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Endoscopic endonasal approaches for reconstruction of traumatic anterior skull base fractures and associated cerebrospinal fistulas: patient series

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BACKGROUND Post-traumatic cerebrospinal fluid (CSF) leaks of the anterior skull base may arise after traumatic brain injury (TBI). Onset of CSF rhinorrhea may be delayed after TBI and without prompt treatment may result in debilitating consequences. Operative repair of CSF leaks caused by anterior skull base fractures may be performed via open craniotomy or endoscopic endonasal approaches (EEAs). The authors' objective was to review their institutional experience after EEA for repair of TBI-related anterior skull base defects and CSF leaks.

OBSERVATIONS A retrospective review of prospectively collected data from a major level 1 trauma center was performed to identify patients with TBI who developed CSF rhinorrhea. Persistent or refractory post-traumatic CSF leaks and anterior skull base defects were repaired via EEA in four patients. Intrathecal fluorescein was administered before EEA in three patients (75%) to help aid identification of the fistula site(s). CSF leaks were eventually repaired in all patients, though one reoperation was required. During a mean follow-up of 8.75 months, there were no instances of recurrent CSF leakage.

LESSONS Refractory, traumatic CSF leaks may be effectively repaired via EEA using a multilayer approach and nasoseptal flap reconstruction, thereby potentially obviating the need for additional craniotomy in the post-TBI setting.

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KEYWORDS cerebrospinal fluid leak; trauma; transsphenoidal surgery; anterior skull base fracture

Post-traumatic cerebrospinal fluid (CSF) leaks may develop after 12%–30% of all closed traumatic brain injuries (TBIs) with associated skull base fractures.[1] Half of post-traumatic CSF leaks become evident within 48 hours of injury, and 95% of reported cases occur within 3 months after TBI.[2] Without timely repair, CSF leaks may result in meningitis, which is associated with high morbidity and up to 10% mortality.[3] Alongside meningitis, untreated post-traumatic CSF leaks can present with symptomatic pneumocephalus in up to 20% of cases.[2] Once diagnosed, repair methods include any combination of direct surgical repair of the skull base defect and/or temporary or permanent CSF diversion. CSF diversion via lumbar drainage or some form of ventricular shunting has an estimated success rate of 53%.[4] Refractory cases of CSF leakage, meningitis, or pneumocephalus often require direct surgical repair, which can be performed via craniotomy (often with pericranial flap repair), which has been reported extensively.[5–7]

Despite the increasing use of endoscopic endonasal approaches (EEAs) and reported outcomes for spontaneous or iatrogenic CSF fistulae, there remains a paucity of data describing indications, surgical technique, and outcomes for post-traumatic anterior skull base defects with associated CSF fistulae.[8] We aimed to review our institutional experience at a high-volume level 1 trauma center with EEA for surgical repair of anterior skull base defects resulting in CSF leakage, as well as to review the relevant existing literature comparing endoscopic and open craniotomy repair techniques for repair of post-traumatic anterior skull base defects and related CSF leaks.

Study Description

Patient Population

A retrospective review of a prospectively collected institutional database was conducted to identify patients with a history of TBI

ABBREVIATIONS CSF = cerebrospinal fluid; CT = computed tomography; EEA = endoscopic endonasal approach; ICP = intracranial pressure; TBI = traumatic brain injury.

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with associated CSF leaks of the anterior skull base who underwent EEAs for repair between 2012 and 2019. Patients with spontaneous or iatrogenic CSF leaks were excluded, and patients with resolution of CSF leaks not requiring surgical intervention were excluded. All operations were performed by the senior author team (B.W. and G.Z.). All operations were performed at Los Angeles County + University of Southern California Medical Center, our high-acuity level 1 trauma center, as well as Keck Hospital. Inclusion criteria were patients aged 18 years or older, confirmed diagnosis of CSF leak, prior TBI, and available clinical follow-up to assess the effectiveness of the repair technique.

Data Analyzed

Clinical data analyzed included patient demographics, clinical presentation, prior surgical details relating to TBI, neurological status, and neuroimaging data. Surgical data included procedure performed, noted site of intraoperative CSF leakage, use of fluorescein, use of CSF diversion, and use of a pedicled flap. Postsurgical data included surgical complications, need for reoperation, CSF leak persistence, and follow-up duration and outcomes.

Operative Technique

All patients underwent EEA using a four-handed binostril approach performed by the neurosurgery and otolaryngology teams. In cases with subtle skull base defects on preoperative imaging, a lumbar drain was placed preoperatively for both temporary CSF drainage and intrathecal fluorescein administration to aid in fistula site identification. Fluorescein (0.1 mL) was diluted with 10 mL of sterile saline and administered in the lumbar drain at 1 mL per minute immediately after intubation in the operating room. Fluorescein was visible in all cases in which it was used. Fluorescein was not used in one case, because it was not required for localization of the defect. For CSF leak repair in all patients, a multilayer repair using a combination of fascia lata autograft and/or a pedicled flap was used as previously described.[9] In general, our repair technique involved a two-layer fascia lata apposition method for dural reconstruction (dural inlay followed by dural overlay/bony inlay), and autologous fat grafting was reserved for regions of anatomical dead space. The repair is then bolstered with a nasoseptal flap. The flap is raised with an initial superior incision along the roof of the nose carrying anteriorly to the middle turbinate, down to the level of the sphenoid sinus, and inferiorly to the choana and along the floor of the nose. The flap is then raised with a spatulated instrument, being careful to maintain the pedicle's vascular supply, and pivoted to provide broad coverage of the comminuted bony skull base fracture. The edges of the flap are secured to the skull base with a fibrin glue sealant and Surgicel. The flap is finally bolstered against the skull base with a combination of Gelfoam and Nasopore.[9]

Statistical Analysis

Results are expressed as mean values and standard deviations for continuous variables. Findings for categorical variables are presented as frequencies (number of responses) and percentage distribution.[10]

Results

Clinical Demographics and Presentation

Analysis identified four patients meeting inclusion criteria. Two patients were identified at our level 1 trauma center, and the remaining two were transferred to and treated at our university hospital. Half of the patients were males (n = 2; 50%), and the mean age at surgery was 31.5 ± 19.1 years. Two patients developed CSF rhinorrhea resulting from TBI without prior craniotomy. Prior TBI episodes included remote TBI (n = 2; 50%), motor vehicle accident (n = 1; 25%), and fall from a height (n = 1; 25%). Two (50%) patients underwent prior craniotomy for TBI for the following indications: frontal sinus cranialization (n = 2; 50%) and repair of post-traumatic mucocele (n = 1; 25%). None of the fractures or CSF leaks were caused by the prior craniotomy. Time from TBI to diagnosis of CSF leak was a mean of 4 weeks. Two patients had a remote history of TBI decades before the onset of CSF leak, thought to be related to the delayed onset of rhinorrhea.

Preoperative symptoms included CSF rhinorrhea (n = 4; 100%), and meningitic symptoms (n = 2; 50%). Three patients (75%) did not have neurological deficits at the time of presentation with post-traumatic CSF leakage. Prior inciting trauma led to cranial nerve deficits in one patient (25%).

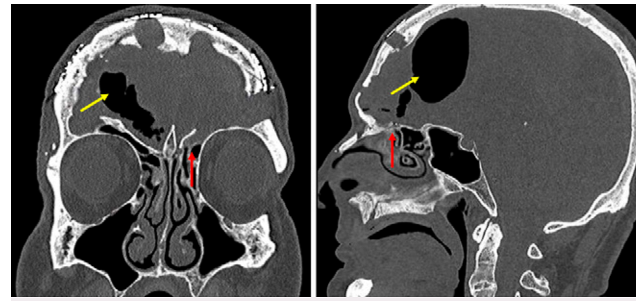

FIG. 1. Case 1. **Left:** Preoperative coronal CT with pneumocephalus (*yellow arrow*) and right frontal sinus fracture (*red arrow*). **Right:** Preoperative sagittal CT with arrows pointing to the same respective defects.

Neuroimaging Characteristics

Neuroimaging included computed tomography (CT) for all cases to characterize and localize potential skull base defects. Magnetic resonance imaging was also available in two (50%) patients. CT confirmed complex, often comminuted fracture patterns of the frontal sinuses (n = 3; 75%), ethmoid (n = 2; 50%), and/or planum sphenoidale (n = 1; 25%). Pneumocephalus was noted in two patients (50%). Concurrent mucocele (n = 1; 25%) and pneumatocele (n = 1; 25%) were also noted. Preoperative neuroimaging is presented in Figs. 1–3.

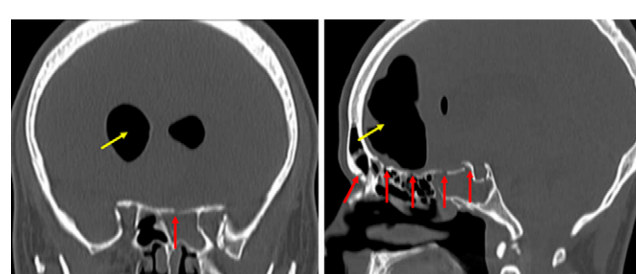

FIG. 2. Case 2. **Left:** Preoperative coronal CT with pneumocephalus (*yellow arrow*) and multiple fractures (*red arrow*). **Right:** Preoperative sagittal CT with pneumocephalus (*yellow arrow*) as well as orbital, ethmoid, and sphenoid fractures (*red arrows*).

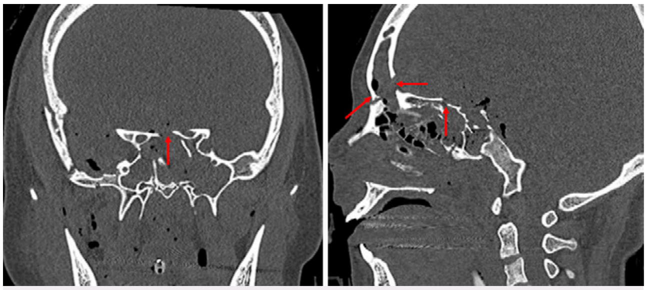

FIG. 3. Case 4. **Left:** Preoperative coronal CT with multiple fractures (*red arrow*). **Right:** Preoperative sagittal CT with frontal sinus and planum sphenoidale fractures (*red arrows*).

Surgical Data

EEAs for repair of CSF leaks were performed on all four patients. Intraoperative CSF leaks were directly observed in all patients, and intrathecal fluorescein was administered to aid with identification of the fistula site(s) in three patients (75%). A lumbar drain was placed preoperatively in all patients (100%). CSF was then drained at 10 mL per hour for three postoperative days, followed by a clamp trial to assess if the leak remained. All patients underwent surgical repair using a multilayer fascia lata apposition technique and pedicled nasoseptal flap coverage (100%).

Surgical Outcomes

CSF leaks were eventually repaired in all four patients; however, reoperation was required in one patient, who presented with delayed tension pneumocephalus related to a frontal sinus fracture unsuccessfully repaired by prior frontal sinus cranialization with a pericranial flap. The mean follow-up for all patients was 8.8 months ± 6.2 months. Brief summaries of the four clinical cases are provided in Table 1.

Complications

The overall surgical complication rate was low. As discussed, tension pneumocephalus developed after EEA repair in one patient (25%), resulting from a frontal sinus fracture from the original TBI, and required repair via open frontal sinus cranialization and a pericranial flap. No patients developed postoperative meningitis or new neurological deficits.

Discussion

Observations

TBI constitutes a leading cause of morbidity and mortality in people under 45 years of age.[11] Of all TBIs, 6%–12% include skull fractures, with 20% of skull fractures involving the skull base.[2] Post-traumatic CSF leakage develops in 12%–30% of patients with skull base fractures.[5,12] The natural history of TBI-related skull base defects and CSF leakage is somewhat favorable overall in the context of TBI, with a reported rate of spontaneous cessation of post-traumatic

TABLE 1. Summary of 4 patients who presented with post-traumatic CSF leak and underwent repair via EEA

	Case 1	Case 2	Case 3	Case 4
Age (yrs)	60	20	21	25
Sex	Male	Female	Female	Male
Presentation	History of TBI w/ skull base defects & pneumocephalus; subsequent rt frontal pneumatocele formation; mucocele; CSF rhinorrhea; confusion	MVA w/ multiple skull base defects; pneumocephalus; encephalocele; CSF rhinorrhea	TBI at age 4 yrs; delayed mucocele (presenting as rt orbital infection) connecting w/ frontal lobe via skull defect; CSF rhinorrhea 1 mo after craniotomy	S/p suicide attempt, multiple skull fractures; CSF rhinorrhea 1 mo after fall from height
Time from trauma to diagnosis of CSF leakage	Decades	4 wks	4 wks	4 weeks
Neurological exam	Intact	Intact	Intact	Rt CN VI, VII palsy
Site of fracture	Rt frontal sinus	Lt/rt sphenoid, lt/rt ethmoid, rt orbit	Lt/rt frontal sinus	Lt orbital roof; lt frontal sinus; cribriform plate; rt orbit
Prior craniotomy?	Yes, 1 mo prior, bifrontal craniotomy for mucocele, frontal sinus cranialization w/ pericranial flap	No	Yes, 1 mo prior; frontal craniotomy for mucocele, sinus cranialization w/ pericranial flap	No
CSF diversion?	Lumbar drain	Lumbar drain	Lumbar drain	Lumbar drain
Fluorescein?	No	Yes	Yes	Yes
Pedicled flap?	Yes, bilateral	Yes	Yes	Yes
Complications	None	Tension pneumocephalus	None	None
Reoperation?	No	Yes, for tension pneumocephalus	No	No
Follow-up	5 mos, no further leak	6 mos, no further leak	6 mos, no further leak	18 mos, no further leak

CN = cranial nerve; MVA = motor vehicle accident; S/p = status post.

CSF leaks of 80%–95%.[12] In cases where intervention is required, the options for management of CSF leakage include direct repair via craniotomy or EEA, with or without CSF diversion.

Conservative therapy for traumatic CSF leaks often involves bed rest, head elevation, and avoidance of exertional activities that increase intracranial pressure (ICP), such as coughing, retching, and Valsalva maneuvers.[2,5] CSF diversion is often indicated in cases of elevated ICP, hydrocephalus, persistent or refractory CSF leakage after initial conservative management, or transiently in cases of operative prophylaxis. CSF diversion via a ventricular or lumbar drain can be used to lower ICP.[2] When conservative management fails, surgical intervention is indicated.[2,5] Surgical intervention includes open craniotomy and endoscopic approaches and was first reported by Dandy in 1926 for a cranionasal fistula repaired by a frontal craniotomy.[10,13] Open craniotomy approaches for anterior skull base defects resulting in CSF leaks have reported success rates of 70%–80%.[10,14] This approach, however, may be associated with a variety of untoward complications in the post-TBI setting, including intracerebral hemorrhage, seizures, cerebral edema, frontal lobe deficits, and anosmia.[5]

In recent years, EEA has been reported for a variety of anterior skull base pathologies and repairs; however, a paucity of data for TBI-related defects exists. First performed in 1981 by Wigand et al., the endoscopic approach involves direct access to the anterior skull base via the nasal cavity.[15] Minimally invasive access, avoidance of frontal lobe retraction, accurate localization of the defect (especially using intrathecal fluorescein), preservation of olfaction in many cases, and less overall morbidity are all attractive features of EEA as compared with craniotomy for CSF leak repair.[16,17] The EEA is also associated with lower costs and higher patient satisfaction, although this does not apply to post-TBI patients.[10,17] When compared with traditional intracranial approaches, EEA yields significantly shorter duration of the repair procedure as well as decreased hospital stay, with a median hospital stay of 20 days for the open craniotomy procedure, compared with 5–9 days in EEA patients.[14,18,19] In contrast to the open craniotomy approach, the success rate of EEA has been cited by several studies to be over 90%,[17,18,20,21] and higher recurrence rates of CSF leakage are more likely after open craniotomy than EEA.[5,14]

In some cases, however, open craniotomy is still indicated for primary repair or if EEA fails, as occurred in one patient in our series who developed tension pneumocephalus after EEA. Skull defects that are depressed or are associated with other intracranial pathologies (e.g., hemorrhagic contusion, hematomas) are likely to require open craniotomy.[2,8,19] Finally, defect location is a major factor in determining method of repair; defects involving the frontal sinus are more likely to require operative management via open craniotomy due to the narrow diameter from the anterior to posterior frontal recess as well as difficulty in accessing frontal sinus defects. In contrast, ethmoidal and sphenoid leak sites can typically be managed successfully via EEA.[5,22]

We report the first surgical series focusing solely on surgical repair using EEA for traumatic anterior skull base fractures with refractory CSF fistulae. Most patients had multifocal, often comminuted fractures with refractory CSF leaks and meningitic signs. Intrathecal fluorescein administration was useful in locating the primary or secondary sites of CSF leakage. Successful CSF leak repair was eventually achieved in all cases; however, reoperation was required in one patient for delayed development of pneumocephalus.

Literature Review

A review of prior studies reporting on EEA for post-traumatic CSF leaks is presented in Table 2. Few prior post-traumatic CSF leak series report using EEA to repair fractures of the ethmoidal roof, cribriform plate, and sphenoid sinus.[13,16,23] Similarly, our study reports complex fracture patterns of the frontal sinuses, ethmoid, and/or planum sphenoidale in all cases. Time from TBI to development of CSF leakage was noted to be 6 weeks in one case report[13] and on the order of months by Locatelli et al.[23] Average time from TBI to CSF leak development is not reported by Ibrahim et al.[16] We report time between trauma and CSF leak development to be 4 weeks (one patient had a remote history of TBI decades before CSF leak onset), which aligns with prior literature stating that half of post-traumatic CSF leaks become evident within 2 days of injury, and the majority of reported cases occur within 3 months.

Ibrahim et al.[16] reported pneumocephalus on imaging before leak repair in 20% of post-traumatic CSF leak cases. In contrast, our study reports 50% of cases presenting with pneumocephalus on imaging, along with concurrent mucocele in 50% and encephalocele in 25% of cases. Other preoperative symptoms in our surgical cohort included concurrent meningitic symptoms in 50% and TBI-related cranial nerve deficits in 25%. A notable difference between our cohort and prior studies is the use of CSF diversion methods including lumbar and external ventricular drains. Past studies report very little to no use of CSF diversion methods, whereas in our study a lumbar drain was used in 100% of cases. The risks and benefits of temporary CSF diversion must be weighed carefully because they may provide a benefit in allowing the reconstruction to take place but also increase the potential risk for pneumocephalus, as occurred in one patient in our series.

Overall CSF leak repair success rates were ultimately similar when comparing our study with others: The post-traumatic CSF leak repair case report was successful; Ibrahim et al.[16] reported a 90% success rate, with one case requiring reoperation; and Locatelli et al.[23] reported a 90% success rate with four cases requiring reoperation. Similarly, our study reports an eventual success rate of 100% in repairing CSF rhinorrhea, with one patient requiring reoperation for pneumocephalus.

Lessons

Our findings suggest that EEA is an effective repair strategy for most severe fractures of the anterior skull base presenting with refractory CSF leakage. Use of a judicious pedicled nasoseptal flap to provide broad coverage of and apposition to the bony skull base is an effective strategy to create durable reconstruction in post-traumatic CSF leaks with comminuted anterior skull base fractures. The width of the flap may be extended by harvesting mucosal tissue from the nasal cavity floor and under the inferior turbinate to aid in maximizing coverage for multifocal fractures.

Limitations of the present study include the small retrospective case nature, heterogeneity in TBI types and time periods of presentation, and variety in related procedures. However, the experience derived from a high-volume TBI center in using EEA for refractory and complex anterior skull base defects is novel and worth relating and offers insight into the often challenging management of TBI-associated skull base defects.

Refractory CSF rhinorrhea is a rare complication of TBI that, without timely repair, may result in severe neurological sequelae. EEA with intrathecal fluorescein is a favorable method of repair for complex,

TABLE 2. Literature review of EEA in cases of traumatic anterior skull base fractures with CSF leakage

Authors & Year	No. of Cases	Time From Trauma to Development of CSF Leak	Duration of Rhinorrhea Before Repair	Fracture Location	Imaging	Repair Method	CSF Diversion (Lumbar Drain, EVD, VP Shunt)	Hospital Postoperative Stay	Success Rate?
Komatsu et al., 2011[13]	1	6 wks		Linear fracture of lt anterior ethmoidal roof		Endoscopic endonasal	N/A	5 days	Yes
Ibrahim et al., 2016[16]	10		3 days–1 yr	Cribriform plate, sphenoid sinus	Pneumocephalus on CT (n = 2; 20%)	Endoscopic endonasal multilayer technique	4 (9.5%) (not specific for post-traumatic cases)	Mean 6 days (range: 4–8 days) (not specific for post-traumatic cases)	9, 90% (1 case, post–road traffic accident, required revision op to repair a missed defect)
Locatelli et al., 2006[23]	39	Mos		Cribriform plate, ethmoid, frontal sinus, sphenoid sinus, multiple fractures		Endoscopic endonasal	2 (lumbar drain, not specific for post-traumatic cases); 1 (VP shunt in a post-traumatic case)	3–5 days	35, 90%

EVD = external ventricular drain; VP = ventriculoperitoneal.

often multifocal refractory CSF leaks of the anterior skull base, especially comminuted fractures involving the ethmoidal and sphenoid regions. Compared with more traditional open craniotomy repair methods, EEA may be favorable for a variety of reasons, especially avoidance of brain retraction.[22] Successful repair of post-TBI CSF rhinorrhea and anterior skull base defects may be achieved using EEA.

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Disclosures

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

Conception and design: Sheth, Strickland, Wrobel, Zada. Acquisition of data: Strickland, Chung, Briggs, Weiss, Wrobel. Analysis and interpretation of data: Sheth, Strickland, Chung, Briggs, Zada. Drafting the article: Sheth, Strickland, Chung, Briggs, Zada. Critically revising the article: Sheth, Strickland, Chung, Briggs, Zada. Reviewed submitted version of manuscript: Sheth, Strickland, Zada. Approved the final version of the manuscript on behalf of all authors: Sheth. Administrative/technical/material support: Sheth, Zada. Study supervision: Zada.

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