

**TITLE: CSF Leaks**

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Cerebrospinal fluid (CSF) leaks are composed of CSF rhinorrhea or otorrhea, which implies an abnormal communication between the subarachnoid space and the nasal cavity or tympanomastoid space. CSF leaks may present in a number of ways, including middle ear effusion, hearing loss, or unilateral rhinorrhea secondary to Eustachian tube drainage. Therefore, the otolaryngologist must keep a high clinical suspicion. The diagnosis must be either confirmed or excluded as the risk of meningitis is high, with reported rates varying between 2-88%. The clinician must be aware of the diagnostic and treatment options available in order to best manage such patients.

## **CSF Rhinorrhea**

CSF rhinorrhea involves a breakdown of all barriers that separate the subarachnoid space from the nasal cavity or paranasal sinuses. Similar to CSF otorrhea, the etiology of CSF rhinorrhea is diverse. CSF rhinorrhea from the anterior cranial fossa may occur after head trauma, ablative tumor surgery, or surgery for paranasal sinus inflammatory disease. Although the incidence of a CSF fistula after endoscopic sinus surgery (ESS) is less than 1%, ESS is a common cause of CSF fistulae. Blunt trauma to the head is another frequent cause of CSF leaks, which are diagnosed in 3% of all patients with a closed head injury and in up to 30% of patients who have skull base fractures.<sup>2</sup> Conditions that increase the ventricular pressure, such as intracranial tumors and post-traumatic and post-infectious hydrocephalus are also important causes of CSF leaks. In addition, arachnoid granulations present along the cribriform plate may also lead to spontaneous CSF rhinorrhea.

The most important factor in its detection is a low threshold of suspicion and this often arises from the history. Any case of unilateral watery rhinorrhea, particularly if increased by posture, should not be empirically treated with intranasal corticosteroids but requires further investigation. It is difficult to identify a leak on routine endoscopic exam, but allows the clinician to formulate a differential diagnosis and may identify an intranasal encephalocele.

## Testing of nasal secretions

Testing the fluid for the beta-2 transferrin is highly sensitive and specific for CSF. The amount of CSF required is extremely small. In an undiluted sample, as little as 1/50<sup>th</sup> of a drop is sufficient for analysis. In the past, the diagnosis was aided by the use of glucose and protein determination. The guidelines used in the past was that a definitive CSF leak exists when the glucose content exceeds 0.4 g/l and the protein content is from less than 1g/l up to a maximum of 2 g/l, but contamination of blood or wound secretions can confound the results.

The electronic nose is new technology that may be able to distinguish CSF from serum. Proponents of the electronic nose argue that it is faster and requires a smaller sample for analysis (0.1-0.2ml). Further studies are needed to confirm these findings.

## Imaging

Imaging plays a pivotal role in the management of CSF rhinorrhea. The most important step in the management of CSF rhinorrhea is the identification of the site of the leak. A high resolution axial and coronal computed tomography scan (CT) may show small defects or fractures in the region of the anterior skull base or sphenoid sinus. However, volume averaging across the thin bone in this area may produce both false negatives and false positives. Congenital dehiscence's can occur at any point on the skull base, however the two most common areas for defects producing CSF rhinorrhea are the cribriform niche adjacent to the vertical attachment of the middle turbinate (fovea ethmoidalis) and the superior and lateral walls of the sphenoid sinus. In cases of temporal bone fractures or iatrogenic defects, the location of the CSF leak will correlate with the imaging studies.

Administration of intrathecal contrast prior to a high resolution coronal CT scan can provide proof of the true site of the leak especially in cases of active leaking. The use of such CT cisternography is currently the optimal imaging modality for demonstration of the site of a CSF leak in the absence of an obvious skull base defect.

MRI cisternography using highly T2 weighted images is advantageous as the patient does not require any intrathecal contrast. However, the MRI lacks the fine bony detail along the skull base which severely limits its accuracy in localizing CSF leaks. A recent study that utilized a small dose of intrathecal gadolinium improved the ability of MRI to localize the site of CSF egress and appears to be a promising new imaging modality.

New MRI techniques that impart great sensitivity to the motion of fluids have already amplified the utility of MRI, as in the widely recognized evaluation of blood flow, MR angiography (MRA). Flow sensitive MRI has also been used to evaluate CSF flow in the head and spine and to evaluate the presence of communication between CSF spaces. Early studies have demonstrated a high sensitivity to fluid motion down to 0.5mm/sec.

Radioisotope cisternography was a popular method of CSF leak identification prior to the development of CT and MRI. Technetium DPTA scans have now been largely abandoned due to both false positive and false negative results and the inability of the technique to show the fine anatomical detail required to locate the site of CSF egress. It is still used in selected cases when

the site of the leak has not been clearly demonstrated or when the leak is less active or intermittent. Endoscopically placed intranasal cottonoids are placed in the middle meatus and sphenoidal recess and are removed and measured for radioactivity within 24 hours of injection to help localize the leak. If a leak is detected, most surgeons will administer intrathecal fluorescein and endoscopically examine the area to help identify the exact anatomic locations of the leak. Identification of the site of the leak is aided by the use of a blue optical filter system introduced into the light source for the endoscopic equipment.

Should the leak not be identified after careful imaging and there remains a strong clinical suspicion, intrathecal fluorescein may be utilized. This is usually combined with an endoscopic approach for repair of the skull base. If a leak is not identified, no surgery is performed. Care must be taken in administering intrathecal fluorescein as potential complications may result. Complications such as lower extremity weakness, numbness, seizures, and cranial nerve defects have been reported. Topical fluorescein dye has also been utilized with successful identification of the site of leak as well.

### **Treatment of CSF Rhinorrhea**

Most cases of CSF leaks occurring after blunt trauma or skull base surgery resolve with conservative measures alone. Bed rest, elevation of the head, stool softeners, avoidance of straining, and decreasing CSF pressure with the use of a lumbar drain or daily spinal taps have been utilized as effective conservative options. Surgical repair is indicated for patients who do not respond to these measures, patients who have traumatic CSF leaks associated with extensive intracranial injury requiring a craniotomy, and patients whose CSF leak is identified intraoperatively.

Prophylactic antibiotics still remain controversial. The proponents of prophylactic antibiotic use believe that because CSF leaks are exposed to potentially pathogenic organisms from the upper respiratory tract. The opponents argue that antibiotic prophylaxis contributes to the development of potentially resistant organisms and more serious infections, and that prophylaxis does not decrease the risk of meningitis. Two meta-analysis reviews of the literature have been conducted. One showed that the incidence of meningitis is statistically lower in patients receiving antibiotics as compared to those who do not. The other study showed that there was an increase in the incidence of meningitis of those who did not receive antibiotics but that did not reach statistical significance. Antibiotics are usually selected on the basis of the nasopharyngeal flora being the source of the infection.

Currently there are three types of techniques use to repair CSF leaks: intracranial, extracranial, and transnasal endoscopic repair. The intracranial approach has the advantage of direct visualization of a leak from above and allows treatment of coexisting intracranial pathology. However, it affords poor visualization of communicating fistulas from the sphenoid sinus to the anterior cranial fossa. Success rates with this technique vary from 50 to 73%. This approach has significant morbidity including anosmia, intracerebral hemorrhage, cerebral edema, seizures, frontal lobe dysfunction with memory loss, osteomyelitis of the frontal bone, and possible death. Repair from this route requires 5-7 days in the hospital, a long incision in the hairline, and a prolonged at home recovery period.

The extracranial approach utilizes facial incisions to gain access to the site of CSF leak. The main disadvantage with this approach is facial scarring however success rates have been very good with upwards of 80% achieving success in closure of the leak.

It is currently accepted that the endoscopic intranasal management of CSF rhinorrhea is the preferred method of surgical repair with higher success rates and less morbidity than the previously described techniques.

There is controversy in regards to the use of an overlay versus an underlay type of graft. In a meta-analysis of endoscopic repair of CSF rhinorrhea, both techniques yielded statistically similar results. It seems surgically sound to reserve underlay techniques to larger bony defects with herniating brain or meninges. The onlay technique is recommended if there is a risk that nerves or vessels may be damaged when dissecting the dura from the surrounding bone, when inserting the graft, or if the inlay technique is not technically possible. Most surgeons utilize gelfoam or gelfilm packing over the repair site to prevent avulsion of the graft during packing removal.

Fibrin glue was found to be used in over half of the cases, which may enhance adhesion of the graft. Nasal packing was shown to be used in all cases and was usually kept in place for 3-7 days. Some authors recommend a spinal drain for 3-5 days to reduce CSF pressure, however drains are not necessary in all cases. They recommend the selective use of a lumbar spinal drain for patients presenting with idiopathic and post-traumatic fistulae that are highly associated with hydrocephalus for recurrent or persistent leaks and for those associated with meningoceles or large skull base defects. In selected cases that do not require a lumbar drain, patients may be discharged home the same day as surgery with strict bed rest, stool softeners, and antibiotics.

A fistula of the sphenoid sinus may be repaired with a free graft technique or with an obliterative technique using abdominal fat. Some authors have also used hydroxyapatite cement for repair within the sphenoid sinus as well. Success rates over 85% may be expected in either case in experienced hands.

Overall success rates with the endoscopic approach are 90% after the first attempt. A second endoscopic approach may be used to close persistent fistulae with success rates in this setting of around 52% giving an overall success rate of 97%. Persistent or recurrent CSF leaks show a statistically significant association with the presence of hydrocephalus. Conversely, hydrocephalus was most commonly diagnosed in patients with traumatic and spontaneous CSF leaks.

The incidence of surgical complications following CSF repair was found to be very low; meningitis (0.3%), brain abscess (0.9%), subdural hematoma (0.3%), smell disorders (0.6%), and headache (0.3%)

## **CSF Otorrhea**

Temporal bone CSF leak is an indication of an abnormal communication or series of communications between the subarachnoid space and the temporal bone. Such leaks may be categorized as either acquired or congenital. Acquired etiologies are by far the most common

and include: trauma (temporal bone fractures), postoperative (delayed or immediate), temporal bone infections, and benign or malignant neoplasms. Congenital, or spontaneous CSF leaks are thought to arise from the congenital bony defect theory or from the arachnoid granulation theory.

### **Temporal bone fractures**

The most common cause of CSF otorrhea is fractures of the temporal bone. Blunt trauma to the skull may produce fractures in the temporal bone with tearing of dura and foramina causing acute leakage. Fractures may also produce defects in the bony tegmen plate, predisposing one to encephaloceles or meningoceles with resultant delayed CSF leakage. Temporal bone fractures have been traditionally divided into transverse or longitudinal, based on the relationship of the fracture line to the otic capsule and axis of the petrous ridge. In reality, however, most fractures are actually oblique in nature. An important factor in temporal bone fracture classification is whether the fracture passes through the otic capsule. Indications for surgical repair of and the approach for CSF fistula is significantly influenced by otic capsule violation. Tympanic membrane or EAC lacerations are frequently seen in longitudinal fractures which allows for the egress of CSF from the ear. However, with transverse fractures, the tympanic membrane is typically intact and the fluid may build within the middle ear and mastoid and eventually drain through the eustachian tube producing CSF rhinorrhea. CSF otorrhea in temporal bone fractures usually occurs within minutes of the accident but may be delayed in its presentation if it is draining through the nasopharynx. A high resolution CT scan can demonstrate the course of the fracture line and give information as to the likely site of CSF fistula. Accurate identification of CSF is important. After trauma, CSF otorrhea is typically serosanguinous and can be mistaken for blood byproducts. The fluid should be sent for beta-2-transferrin, as this protein is highly specific to the CSF. As discussed earlier, measurements of glucose and protein in the fluid have fallen out of favor for CSF identification. Bed rest with head elevation, stool softeners, and occasionally the use of lumbar drains is indicated. Sterile cotton should be used to prevent contamination of the ear. Antimicrobial ear drops are unnecessary and may actually confuse the clinician in regards to cessation of CSF flow.

In a study by Brodie and Thompson, 820 temporal bone fractures were treated over a 5 year period. There were 122 patients with CSF fistulae (97 with otorrhea, 16 with rhinorrhea, and 8 with both). Ninety-five of the patients had the fistulae close spontaneously within 7 days, 21 closed within 2 weeks, and only 5 had persistent drainage over 14 days. Only seven patients underwent surgery for repair of the CSF leak (middle cranial fossa, transmastoid, or combined). Nine of the 121 developed meningitis (7%). The use of prophylactic antibiotics was not statistically correlated with the development or prevention of meningitis in this study. A later meta-analysis by the same author, however, did reveal a statistically significant reduction in the incidence of meningitis with the use of prophylactic antibiotics.

The overall incidence of pediatric basilar skull fractures is lower than that of adults. The adult to child ratio is 10:1. This lower incidence is thought to be because of the increased skull flexibility and underdeveloped sinuses. The incidence of otorrhea is greater than rhinorrhea. Despite having a small number of cases, a meta-analysis showed that the use of prophylactic antibiotics did not influence the development of meningitis.

## Spontaneous CSF Otorrhea (Congenital)

Spontaneous cerebrospinal fluid otorrhea is a rare but potentially life-threatening condition with two different subtypes. In one type, known as the congenital defect theory, a preformed bony pathway around and through the bony labyrinth allows the higher subarachnoid pressure to communicate to the middle ear or mastoid. The three preformed bony pathways are 1) enlarge petrosal fallopian canal, 2) patent tympano-meningeal (Hyrtl's) fissure, and 3) communication of the internal auditory canal with the vestibule (Mondini dysplasia). This form of spontaneous CSF leak usually presents early in life, from the ages of one to five years. 82% will have sensorineural hearing loss, 93% will have meningitis, and 83% will have a Mondini dysplasia. Often the CSF in the middle ear is first recognized after myringotomy. The second type of congenital defect, known as the arachnoid granulation theory, manifests itself later in life (usually over the age of 50). This is because congenital structures (arachnoid villi) carrying CSF enlarge with age and physical activity as a result of intermittent changes in subarachnoid pressure. This pulsatile pressure and the weight of the temporal lobe is capable of bony erosion over the course of many years. The clinical presentation is usually a unilateral serous otitis media, which at first is recurrent but eventually is persistent. The incidence of meningitis is much lower (36%), and profound sensorineural hearing loss or Mondini dysplasia is not encountered. It is hypothesized that the responsible congenital structures are arachnoid granulations which are aberrantly located over a pneumatized part of the skull rather than invaginated in the intracranial venous system enclosed in dura. 88% of these defects occur on the floor of the middle fossa, and can be from multiple defect sites.

Timely diagnosis of adult spontaneous CSF otorrhea begins with a high degree of clinical suspicion. Stone et al. compared the usefulness of non-contrast, high resolution CT to contrast-enhanced CT cisternography and radionuclide cisternography. HRCT showed bone defects in 30 of 42 (71%) patients with CSF leak. High resolution, radionuclide cisternography and CT cisternography did not show bone defects of CSF leak in 12 (29%) patients who had clinical evidence of CSF leak. Among the 30 patients with bone defects, 20 (66%) had positive results on radionuclide cisternography or CT cisternography. For the 21 patients who underwent surgical exploration and repair, intraoperative findings correlated with predictions made on the basis of HRCT in all cases. HRCT identified significantly more patients with CSF leak than did radionuclide cisternography and CT cisternography.

Surgical repair is recommended for those cases that do not resolve in order to prevent the morbidity and mortality associated with meningitis. Tegmen defects may be multiple rather than single, and identifying only one defect may not be sufficient for achieving definitive repair. Because surgical repair by way of a mastoidectomy approach alone can be inadequate if there are multiple tegmen defects, a middle fossa approach alone or in combination with a transmastoid approach should be considered in most cases.

The success rate is significantly higher for those patients who undergo primary closure with a multi-layer technique (using bone wax plus 2 additional materials, such as Oxycel cotton, muscle, fascia, or abdominal fat) versus those patients who underwent primary closure with a single-layer technique. The surgeon should also be prepared to deal with an encephalocele encountered incidentally during surgery. This herniated, pedunculated tissue is functionless and can be amputated. Closing off the external auditory canal and obliteration of the Eustachian tube

and mastoid cavity may be indicated when CSF otorrhea has been refractory to medical and surgical interventions.

## **Conclusions**

The successful management of a patient with a history suggestive of a CSF leak involves ensuring that it is a true leak by testing the fluid for beta-2-transferrin. Imaging studies should be performed in order to anatomically localize the site. Surgery, if necessary, should minimize morbidity while maximizing the chances of a successful outcome. This may be achieved by meticulous preoperative assessment and meticulous intraoperative techniques. Success rates of over 90% can be expected with proper patient and surgical selection.

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