatrogenic CSF leaks, meningoceles, and meningoencephaloceles has an extensive history characterized by a collection of surgical approaches and different graft materials used to repair the skull base defects. Surgical repair of encephaloceles is recommended to prevent recurrent meningitis, intracranial abscess, and pneumocephalus. Encephaloceles and CSF leaks could be managed via a craniotomy with a good successful closure rate. Advantages of the transcranial approach include direct visualization of the dural or skull base defect, the ability to address associated brain injury, and the potential to use a large vascularized pericranial flap. Some studies have reported up to a 40% recurrence rate with this approach as well as potential morbidity including anosmia, frontal lobe retraction, seizures, memory deficits, and intracranial hemorrhage. In attempt to avoid these complications and improve closure rates, the endonasal endoscopic approach has evolved to address CSF leaks and some encephaloceles of the anterior skull base. This involves pathologies along the cribiform plate, fovea ethmoidalis, sphenoid bone, and temporal bone. The endoscope can provide excellent visualization. Outcome studies have demonstrated decreased morbidity and improved closure rates. Nevertheless, many neurosurgeons still continue to close CSF leaks of the anterior skull base encephaloceles via a craniotomy.3,15 We used the open craniotherapy approach in this case because of the complicated clinical history including recurrent meningitis in a patient with TSC and previous craniotomy for SEGA resection. We believe that harvesting a large vascularized pedicle of the pericranium is crucial for reconstruction of the anterior skull base in selected cases.

Conclusions

This report demonstrates that TSC frontal tubers can protrude into the frontal sinus as acquired encephaloceles and present with recurrent meningitis. To our knowledge, recurrent meningitis is not known to coincide with TSC. We conclude that patients with TSC who present with signs and symptoms of meningitis should be carefully assessed. We also recommend careful clinical and radiographic follow-up for frontal tubers in patients with TSC.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Elbabaa. Acquisition of data: Elbabaa, Riggs. Analysis and interpretation of data: Saad. Drafting the article: Elbabaa. Administrative/technical/material support: Riggs, Saad. Study supervision: Elbabaa.

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