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ORIGINAL RESEARCH—SINONASAL DISORDERS

Spontaneous CSF leaks: A paradigm for definitive repair and management of intracranial hypertension

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OBJECTIVE: To report our outcomes with the repair of spontaneous cerebrospinal fluid (CSF) leaks and to demonstrate how management of underlying intracranial hypertension improves outcomes.

STUDY DESIGN: Retrospective review of spontaneous CSF leaks treated at the University of Pennsylvania Health System from 1996 to 2006. Data collected included demographics, nature of presentation, body mass index (BMI), site of skull base defect, surgical approach, intracranial pressure, and clinical follow-up.

RESULTS: Fifty-six patients underwent repair of spontaneous CSF leaks. Eighty-two percent (46 of 56) were obese (average BMI 36.2 kg/m^2). Nine patients had multiple CSF leaks. Fifty-four patients (96%) had associated encephaloceles. Fifty-three CSF leaks (95%) were successfully repaired at first attempt (34 months of follow-up). Intracranial pressures averaged 27 cm H_2O. Patients were treated with acetazolamide or, in severe cases, with a ventriculoperitoneal shunt.

CONCLUSIONS: Spontaneous CSF leaks have the highest recurrence rate of any etiology. With treatment of underlying intracranial hypertension coupled with endoscopic repair, the success rate (95%) approaches that of other etiologies of CSF leaks.

Repair of cerebrospinal fluid (CSF) leaks of the sinonasal cavities using accepted endoscopic techniques has had relatively high success rates for nearly 20 years. Success rates of over 90 percent are quoted in multiple patient series.[1-3] However, separating and classifying CSF leaks according to the underlying pathophysiology and etiology is critical to achieving these successful outcomes. Most CSF leaks can be broadly classified into traumatic (including accidental and iatrogenic trauma), tumor, spontaneous, and congenital causes. Although this classification varies in the literature, those leaks that do not have an identifiable cause are generally referred to as "spontaneous" or "idiopathic." In this subset of patients, successful repair rates are dismal, with recurrences reported anywhere from 25 to 87 percent over time.[4,6-8] Fortunately, our knowledge and experience with idiopathic/spontaneous CSF leaks have increased dramatically over the last decade.[5-11] We now know that the majority of these patients exhibit clinical symptoms and radiographic signs of elevated intracranial pressure (ICP).

Elevated ICP most commonly manifests itself in the syndrome of benign intracranial hypertension (BIH) also known as pseudotumor cerebri. Patients with BIH typically present clinically with headache, pulsatile tinnitus, balance problems, and visual disturbances. Our prior studies have indicated that the "spontaneous" etiology of patients most often represents a variant of BIH, according to modified Dandy criteria.[9] Evaluating clinical, radiographic, and ICP data for the most rigid diagnosis of BIH reveals that more than 70 percent of patients with spontaneous leaks meet these diagnostic criteria. Radiographically, many of these patients have total or partial empty sella syndrome (ESS) caused by dural herniation through the sellar diaphragm into the sella turcica.[6] The sella has the radiographic appearance of an absent pituitary gland because it fills with CSF. Other radiological findings associated with elevated ICP include abnormalities of the optic nerve sheath complex, encephaloceles, arachnoid pits, and dural ectasia.[12]

Spontaneous CSF leaks are associated with the highest rate (50%-100%) of encephalocele formation, because there are often large meningoencephaloceles herniating through relatively small bony defects.[3,4] Furthermore, our previous studies have found direct evidence of elevated ICP in most patients with "spontaneous" CSF leaks, either by obtaining an opening pressure during lumbar tap or through monitoring of lumbar CSF pressure in the postoperative period.[7-9] These findings have truly affected our treatment philosophy in the management of patients with spontaneous CSF leaks.

The purpose of the current study is to report our outcomes with the repair of spontaneous CSF leaks and to demonstrate how management of underlying intracranial hypertension improves results. We provide important clinical information that affects treatment and long-term outcomes of these patients.

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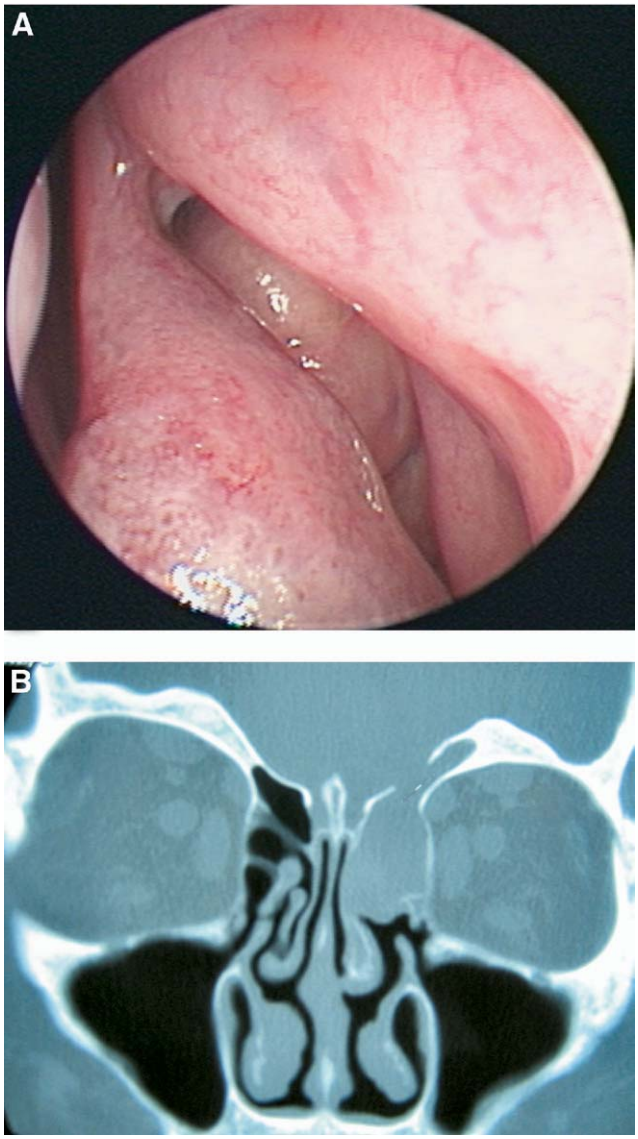

Figure 1 (**A**) Transnasal endoscopic view of a left supraorbital ethmoid encephalocele. Clinically, intracranial pressure is transmitted to the encephalocele sac, resulting in pulsations. (**B**) The encephalocele originated from a skull base defect in the roof of the left supraorbital ethmoid sinus, as demonstrated by coronal CT scan.

METHODS

The present study is a retrospective case series of all patients with spontaneous CSF leaks treated at the University of Pennsylvania Health System from 1996 to 2006. Institutional review board approval was obtained prior to the initiation of this study. All cases were performed at the Hospital of the University of Pennsylvania in Philadelphia. Electronic medical records and archived paper charts were reviewed to obtain the following data: age, gender, clinical presentation, body mass index (BMI), site and size of skull base defect, presence of ESS, CSF pressure, associated encephalocele, surgical technique, peri- and postoperative morbidity, recurrence rates, and clinical follow-up. Patients with a BMI >30 kg/m^2 were considered obese; those with a BMI >25 kg/m^2 were considered overweight. Only patients with either indirect (radiographic) or direct (lumbar pressure) evidence of intracranial hypertension were included in the study.

RESULTS

Fifty-five patients had spontaneous CSF leaks with evidence of intracranial hypertension. Average age of presentation was 61 years (range 19-79 years) with an average BMI of 36.2 kg/m^2 (range 24.5-66.4 kg/m^2). Seventy-seven percent (43 of 56) of patients were women. Forty-six patients were considered obese with a BMI >30 kg/m^2. Only one patient had a BMI <25 kg/m^2. All patients presented with CSF rhinorrhea; 10 presented with meningitis. The most common defect was the lateral sphenoid sinus (n = 23) followed by ethmoid roof (n = 17), cribriform plate (n = 12), central sphenoid (n = 7), and frontal sinuses (n = 7). Nine patients had multiple CSF leaks at presentation. Fifty-three (96%) patients had associated encephaloceles (Fig 1). For operative repair, 36 bone grafts derived from septal, mastoid, or turbinate bone were used in an underlay fashion. Fifty-three (95%) CSF leaks were successfully repaired at the first attempt. However, the overall CSF leak control dropped to 89 percent with the inclusion of new CSF leaks from a site distant to the original repair.

Lumbar drain pressures were recorded on 48 of 56 patients (average 27 cm H_2O; range 9-60 cm H_2O). Forty-five (94%) of these patients had elevated ICPs measured via lumbar puncture or lumbar drains from our previously described protocol.[8] Three patients did not meet the lumbar drain criteria for elevated ICP; however, these patients were included because of radiographic signs of intracranial hy-

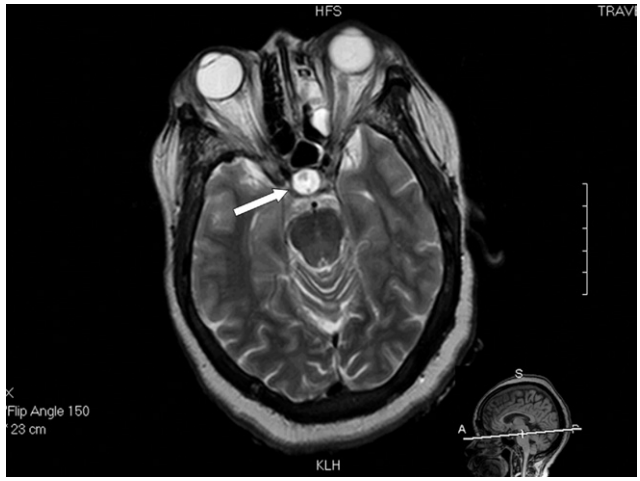

Figure 2 Axial T2-weighted MRI scan demonstrating a completely empty sella (*white arrow*). This structure is a CSF-filled dural evagination into the pituitary fossa. Eighty-five percent of patients with spontaneous CSF leaks in this study had a partially or totally empty sella.

Table 1
Recurrences

Pt	Primary site	BMI (kg/m^2)	Approach	Recurrence	Empty sella	Approach	ICP	Time to recurrence (mo)	F/U (mo)
1	L PE	42.5	Endo	L PE	Yes	Endo	32	2	52
2	L Central SS	38	Endo	L central SS	Yes	Endo	20	14	36
3	L LR SS	32.4	Endo, TPG	L LR SS	Yes	Endo, TPG	20	1	36
4	R PE	32.8	Endo	Left FS	Yes	OPF with obliteration	Refused LD	3	57
5	L LR of SS	32.9	Endo, TPG	R LR of SS	Yes	Endo, TPG	35	3	87
6	L cribriform	32.3	Endo	L LR of SS	Ptl	Endo	21	1	24

Pt, Patient; *ICP,* intracranial pressure;*F/U,* follow-up; *L,* left; *R,* right; *PE,* posterior ethmoid; *SS,* sphenoid sinus; *LR,* lateral recess; *BMI,* body mass index; *Endo,* endoscopic; *TPG,* transpterygoid approach; *OPF,* osteoplastic flap; *LD,* lumbar drain.

pertension (ie, empty sella) (Fig 2). No lumbar pressure data were available on eight of the 56 patients; however again, they met radiographic criteria for elevated ICP. Lumbar pressure data in these eight patients were either lost or unreliable because of lumbar punctures performed in a sitting position. Some of these patients were repaired early on in this series before the establishment of our lumbar drain protocol for measuring pressures. Patients were treated with 500 mg of acetazolamide taken twice daily or, in severe cases, a ventriculoperitoneal (VP) shunt (n = 13) for intracranial hypertension. Forty-nine patients had MRI scans available for evaluation of the sella turcica. Forty-two (85%) patients had evidence of empty sella on imaging—26 totally empty sellas and 16 partially empty sellas. This finding is similar to that of previously reported studies.[5,6] However, one of the patients without an empty sella had radiographic evidence of elevated ICP with the identification of bilaterally distended Meckel's caves.

Forty-six patients were repaired with a strictly endoscopic approach. Fourteen patients required a transpterygoid approach for CSF leaks in the lateral recess of the sphenoid. One of these patients also required an additional Caldwell-Luc procedure. Three patients required an adjuvant osteoplastic flap for frontal sinus CSF leaks. Two of these patients underwent fat obliteration. There were no major complications in this series of patients.

The overall recurrence of spontaneous CSF leak in this series was 11 percent (six of 56) with a mean follow-up of 34 months (range 6-96 months) (Table 1). In three of six cases, the leak occurred at the site of the original repair; in the other three cases, it occurred at a new distant site. Because subsequent CSF leaks in patients 4, 5, and 6 occurred at another site, we considered these leaks a failure of management of elevated ICP, rather than a failure of operative repair. Furthermore, patients 2, 5, and 6 had clogged VP or lumboperitoneal shunts. Thus, direct evidence of failure to reduce ICP was available in these three individuals. Patient 5 currently has a left middle cranial fossa leak into the middle ear attributable to another shunt failure. She has had multiple shunt revisions. In addition, patients 1 and 3 elected to have a VP shunt placed during the second repair because of failure of acetazolamide to lower their ICP following the first operation. Patient 4 refused intervention for her elevated ICP.

DISCUSSION

Because a wide variety of clinical conditions have been classified as "spontaneous" CSF leaks in the past,[4] we recommend that a distinction be made between high-pressure and low-pressure leaks. Based on the data from this study, we suggest that the term *idiopathic* not be used in the presence of high CSF pressure. The evidence presented in this study lends credence and strong support to the theory that chronically elevated ICP is the underlying cause of spontaneous CSF rhinorrhea and encephalocele formation in this population. Lumbar drain pressures were an average of 27 cm H_2O pressure in this study—well above the normal range of 10 to 15 cm H_2O pressure. Although three patients had an ICP below 15 cm H_2O pressure, they all had radiological evidence of elevated pressure (ie, empty sella) and were included in this study. The reasons for low readings in these patients are potentially due to a number of factors: faulty readings, depleted CSF from postoperative diuresis or excessive drainage, or measurement of a single time point during natural variations of the ICP. Maira et al[13] performed continuous ICP monitoring on 11 patients with ESS and found major fluctuations in ICP that ranged from normal to pathological elevation throughout the course of the day. Thus, these patients may have had natural fluctuations in intracranial hypertension that led to periodic pressure shifts that were significant enough to create a skull base erosion and herniated sellar diaphragm. Importantly, there was a wide range of elevated ICP in the present study, indicating that intracranial hypertension could represent a spectrum of disease. It is also possible that patients who manifest meningoencephalocele and/or spontaneous CSF leak, but have a normal ICP, might have a local or focal ICP elevation. An arachnoid gran-

ulation might develop into a small arachnoid cyst and manifest as a ball-valve phenomenon, whereby CSF is trapped within the cyst resulting in increased pressure that could eventually erode the skull base.

The clinical similarities between patients with high-pressure spontaneous CSF leaks and those with BIH are striking. In terms of demographics, the majority of patients who develop the diagnosis of BIH are obese, middle-aged women. Seventy-seven percent of the patients in the present study were women. Furthermore, the average BMI in our spontaneous CSF leak population was 36.2 kg/m^2 (range 24.5-66.4 kg/m^2). Forty-six patients were considered obese with a BMI >30 kg/m^2, whereas only one patient was not considered overweight (BMI 24.5 kg/m^2). The association of obesity with BIH has been reported in many studies.[14] Radhakrishnan et al[14] calculated an increase in incidence to 21.4 per 100,000 for obese females with a BMI of 30 kg/m^2, approximately 10- to 20-fold of the incidence in the total population. Because of these similarities, the large body habitus of patients in this study does indicate a potential role for obesity in the underlying pathophysiology of high-pressure spontaneous CSF leaks and indicates that this patient population is a likely variant of BIH. However, given that the prevalence of obesity is as high as 16 percent in the population, one would expect spontaneous CSF leaks to be much more common if obesity were the major inciting factor in elevated ICP.[15] Ultimately, an additional etiological factor, such as an underlying anatomic abnormality of the arachnoid villi, must be present to account for this discrepancy.

Regardless of the underlying mechanism leading to elevated ICP, constant pulsatile pressure applied to the skull base over time ultimately leads to erosion at sites of inherent structural weakness. Examples of this include erosion of the dura of the sellar diaphragm, and perforations in the cribriform plate and adjacent to natural foramina of the skull base. It is likely that individuals with a thicker skull base who have elevated ICP could manifest as BIH, whereas those who develop erosions in the skull base result in CSF rhinorrhea.

The most common location for a defect in this study was adjacent to the foramen rotundum in a pneumatized lateral recess of the sphenoid sinus (35%). Until recently, encephaloceles of the lateral recess of the sphenoid sinus were relatively undocumented.[16] These lesions evolve from herniation of temporal lobe tissue through a middle cranial fossa defect lateral to the foramen rotundum and vidian canal. There is excessive pneumatization of the pterygoid process with an attenuated sphenoid sinus recess roof and skull base. In combination with elevated ICP, the presence of thin bone increases the likelihood of defects developing in the floor of the middle fossa.[16] Although some authors have postulated that lateral sphenoid encephaloceles are congenital in origin, secondary to a persistent lateral craniopharyngeal canal (Sternberg's canal),[17] the location of this canal as it was originally described is actually posterior and medial to the foramen rotundum.[18,19] The advanced age of our patients at diagnosis, the lumbar pressure data, and the fact that the majority of our CSF leaks were lateral to the foramen rotundum give less credence to a congenital origin for these CSF leaks.

Intrathecal fluorescein was used in all individuals in this study. Fluorescein is not approved by the Food and Drug Administration (FDA) for intrathecal injection, because seizures and neurotoxicity have been reported with the use of higher concentrations or more rapid injections. We have used a mixture of 0.1 ml of 10-percent fluorescein diluted in 10 ml of the patient's CSF injected slowly over 10 to 15 minutes and have had no complications in over 15 years of use.[10,11] We obtained from all patients informed written consent regarding the risks and benefits of intrathecal fluorescein and its lack of FDA approval. We find fluorescein particularly helpful in cases of spontaneous CSF leaks because of the frequent presence of several defects. Despite multiple encephaloceles, only one may be actively leaking. Nine patients in this study had more than one CSF leak identified intraoperatively. Fluorescein is useful for identifying all encephaloceles intraoperatively and determining the area of an active leak. Because CSF is more easily visualized, fluorescein also ensures a watertight closure. If it is not readily apparent where the fluorescein is originating, we perform a thorough skull base exposure for evaluation. The fluorescein may be significantly diluted or excreted by the time skull base exposure is attained, depending on the rate of the leak, the rate of CSF turnover, and the timing of the intrathecal injection. The addition of a blue light filter helped improve the detection of dilute fluorescein in many cases.

Our success in repairing these defects is likely secondary to our management of intracranial hypertension in these individuals through the use of acetazolamide and VP shunts. Acetazolamide is a carbonic anhydrase inhibitor diuretic that is a useful adjunct in patients with elevated CSF pressure. It decreases production of CSF in these individuals and may decrease recurrence of CSF leaks. However, with the passage of additional time, it is still possible that the incidence of repeat leaks or recurrent encephaloceles may increase in patients without shunts. Of note, one patient with a recurrent CSF leak refused both acetazolamide and a VP shunt. Thirteen patients in our study eventually underwent shunt placement for management of their ICP. Of note, three patients who recurred had elevated ICP in the presence of a failed shunt on revision surgery. Although weight loss therapies are promoted in these individuals, significant weight loss appears to be required for this approach to become an effective treatment.[14] Thus, we feel the most important factor for a successful repair in these patients is decreasing their ICP through nutritional, medical, or surgical means.

Operative techniques varied according to the site and size of the defect and according to surgeon preference. Thus, very little information can be gleaned from the specific method of repair. However, the placement of bone grafts in the epidural space was performed on 36 patients and was a common technique among surgeons. This procedure may provide improved structural support in the presence of elevated ICP.

The complementary imaging modalities of CT and MRI were performed in the majority of patients in this study. MRI was useful for discerning evidence of encephaloceles and radiological signs of elevated ICP, whereas bony defects and a broadly attenuated skull base were seen more clearly on CT. MRI showed evidence of totally or partially empty sella in 85 percent of this patient population. This finding is similar to that of prior case series of patients with spontaneous CSF leaks.[20] Thus, patients with spontaneous CSF leaks should be evaluated for this finding, because it was present in the majority of spontaneous CSF leaks in this study and is representative of elevated ICP.

Although our average follow-up is almost 3 years in this series, it must be pointed out that future failures are possible if intracranial hypertension is not effectively managed. Unfortunately, we cannot measure CSF pressures periodically in our patients due to the invasive nature of lumbar punctures. For now, medical treatment with acetazolamide or frequent monitoring by neurosurgeons of implanted VP shunts will continue. We provide reasonable evidence that continued management of intracranial hypertension will result in better outcomes. However, longer-term follow-up of these patients is still needed, and some additional failures should be expected over time. Future studies are required to develop methods of monitoring ICP in a noninvasive fashion to provide long-term ICP data in these patients.

CONCLUSIONS

The present study is the largest reported case series of spontaneous CSF leaks with the longest average clinical follow-up. The evidence provided in this study indicates that treatment of underlying intracranial hypertension coupled with endoscopic repair can provide success rates (95%) approaching that of other etiologies for CSF leaks. Decreasing the underlying intracranial hypertension is essential for increasing success rates, although additional failures may occur over a longer follow-up period.

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Bradford A. Woodworth, data collection, author; **Anthony Prince,** data collection; **Alexander G. Chiu,** critical review of manuscript; **Noam A. Cohen,** critical review of manuscript; **Rodney J. Schlosser,** critical review of manuscript; **David W. Kennedy,** critical review of manuscript; **William E. Bolger,** critical review of manuscript; **James N. Palmer,** critical review of manuscript.

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Bradford A. Woodworth, none, **Anthony Prince,** none **Alexander G. Chiu,** consultant: Medtronic, BrainLAB; speaker's bureau: Sanofi-Aventis; **Noam A. Cohen,** consultant: Medtronic; **Rodney J. Schlosser,** consultant: BrainLAB, Gyrus, Xomed, Johnson & Johnson; speaker's bureau: GlaxoSmithKline, Sanofi-Aventis; **David W. Kennedy,** consultant: Aventis, Novartis, Schering-Plough, Medtronic Xomed; royalties: Medtronic Xomed; speaker's bureau: Merck; chair of research fund: Xoran; **William E. Bolger,** scientific advisor, consultant, stockholder: Acclarent; scientific advisor, consultant, royalties: Gyrus; **James N. Palmer,** consultant: Medtronic, GEMSNAV; speaker's bureau: Ortho-McNeil, Sanofi-Aventis.

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