Refractory Cerebrospinal Fluid Rhinorrhea Secondary to Occult Superior Vena Cava Syndrome and Benign Intracranial Hypertension: Diagnosis and Management

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ABSTRACT

Objective: This study is designed to describe the association between benign intracranial hypertension (BIH) and spontaneous cerebrospinal fluid (CSF) rhinorrhea and address the effect of extracranial venous flow dynamics on intracranial pressure (ICP). **Methods:** We present a 58-year-old woman with refractory spontaneous CSF rhinorrhea who was later found to have superior vena cava syndrome. The patient had undergone two prior transnasal endoscopic repair attempts. In retrospect, a preoperative magnetic resonance venogram (MRV) suggested very prolonged cerebral transit time, despite otherwise normal intracranial venous anatomy. **Results:** The CSF leak was repaired through a bifrontal craniotomy. The intraoperative and postoperative course was complicated due to the patient's significant comorbidities. She ultimately made a good recovery and has not had any further CSF rhinorrhea in more than 2 years of follow-up. **Conclusions:** Refractory, spontaneous CSF leak must prompt aggressive investigation for multiple causes of elevated ICP. A cerebral transit time can be obtained from scout imaging when a magnetic resonance angiogram or MRV is performed, and this may disclose elevated ICP if it is prolonged. If endoscopic transnasal repair fails, craniotomy and direct suture repair and autologous tissue reinforcement of the skull base may prove successful and durable, even if BIH persists.

KEYWORDS: Cerebrospinal fluid rhinorrhea, benign intracranial hypertension, superior vena cava syndrome, craniotomy

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Cerebrospinal fluid (CSF) rhinorrhea is a rare condition resulting from a pathological communication between the subarachnoid space and a paranasal air sinus or the middle ear. It is most commonly associated with trauma. Alternatively, it may occur following surgery for skull base tumors, sinus disease, or otologic disorders. Other rare causes include direct tumor erosion through the skull base, hydrocephalus, empty sella syndrome, and idiopathic causes. Idiopathic or spontaneous CSF rhinorrhea occurs in 4 to 40% of cases, depending on the inclusion criteria.¹⁻⁶ The more recent literature has demonstrated that a significant portion of patients with spontaneous CSF rhinorrhea are also found to have benign intracranial hypertension (BIH).^{4,6-11}

The primary indication for repair of CSF rhinorrhea is an increased risk of meningitis.² Treatment includes CSF diversion versus direct surgical repair. Endoscopic, transnasal repair has demonstrated initial success rates of up to 90%, and second revisions are nearly 97% successful.³ This has provided a safe and effective alternative to intracranial approaches in most cases. However, patients with spontaneous CSF rhinorrhea and elevated intracranial pressure (ICP) have a reported increased recurrence rate of 21 to 87% after endoscopic treatment.^{2,3,12-14}

Benign intracranial hypertension is characterized by elevated ICP without apparent pathology on conventional intracranial imaging and normal CSF studies. Patients typically present with headache, and papilledema may be found on examination. Epidemiologically, large portions of these patients are young, obese females. Conditions associated with BIH include steroid administration, autoimmune disorders (e.g., systemic lupus erythematosus [SLE]), antibiotics (e.g., tetracycline), chronic renal failure, and hypervitaminosis A. Several pathophysiological mechanisms have been proposed including alterations in CSF production and absorption, cerebral edema, endocrine disorders, and cerebral venous hypertension.¹⁵⁻¹⁷ Studies have supported obstructed intracranial venous flow as a cause of elevated intracranial venous pressures

and, subsequently, raised ICP.¹⁸⁻²³ Few studies have demonstrated increased ICP as a result of reduced extracranial venous flow dynamics.²⁴⁻³¹

We present a patient with refractory spontaneous CSF rhinorrhea and superior vena cava (SVC) syndrome secondary to idiopathic multifocal fibrosclerosis and discuss current literature for the pathology and treatment of spontaneous CSF rhinorrhea secondary to BIH with elevated extracranial venous pressures.

CASE

A 58-year-old woman presented initially elsewhere in May 2005 with a 4-month history of right-ear fullness and hearing loss and was noted to have fluid in the middle ear. A tympanostomy tube was placed, and the fluid was noted to be clear. The ear quit draining after several weeks, but by August of that year she developed copious right-sided clear fluid rhinorrhea. Also, at that time she developed severe swelling of her right arm and was diagnosed with deep venous thrombosis (DVT) of the right upper extremity and had been placed on Coumadin. Examination of the nasal fluid for beta-2 transferrin was positive, indicating CSF leak. She had no history of headache, meningitis, prior cranial or sinus surgery, or head trauma.

The past medical history was complicated by a diagnosis of idiopathic multifocal fibrosclerosis, a type of retroperitoneal fibrosis. This had resulted in bowel obstruction ~20 years earlier, requiring multiple surgeries and blood transfusions. She presumably developed hepatitis C from one of the blood transfusions at that time. She was noted to be chronically thrombocytopenic, and her DVT was felt secondary to her fibrosclerosis involving the upper mediastinum.

She was referred to the Mayo Clinic in September 2005. Endoscopic nasal examination revealed no obvious meningocele or encephalocele. Her middle ears were well aerated and clear. Magnetic resonance imaging (MRI) and computed

tomography (CT) cisternography performed elsewhere suggested a bony defect at the right cribriform with accumulation of subarachnoid contrast in the right posterior ethmoids.

On October 26, 2005, after withholding Coumadin for several days and allowing her international normalized ratio (INR) to normalize, she underwent endoscopic transnasal repair of the cribriform plate defect to seal the CSF leak. The bony and dural defect was readily apparent and was patched with two layers of autologous fascia lata harvested from the right thigh and Tisseel fibrin sealant. Postoperatively, the patient did well, was restarted on Coumadin, and had no further rhinorrhea.

She presented 4 months later, in February 2006, with recurrent, intermittent, right-sided rhinorrhea. Repeat testing of the fluid was once again

positive for beta-2 transferrin. A repeat CT cisternogram (Fig. 1) again showed leakage of contrast from the subarachnoid space into the right posterior ethmoid sinuses at the site of the prior repair. Her anticoagulation was again stopped, and on February 22, 2006, she once again underwent transnasal endoscopic repair of her anterior skull base defect with autologous fascia lata and Tisseel fibrin sealant without complication.

She returned 2 months later, in April 2006, with right-sided CSF rhinorrhea, now for the third time. A noninvasive investigation was undertaken to investigate for elevated ICP. Coronal MRI demonstrated a right cribriform plate defect with inferior herniation of the right frontal lobe into the right ethmoid sinus (Fig. 2). A magnetic resonance venogram (MRV; Fig. 3) revealed all intracranial venous sinuses were patent. Interestingly, the radiologist noted that the cerebral venous transit time was markedly prolonged after the gadolinium bolus was delivered for the MRV, but this information was not relayed to the surgical team. We elected not to do a spinal tap as this would require taking her off her anticoagulation, and considering

Figure 1 Coronal computed tomography of the head at time of cisternogram performed after patient developed cerebrospinal fluid rhinorrhea following her first transnasal endoscopic procedure. Image demonstrates the absence of the right ethmoid roof with probable herniation of the frontal lobe inferiorly.

Figure 2 Magnetic resonance imaging for preoperative evaluation following second endoscopic repair and before craniotomy procedure. Gadolinium-enhanced coronal T1-weighted image continues to show a right cribriform plate defect with inferior herniation of the right frontal lobe into the right ethmoid sinus.

Figure 3 Magnetic resonance venogram revealing normal venous anatomy and patent major dural sinuses.

her active leak the opening pressure may not have been very reliable. Also, it was apparent to us that to completely fix this leak would require a craniotomy and direct repair.

On April 17, 2006, we performed a bifrontal craniotomy and direct repair of the dura and skull base defect using additional autologous fascia lata and pericranium. The site of the leak was readily identifiable. At the time of surgery, the brain was extremely friable, and there was a moderate amount of cerebral swelling and venous bleeding from the entire craniotomy site. She had been initially transfused with platelets for a platelet count of 71,000, but her platelets remained between 53,000 and 68,000 during the operation. Her activated partial thromboplastin time (aPTT) was mildly elevated to 40 seconds, and she was also given fresh frozen plasma. We were able to achieve good hemostasis, and, being confident that we had repaired the defect causing repeated CSF rhinorrhea, the wound was closed. An immediate postoperative CT scan of the

head showed no significant intracranial hemorrhage.

Postoperatively, she remained thrombocytopenic but had no hemorrhagic complications. Further investigation confirmed presence of SVC thrombosis, including thrombosis of her left internal jugular vein (IJV) and partial thrombosis of the right IJV (Fig. 4). She made a good recovery and was able to be discharged on postoperative day 16. Magnetic resonance imaging performed 4 months postoperatively showed sustained graft repair of the cribriform plate defect (Fig. 5), and she has had no evidence of recurrent CSF leak at almost 2 years of follow-up.

DISCUSSION

Spontaneous CSF rhinorrhea is a rare condition that presents unique diagnostic and therapeutic challenges to the treating surgeon. The literature has demonstrated a strong association between spontaneous CSF rhinorrhea and BIH.^{4,6-11} Schlosser et al reviewed 16 patients with spontaneous CSF rhinorrhea who developed symptoms and signs of elevated ICP after surgical repair.⁹ Postoperative measurement of CSF pressures with lumbar puncture for cisternogram revealed elevated ICP in 10 of 16 patients, with a mean of 26.5 cm H₂O. Furthermore, a study that included patients with spontaneous CSF rhinorrhea or encephalocele showed 72% met the modified Dandy criteria used by neuro-ophthalmologists for the diagnosis of BIH.¹¹ Ransom et al presented a patient successfully treated with ventriculoperitoneal shunt for BIH who presented with spontaneous CSF rhinorrhea and was found to have shunt failure.⁸ Cerebrospinal fluid rhinorrhea ceased after shunt revision.

Many authors have proposed elevated intracranial venous pressure as the pathophysiology for BIH.¹⁸⁻²³ Increased venous pressure in the major intracranial venous sinuses will translate into increased CSF pressure.³² Johnston et al³³ and

Figure 4 Computed tomography of the chest with contrast for pulmonary embolus protocol. (A) Multiple dilated superficial venous collaterals (arrows) over chest wall characteristic of superior vena cava (SVC) syndrome are seen. (B) Diminutive and unopacified SVC (arrow) is seen. (C) Small venous collaterals (arrow) are attempting to fill superior azygous vein.

Figure 5 Postoperative magnetic resonance imaging performed 4 months after the bifrontal craniotomy. Coronal T1-weighted image with contrast reveals persistent fascia lata graft repair of the cribriform plate defect.

Malm et al³⁴ independently demonstrated elevated CSF pressure associated with increased superior sagittal sinus (SSS) pressure in BIH patients.

This theory has predominantly been applied to intracranial venous pathology. However, any disruption in venous flow proximal to the right heart chambers could potentially result in elevated intracranial venous pressures, decreased CSF absorption, and increased ICP. A prime example of this includes infants who developed hydrocephalus after cardiac surgery, producing restricted venous flow in the SVC.^{25,27,28,30,31} Further evidence is seen in patients who develop BIH after radical neck dissection and occlusion of one or both IJVs.^{26,35} Alperin et al evaluated extracranial venous flow in eight patients with BIH and eight control patients.²⁴ The patients with BIH showed a four-fold increase in mean venous flow rate in epidural and vertebral veins compared with controls. Additionally, one of the healthy patients was studied while compressing the IJV and demonstrated

increase in epidural venous flow and ICP, as measured by MRI. Our patient had extensive fibrosis and thrombus in her SVC and bilateral IJV resulting in occlusion and SVC syndrome.

Patients with spontaneous CSF rhinorrhea, especially those refractory to treatment, should be evaluated for elevated ICP or BIH. Unfortunately, diagnosing BIH in patients with spontaneous CSF rhinorrhea can be difficult until the CSF leak is successfully treated. With the recent evidence implicating venous flow obstruction as a pathophysiological mechanism for BIH, many physicians include MRV in the initial workup for BIH. In an attempt to identify noninvasive tests for elevated ICP, Bateman evaluated vascular flow and pulsatility characteristics using MRI.¹⁸ After comparing MR vascular studies in 12 BIH and 12 control patients, he found that a 30 to 40% reduction in major intracranial venous sinus pulsatility might represent a marker of raised ICP. Additionally, MRV in patients with intracranial hypertension secondary to venous outflow obstruction had 25% reduced blood flow in the SSS compared with controls.

When performing an MRV at our institution, a timing study from the initial gadolinium bolus to maximum venous opacification is performed before diagnostic imaging to determine the point of optimal visualization in the desired vessels. This study typically averages between 10 and 20 seconds, depending on the patient's age, venous access, and cardiac function. Our patient's transit time was 40 to 45 seconds on two separate attempts. The venous access was felt to be adequate, and her cardiac function was not impaired. Given Bateman's finding of reduced SSS flow with obstructed intracranial venous flow resulting in intracranial hypertension, it is feasible to conclude that reduced transit time for contrast in MRV may be another finding suggestive of venous pathology and increased ICP. Although further studies need to be performed to examine the validity of these tests, they may represent noninvasive information to aid surgeons in the diagnosis and treatment planning for these challenging cases.

Our patient was discovered to have extensive thrombosis of the SVC and IJVs. This undoubtedly led to elevated ICP and spontaneous CSF leakage. Although endoscopic repair typically has a high success rate, in our case it failed after two attempts. Bifrontal craniotomy and direct suture repair and autologous tissue reinforcement of the skull base has resulted in a very durable repair without the need for CSF diversion.

CONCLUSION

Patients with spontaneous CSF rhinorrhea have elevated failure rates when compared with post-traumatic or postsurgical cases. The presence of BIH in these patients provides a reasonable explanation. A thorough search for possible causes of BIH, including evaluating the extracranial venous system, may reveal an etiology of the elevated ICP that should be taken into account in the preoperative planning. The use of lumbar drains, acetazolamide, or permanent CSF diversion may help reduce the failure rate of endoscopic repair for spontaneous CSF rhinorrhea. Direct repair via craniotomy and an intracranial approach may provide an effective, durable repair even if the cause of the BIH cannot be remedied. Heightened awareness of these patients should result in improved outcomes.

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