Spontaneous Cerebrospinal Fluid Leak Repair: A Five-Year Prospective Evaluation

Mohamad R. Chaaban, MD; Elisa Illing, MD; Kristen O. Riley, MD; Bradford A. Woodworth, MD

Objectives/Hypothesis: Mounting evidence indicates the majority of spontaneous cerebrospinal fluid (CSF) leaks are associated with intracranial hypertension. The objectives of the current study were to assess outcomes regarding spontaneous CSF leaks focusing on premorbid factors, surgical technique, and management of intracranial pressure.

Study Design: Prospective cohort.

Methods: Prospective evaluation of patients with spontaneous CSF leaks was performed. Data regarding demographics, nature of presentation, body mass index (BMI), location and size of defect, intracranial pressure, clinical follow-up, and complications were collected.

Results: Over 5 years, 46 patients (average age, 51 years) with 56 spontaneous CSF leaks were treated by a single otolaryngologist. Twenty-one subjects presented with recurrence of their CSF leak following previous endoscopic and/or open approaches by other physicians. Obesity was present in 78% of individuals (average BMI, 35.6). Fifty-two CSF leaks (93%) were successfully repaired at first attempt. With secondary repair, all CSF leaks were closed at last clinical follow-up (average, 93 weeks). Three patients developed late failures (>2 months), with one recurrence at a distinct location from the primary site at 8 months postprocedure (associated with ventriculoperitoneal shunt failure). Opening pressures via lumbar puncture averaged 24.3 ± 8.3 cm H2O, which increased significantly to 32.3 ± 9.0 cm H2O (P < .0001) following closure of the skull base defect(s). Management of intracranial hypertension included acetazolamide (n = 23) or permanent CSF diversion (n = 19, including five revisions of failed preexisting shunts).

Conclusions: Although spontaneous CSF leaks have the highest recurrence rate of any etiology, prospective evaluation demonstrates high success rates with control of intracranial hypertension.

Key Words: Encephalocele, cerebrospinal fluid rhinorrhea, cerebrospinal fluid leak, intracranial hypertension, spontaneous, endoscopic sinus surgery, skull base defect, cerebrospinal fluid leak repair, pseudotumor cerebri, empty sella.

Level of Evidence: 4.

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INTRODUCTION

Cerebrospinal fluid (CSF) leaks are relatively rare, but their sequelae, such as ascending meningitis or brain abscess, are life threatening. A CSF leak develops when there is disruption in the arachnoid and dura mater, coupled with an osseous defect, and an intracranial pressure (ICP) gradient that is continuously or intermittently greater than the tensile strength of the disrupted tissue. An associated herniation of dura and sometimes brain parenchyma (encephalocele) through the defect may be present, but can also exist in the absence of a leak (e.g., congenital). Because the underlying reason for the disruption affects the treatment philosophy, skull base defects are most commonly classified according to etiology (traumatic, spontaneous, congenital, neoplasm).

Spontaneous CSF leaks are associated with sustained increases in ICP and may represent a variant of benign (now called idiopathic) intracranial hypertension (also known as pseudotumor cerebri). Patients with idiopathic intracranial hypertension (IIH) are typically obese (BMI > 30) females who may present with headache, pulsatile tinnitus, and visual disturbances. High-resolution computed tomography (CT) or magnetic resonance imaging (MRI) scans reveal common characteristics of patients with IIH and spontaneous CSF leaks not typically present in CSF leaks of other etiologies. Distinguishing findings on CT include thinning or attenuation of the skull base, demonstration of arachnoid pits in up to 63% of patients, and the presence of multiple defects in up to 31%. MRI may reveal encephaloceles in up to 50% to 100% of patients, empty sella, and dilated optic nerve sheaths. The presence of empty sella on MRI is strongly associated with both increased ICP in IIH as well as spontaneous CSF leaks, with one study demonstrating its reversibility following control of intracranial hypertension. Finally, direct...
evidence of elevated ICP in patients with spontaneous CSF leaks has been documented in numerous studies by obtaining an opening pressure during lumbar tap or through monitoring of lumbar CSF pressure in the postoperative period.\(^{10-14}\) Spontaneous CSF leaks have the highest rate (50% to 100%) of encephalocele formation, and the highest recurrence rate following surgical repair of the leak (25%–87%), compared to <10% for most other etiologies.\(^{2,5,15,16}\)

The objectives of the current study were to prospectively evaluate outcomes regarding spontaneous CSF leaks focusing on premorbid factors, surgical technique, and management of ICP.

**MATERIALS AND METHODS**

**Subjects**

Prospective evaluation and data collection of subjects was approved by the institutional review board at the University of Alabama at Birmingham. All patients treated by a single otolaryngologist (B.A.W.) with CSF leaks of spontaneous etiology were enrolled over a 5-year period. CSF leaks were considered spontaneous when there was no previous history of skull base fracture/truma or tumor. Preoperative evaluation of all patients consisted of a thorough history and physical examination (plus nasal endoscopy), including inquiries about previous history of head trauma, prior sinus or neurological surgery, congenital abnormalities (e.g., midline craniofacial cleft/morning glory syndrome),\(^{17}\) prior episodes of meningitis (or other intracranial event), and obesity with body mass index (BMI) calculation. Radiographic imaging assessment included image-guided surgical navigation CT scans in all cases and MRI scan unless otherwise contraindicated. Data regarding demographics, nature of presentation, radiographic signs (e.g., empty sella), location and size of defect, surgical approach, reconstructive technique, management of ICP, clinical follow-up, and complications were collected.

**Surgical Technique**

The technique for endoscopic management varied depending on the site and size of the defect, presentation, and other factors but generally outlined those previously described.\(^{3,18-22}\) Lumbar drains (LDs) (or ventriculostomies) were used in all patients with spontaneous CSF leaks unless contraindicated and opening ICP assessed with manometry.\(^{11}\) Fluorescein was also utilized according to previously published protocols to localize defects, identify multiple CSF leaks, and inspect for a watertight closure at the conclusion of the case.\(^{15}\) We use a mixture of 0.1 mL of 10% fluorescein diluted in 10 mL of the patient’s CSF slowly injected over 10 to 15 minutes.

Surgical exposure is characterized according to transethmoid technique (sphenethmoidectomy) with additional exposures (e.g., transpterygoid, Draf IIB frontal sinusotomy). The transpterygoid approach is performed as previously described for nearly all lateral sphenoid recess CSF leaks.\(^{13}\)

**LD Management**

Although the use of LDs in CSF leak repair has recently been labeled controversial,\(^{1,14,23,24}\) we utilize drains when we feel the benefits far outweigh the risks. Because spontaneous CSF leaks often have multiple defects, the administration of intrathecal fluorescein is useful for identifying other leaking sites that may not be readily apparent on preoperative imaging. LDs (or ventriculostomies) are managed according to previously described protocols with slight alterations.\(^{11}\) In general, LDs are opened at the time of graft placement, and the height of the collection chamber is adjusted to maintain drainage at approximately 10 mL/hr. The drain is clamped on the morning of postoperative day 2 or 3, and at least 6 hours is allowed to help equilibrate the patient’s CSF volume. A pressure transducer or manometer is connected to the lumber drain with the patient in the lateral decubitus position zeroed at the spinal column. Normal CSF pressure is between 5 and 15 cm H\(_2\)O in this position. If pressure is elevated, oral acetazolamide (500 mg) is administered and read again at 4 to 6 hours to assess the effect of the diuretic. Acetazolamide is a carbonic anhydrase inhibitor diuretic that decreases CSF production.

In patients with significantly elevated ICP (generally >35 cm H\(_2\)O at baseline), multiple defects, or an inadequate response to medical therapy with diuretics (generally <10 cm H\(_2\)O decrease) permanent ventriculoperitoneal (VP) shunting is recommended. Patients are otherwise placed on acetazolamide (or if refused a shunt) and electrolytes are checked periodically to ensure no life-threatening abnormalities.

**Postoperative Management**

Patients are instructed on movement techniques to avoid breath holding and Valsalva maneuvers. An antistaphylococcal antibiotic is prescribed until the packing is removed at the first postoperative visit 9 to 13 days postoperatively. A stool softener is prescribed for every patient and light activity is continued for 6 weeks after surgery. Patients are seen anywhere from 1 to 4 weeks after the first visit.

**RESULTS**

Over 5 years, 46 patients (average age, 51 years) with 56 spontaneous CSF leaks were treated by a single otolaryngologist. Average clinical follow-up was 22 months, with a range of 4 to 49 months. Patient demographics and clinical data are detailed in Table I. The most common major presenting major symptoms encountered by patients were clear rhinorrhea (98%), meningitis (9%), and seizures (7%). The estimated duration of symptoms at presentation averaged 14.3 months (range, 1–120 months). Thirteen patients reported a remote history of meningitis (28%). Twenty-one subjects (46%) presented with recurrence of a CSF leak following previous endoscopic and/or open approaches by other physicians. Factors associated with recurrence included failure to 1) control elevated ICP (n = 21), 2) repair at the level of the defect (n = 10), and 3) recognize the actual site of the defect (n = 4). Empty sella was present in 35/41 patients (85%) with available MRI scans, and 21/46 (46%) had multiple skull base defects present on preoperative CT imaging.

Although 21 subjects had radiographic evidence of multiple skull base defects, only 12 of these patients had multiple sites of active leakage. One patient developed a new site of spontaneous CSF leakage addressed 8 months following his initial repair due to a shunt failure, and 2 other subjects had active leaks in the middle ear (tympanum) that were never addressed surgically. Leak sites separated by a clear boundary (e.g., presence of two encephaloceles from two distinct areas) were counted as separate defects, but some single defects involved two subsites. Thirty-six percent (n = 20) of leak...
sites were located in the posterior table (PT) of the frontal sinus, making it the most common site of defect involvement, followed by the lateral recess of the sphenoid (n = 18), cribriform plate (n = 14), supraorbital ethmoid (n = 5), planum sphenoidale (n = 4), anterior ethmoid (n = 3), posterior ethmoid (n = 2), and optic nerve sheath (n = 1). The mean dimensions were 6.7 mm in length (range, 2–24 mm) by 6.2 mm in width (range, 2–12 mm). Encephaloceles were present in all but two sites (54/56, or 98%) and were usually very large compared to the relative size of the skull base defect (Fig. 1).

An endoscopic transethmoid approach alone was the most common surgical technique in 41 of 56 repairs (75%). For lateral recess of the sphenoid defects, a transpterygoid approach was required in 17/18, with a partial transpterygoid (some displacement of the greater palatine nerve but without sacrifice of the internal maxillary artery) for a patient with a blunted lateral recess and sagittally oriented defect as previously reported.13 For PT defects, a Draf IIB was required for 18/19 frontal sinus openings. The choice of graft and nasoseptal flap to repair defects was diverse, and depended on location and size of the defect and availability of nasoseptal flap blood supply. A bone graft was placed in an epidural fashion in 34 defects in 28 individuals. A nasoseptal flap was harvested for reconstruction in 34 subjects. We used a multilayer technique with use of cadaveric or xenograft materials in underlay and/or overlay fashion in all patients (Table II). A LD was used in 38 of 46 patients, and an external ventricular drain (EVD) was used in four people. Five patients had nonfunctional VP (n = 4) or lumboperitoneal shunts (n = 1) that were placed during or following previous surgical intervention at outside facilities. Opening pressures via lumbar puncture averaged 24.3 ± 8.3 cm H2O, which increased significantly to 32.3 ± 9.0 cm H2O (P <.0001) following closure of the skull base defect(s).

Whereas four subjects developed a CSF leak recurrence at the primary site, one additional patient developed a new fistula from a defect not leaking at the original surgery. This was associated with shunt malfunction and was present at a location distinct from the original site 8 months postprocedure. The original site of the leak was addressed through a transpterygoid approach lateral to the second branch of the trigeminal nerve, and this area was noted to be well sealed and obliterated by both preoperative CT and intraoperative exam. This patient had a large number of nonleaking arachnoid pit defects above both lateral recess of the sphenoid (LRS) locations, but the new leak site was through a pit just medial to the second branch of the trigeminal nerve that was accessed via a transpterygoid approach/sphenoidotomy. Two late (>2 months) primary repair failures were noted. Two of the four individuals with recurrence were intolerant of acetazolamide therapy postoperatively (initially refused shunt), and another had recurrence several days after voluntarily discontinuing the drug. Two of these patients subsequently had VP shunts placed at time of the second repair. Overall management of intracranial hypertension included acetazolamide in 24 subjects (52%), whereas 19 patients (41%) had permanent CSF diversion.

Other complications included a small inconsequential 3-mm intraparenchymal hematoma and respiratory acidosis secondary to severe underlying obstructive sleep apnea requiring a tracheostomy.

**DISCUSSION**

**Premorbid Factors**

The current study indicates that spontaneous CSF leaks are more common in the presence of obesity and female gender and remains consistent with other reports in the literature.12,14 The majority of subjects (78%) qualified as obese (BMI >30), with an overall average

<table>
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<tr>
<th>Table I. Demographic and Clinical Data.</th>
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<td>Age Presenting Symptoms Prior Surgical Attempts</td>
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<td>51.2 years (range, 27–72 years) CSF leak (98%), meningitis (9%), seizures (7%) 21/46 (46%)</td>
</tr>
<tr>
<td>Gender Estimated Duration of CSF Leak Opening ICP</td>
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<td>32 females, 14 males 14.3 months (range, 1–120 months) 24.3 ± 8.3 cm H2O</td>
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<tr>
<td>Race Prior History of Meningitis Postoperative ICP</td>
</tr>
<tr>
<td>24 white, 21 black, 1 Hispanic 13/46 (28%) 32.3 ± 9.0 cm H2O</td>
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<tr>
<td>BMI Empty Sella ICP Management</td>
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<td>35.6 (range, 19.6–52.1) 35/41 (85%) Acetazolamide (n = 23), VP shunt (n = 20)</td>
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<tr>
<td>% Obese (BMI &gt;30) Multiple Skull Base Defects Clinical Follow-up</td>
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<tr>
<td>36/46, 78.3% 21/46 (46%) radiographic, 12/46 (24%) active leaks 22 months (range, 3–49 months)</td>
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BMI = body mass index; CSF = cerebrospinal fluid; ICP = intracranial pressure; VP = ventriculoperitoneal.
BMI of 35.6. Additionally, 70% of patients were female in this evaluation. Like IIH, spontaneous CSF leaks are increasing in incidence in parallel with the current epidemic of obesity in the United States.\textsuperscript{25,26} Overall, this suggests, at least in part, that lifestyle is an important contributor to this phenomenon. Furthermore, the growing pervasiveness of childhood obesity is strongly associated with an increased risk of pediatric IIH in female adolescents and indicates the incidence of spontaneous CSF leaks in the general population will only increase in the future.\textsuperscript{27}

Clinical presentation and radiologic findings of subjects were similar to previously reported data. Major clinical symptoms included CSF rhinorrhea (98%), meningitis (9% at presentation, 27% by history), and seizures (7%). Comparatively, a pooled systematic review found a 79.7% and 23% incidence of rhinorrhea and meningitis, respectively.\textsuperscript{26} Empty sella was present in 85% of subjects with MRI scans in the current study. A high incidence of empty sella may be present in up to 100% of patients with multiple spontaneous CSF leaks, which is in striking contrast to the low prevalence (11%) noted in individuals with leaks from other causes.\textsuperscript{28}

Additional radiographic findings in the current study included attenuation of the skull base, dilated optic nerve sheaths, dilated Meckel's caves, and multiple arachnoid pits.

Table II.
Operative Data.

<table>
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<th>Site of Defect Involvement</th>
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<td>20 PT, 18 LRS, 14 CP, 5 SOE, 4 PS, 3 AE, 2 PE, 1 ONS</td>
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<tr>
<th>Size of Defect</th>
<th>Extended Surgical Access</th>
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<tr>
<td>Length 6.7 ± 4.4, width 6.2 ± 2.8</td>
<td>17 TP, 18 Draf IIB</td>
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<tr>
<th>Defect Repair</th>
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<tr>
<td>56 cadaveric/xenograft, 34 bone graft, 34 nasoseptal flap</td>
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</table>

AE = anterior ethmoid; CP = cribiform plate; LRS = lateral recess of the sphenoid; ONS = optic nerve sheath; PE = posterior ethmoid; PS = planum sphenoidale; PT = posterior table; SOE = supraorbital ethmoid; TP = transpterygoid.
**Location/Localization**

The most common location of spontaneous CSF leaks has varied in the literature, with the cribriform plate and the lateral recess of the sphenoid sinus the most frequently quoted areas. Small series and dissimilarities regarding defect site characterization likely account for this variability. The current prospective evaluation is the first cohort of spontaneous CSF leak patients to report the frontal sinus posterior table as the most common site of involvement. Remarkably, the posterior ethmoid was rarely involved in the current series of patients, which stands in marked contrast to this frequent site of iatrogenic CSF leak created during endoscopic sinus surgery. Others have proposed a congenital origin for CSF leaks within the lateral recess of the sphenoid sinus, such as those evaluated in the current series of patients, through a lateral craniopharyngeal (Sternberg’s) canal. However, such a theory ignores the known pattern of pneumatization of the sphenoid sinuses, in which the lateral recess is not present at the time of birth. Furthermore, the location of Sternberg’s canal in anatomic studies is inconsistent with the majority of lateral sphenoid sinus CSF leaks, as these are nearly all located lateral to the second branch of the trigeminal nerve (V2). Thus, a congenital etiology underlying LRS sinus CSF leaks has been largely disproven, and mention of this should be removed from the literature.

**Factors Associated With Recurrence**

Important information can be gleaned from the analysis of 21 individuals who presented with recurrences following previous surgical interventions at outside institutions. The most common factor associated with recurrence in this group was failure to control (five failed shunts) or recognize intracranial hypertension in all 21 subjects. All patients in this group had documented elevated ICP on opening pressure and/or monitoring following the procedure at our institution. For example, one subject had an endoscopic repair of a right ethmoid roof encephalocele in 2003 with a normal contralateral skull base on prior imaging. However, ICP was not measured or addressed during or following that surgical intervention. She subsequently presented 9 years later with three left-sided defects (Fig. 2). Another individual also presented with a late CSF leak recurrence 14 years after initial repair. Even though her recurrent leak was identified at the same site of the original repair, she also exhibited new nonleaking skull base defects and arachnoid pits. Additional factors included lack of repair at the level of the defect (e.g., attempting to block a sinus rather than remove the encephalocele and mend the hole) in 10 individuals and poor recognition of defect location by the outside surgeon (n = 4).

We attributed failure of primary repair in the four recurrences in the present cohort of patients to elevated ICP after discontinuation of acetazolamide in three individuals. Although a failed shunt was thought to be responsible for a late recurrence in patient 18, lumbar puncture revealed normal ICP indicating a functioning apparatus at the time of repair. Three defects were associated with the cribriform plate where a bone graft was not utilized in the reconstruction, but whether this increases the risk of failure cannot be definitively stated. Additional clinical follow-up will be useful to monitor other recurrences over time.

**Management of Intracranial Hypertension**

A common theory underpinning spontaneous CSF leak development is the creation of a release valve for chronically elevated ICP. Support for this theory is derived from postoperative ICP data and individuals who have developed clinical symptoms of IIH following...
closure of the defect. Diurnal variations in CSF pressure have been described in normal patients as well as patients with empty sella. In this study, the opening pressures in the current cohort of patients were elevated at 24.3 ± 8.3 cm H2O on instillation of the LD or EVD. Subsequent pressure measurements postclamping several days later caused a significant increase in the average ICP of 32.3 ± 9.0 cm H2O (P < .0001). Although we credit the high success rate in the current study to lowering the ICP through the use of acetazolamide and permanent CSF diversion, our data contradict a previous report noting a decrease in ICP of 15 ± 6 cm H2O post-clamping in a series of 16 patients. Regardless, there is overwhelming evidence in the literature, including the prospectively collected data in the current study, that the underlying cause of the vast majority of spontaneous CSF leaks is elevated ICP, and that the entity represents a variant of IIH. Although the use of VP shunts failure to control elevated ICP can result in recurrent CSF leakage in either the same or a different locale many years later as illustrated in the current cohort of subjects. Like the treatment of IIH, weight loss therapies are promoted in these individuals, including hiraric surgery for morbid obesity. Unfortunately, significant weight loss appears to be required for this to become an effective treatment.

CONCLUSION

The data presented in the current prospective evaluation provide solid evidence that the majority of spontaneous CSF leaks are secondary to intracranial hypertension. Successful treatment of elevated ICP in combination with endoscopic repair can provide high success rates (93% primary and 100% secondary) approaching that of other etiologies.

BIBLIOGRAPHY


Laryngoscope 124: January 2014

Chaaban et al.: Spontaneous CSF Leak Repair

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