Imaging review of cerebrospinal fluid leaks

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Abstract
Cerebrospinal fluid (CSF) leak occurs due to a defect in the dura and skull base. Trauma remains the most common cause of CSF leak; however, a significant number of cases are iatrogenic, and result from a complication of functional endoscopic sinus surgery (FESS). Early diagnosis of CSF leak is of paramount importance to prevent life-threatening complications such as brain abscess and meningitis. Imaging plays a crucial role in the detection and characterization of CSF leaks. Three-dimensional, isotropic, high resolution computed tomography (HRCT) accurately detects the site and size of the bony defect. CT cisternography, though invasive, helps accurately identify the site of CSF leak, especially in the presence of multiple bony defects. Magnetic resonance imaging (MRI) accurately detects CSF leaks and associated complications such as the encephaloceles and meningoceles. In this review, we emphasize the importance and usefulness of 3D T2 DRIVE MR cisternography in localizing CSF leaks. This sequence has the advantages of effective bone and fat suppression, decreased artefacts, faster acquisition times, three-dimensional capability, and high spatial resolution in addition to providing very bright signal from the CSF.

Key words: Cerebrospinal fluid leaks; Cisternography; T2 Drive

Introduction
Cerebrospinal fluid (CSF) is an egress of CSF from the skull base osseous dural defect leading to a direct communication of extracranial space to the subarachnoid space.[1] When the leak is through the ear it is called CSF otorrhea and when it is through the nose, it is called CSF rhinorrhea. When there is an intact tympanic membrane, but a defect/fracture in the petrous temporal bone, the CSF may leak through the Eustachian tube into the nasopharynx/nasal cavity and this condition is called CSF otorhinorrhea. Congenital anomalies such as cephaloceles, persistent craniopharyngeal canal, or cribiform plate defect may present with CSF leak. The acquired CSF leaks can be posttraumatic or iatrogenic. Iatrogenic causes are now becoming the important causes owing to the wide and routine use of complex skull base surgeries and functional endoscopic sinus surgery (FESS).[2] Posttraumatic CSF leaks occur with fractures of the cribiform plate, sphenoid sinus, or ethmoid roof. Spontaneous intracranial CSF leaks are most commonly associated with large arachnoid granulations in the lateral sphenoid sinus. Undiagnosed and untreated CSF leaks may have the risk of complications such as headache, meningitis, and brain abscesses and hence, accurate diagnosis is essential.[3] High resolution computed tomography (HRCT) provides an excellent bony detail but it is difficult to differentiate paranasal sinus (PNS) secretions...
from leaked CSF. Magnetic resonance imaging (MRI) is an excellent noninvasive modality which accurately localizes the site of CSF leak, but has the limitation of poor spatial resolution and loss of bony detail. Thus, CT and MRI act as complimentary modalities in diagnosing CSF leaks.[4,5]

Epidemiology

CSF leaks can occur in patients of all ages. Most patients reveal a history of trauma or surgical procedures. However, spontaneous CSF leaks are not uncommon and are often described in middle-aged obese women with signs of intracranial hypertension.

The commonest presentation is CSF rhinorrhea. The nasal discharge increases and becomes copious with valsalva or with head down maneuvers (Reservoir test). Clinically, a typical pattern of bloody CSF staining the pillow when one raises in the early morning is a characteristic finding. The rings of the stain are formed, the center being the blood mixed CSF and the periphery being the less viscous CSF (Halo Sign). Imaging plays a pivotal role in identification and characterization of CSF leaks. CSF leaks can be broadly divided into three categories—post-traumatic, non-traumatic, and spontaneous.

Posttraumatic CSF leaks are commonly seen within the first 2 days of injury. Most of these leaks heal spontaneously, but some become persistent and might present with meningitis years after the initial event.[3] The most common injuries include the anterior cranial fossa fractures, central skull base—fractures and lateral skull base—fractures involving the temporal bone. CSF otorrhea has greater chances of spontaneous resolution than that of the CSF rhinorrhea but it is more commonly associated with meningitis. Skull base surgeries, transnasal pituitary gland surgery, and otological surgeries are associated with development of CSF fistulas.[4] CSF leaks are more common in the case of revision surgeries where the anatomical land mark of middle turbinate is absent. These CSF leaks are most commonly identified during the surgery and are closed intraoperatively, but sometimes, the CSF leaks are very small and might need imaging to identify and characterize.

Nontraumatic CSF leaks occur secondary to nontraumatic pathologies such as tumors, infections, and congenital cephaloceles. The skull base tumors and infections can erode the dura and—the skull base leading to CSF leak. Similarly, radiation and radiation necrosis might also result in osseodural defects leading to CSF leaks.[3] Meningoceles and meningo-encephaloceles are other commonly identified congenital causes of CSF leaks [Figure 1].

Spontaneous CSF leaks can be considered as primary CSF fistulas. They are commonly seen in middle-aged obese women and are associated with intracranial hypertension. Other important imaging findings that are commonly seen in these patients include empty sella syndrome and cystic lesions in the petrous part of the temporal bone.[3] Many hypotheses are centered on the possibility of arachnoid granulations which increase the volume of CSF resulting in increased intracranial pressure and resultant CSF fistula and leaks. Presence of smooth margined defects around the leak, and along the inner table of the sinus wall and calvarium supports the hypothesis of arachnoid granulations as the cause of primary CSF leak.[1] The most common site for spontaneous CSF leak is the cribriform plate followed by the ethmoid roof. Primary CSF leaks can also involve the sphenoid sinus, peri sella, or pterygoid recesses.

Accurate diagnosis of CSF rhinorrhea involves confirmation of the nasal secretions as CSF for which beta-2-transferrin test is greatly helpful. Beta-2 transferrin is highly specific for human CSF. The nasal fluid, even as low as 0.5 mL can be evaluated for the presence of beta-2-transferrin and its presence confirms the CSF leak.[1] In patients with recurrent attacks of meningitis, the possibility of CSF leak is to be considered even though there is no actual rhinorrhea.

Imaging

Various imaging tests are used for identification of CSF leak.[3] These include radionuclide cisternography, HRCT of the skull base, CT cisternography, and MR cisternography. Table 1 for advantages and disadvantages of various Imaging Modalities.

Radionuclide cisternography is rarely performed now-a-days. Most ideal radiotracer is Technetium (Tc) 99m labeled diethyleneetriamine pentaacetic acid. Active CSF leakage should be present at the time of study for accurate diagnosis. Intermittent CSF leaks are poorly demonstrated by Tc-99m radionuclide study. In such cases, a prolonged cisternography can be performed with a radiotracer having a longer biological half-life such as the Indium (In) 111 diethyleneetriamine pentaacetic acid. Delayed imaging
can be performed with this radionuclide for up to 72 h for diagnosis of intermittent CSF leak.\[1\]

HRCT of the skull base can identify the site of CSF fistula as dural and osseous defect. Multidetector CT imaging with volumetric acquisition using thin collimation allows isotropic multi-planar reconstruction for accurate identification of CSF leak. The dural defect may not be identified but the bone defect with fluid opacification of adjacent sinuses is clinching point in diagnosis of CSF leak [Figure 2]. Care should be taken to evaluate the temporal bone along with anterior skull base for the possibility of CSF otorhrea as it can present as CSF rhinorrhea when the tympanic membrane is intact. CT is less valuable in identification of nontraumatic CSF leaks such as those associated with the meningocele and meningoencephalocele. The identification of meningocele or meningoencephalocele is important because in such conditions, the herniating structure is also to be resected along with overlay and underlay repair of the dural defect.

Shetty et al.\[6\] evaluated the role of HRCT and MR cisternography in the diagnosis of CSF leaks. In their study the most common site of CSF fistula was cribiform plate followed by junction of cribiform plate and fovea ethmoidalis. HRCT showed an accuracy of 92%, sensitivity of 92% and specificity of 100% as opposed to MR cisternography where the accuracy, sensitivity, and specificity were 89%, 87%, and 100% respectively. They identified thinner sections possible with HRCT yielded better results when compared to MR examination.

When multiple bony defects are seen on HRCT, it is difficult to identify the defect that is primarily responsible for the CSF leak. Mostafa et al. combined HRCT and MRI for detection of CSF rhinorrheas. By super-imposing the CT and MR data, his team accurately localized the CSF leaks with a sensitivity of 89%\[4,7\].

CT-cisternography is considered the gold standard examination for evaluation for CSF fistula. In our hospital, a non-contrast HRCT of the skull base in the axial plane is performed first. CT-cisternography with intrathecal injection of low-osmolar contrast material is performed for equivocal cases. After intrathecal administration of contrast material, the patient is requested to lay down in prone position with the head in the dependent position. Imaging involves thin section coronal CT scan of the skull base [Figure 3]. We believe pre-cisternography non-contrast images are important for comparison and evaluation with postcontrast imaging. The greatest advantage of this technique is precise anatomical localization of the osseous defect with definitive proof of CSF leak. In addition, we place nasal pledgets which are imaged along with CT cisternography to confirm the CSF leak. CT cisternography is a minimally invasive procedure, but the major side effects include headache, meningeal irritation, and seizures. The possibility of

**Table 1: Importance of various imaging modalities**

| Modality                 | Advantages                                      | Disadvantages                                      |
|--------------------------|-------------------------------------------------|---------------------------------------------------|
| HRCT                     | Bony defect characterization                     | Radiation, differentiation from mucosal pathology is difficult |
| CT cisternography        | Accuracy in bony defect detection, characterization of defect, less time | Radiation, invasive, poor patient acceptance, intermittent leak may be missed |
| MR cisternography        | No radiation, noninvasive, good patient acceptance | Lack of bony detail, false negatives |
| Radionuclide cisternography | Intermittent leaks can be detected              | Radiation, invasive, poor patient acceptance, lengthy procedure |

HRCT: High resolution computed tomography, MR: Magnetic resonance
seizures is quite low and we have not encountered a patient with seizures in our experience. The headache and meningeal irritation are relatively common and are seen in approximately 10% of patients undergoing CT cisternography.

MR cisternography is one of the robust techniques for demonstration of CSF leaks. It was first reported in 1986 by Dichiro et al.\[8\] using cisternal injection of contrast material to enhance CSF in dogs, but with advances in the MR technology, the intrathecal injection is discouraged. Almost all the studies of MR cisternography are performed on 1.5 tesla and high strength MRI scanners. One of the basic principles of imaging CSF fistula is to keep the patient in the prone position which will provoke the leak. For patients who are not comfortable in laying prone for long time, a supine position can also be used. The principle of MR cisternography is to demonstrate a contiguous fluid signal between the cisternal space and nasal sinus on heavily weighted T2 images. Hence, imaging during prone position though superior, is not always necessary. A complete study of MR cisternography takes approximately 20 min. The development of heavily T2W and gradient sequences such as 3D T2 DRIVE, B FFE (Philips), CISS (Siemens), FIESTA (GE) has greatly helped in identification of the exact site of CSF leak [Figure 4]. We used 3D T2 DRIVE sequence on a 1.5T scanner (Philips) in all our patients. Examination was performed in prone position. T2W axial sections of the brain and skull base were obtained initially to rule out intracranial mass lesions. In addition to coronal T2 weighted images, thin 1–1.5 mm coronal sections were also obtained using 3D T2DRIVE sequence. DRIVE sequence refers to “Driven Equilibrium Pulse sequence” which uses 3D turbo-spin echo (TSE) technique for producing high resolution T2 weighted images. It has high signal to noise ratio and low sensitivity for flow voids than multislice sequences. DRIVE pulse consists of 90° radiofrequency pulse in combination with gradient refocusing pulse and a spoiling gradient. This 90° pulse is given exactly when the echo appears, which rebuilds the vertical magnetization of the fluid. TSE factor should be set to highest possible value to minimize the sensitivity for flow voids and achieve short scan time. A short TR is used to reduce the total scanning time. Image contrast is determined by TR and TE. Contiguous interleaved images are obtained at a slice thickness of 2 mm and field of view of 16 cm. The brain parenchyma and fat are suppressed well on this sequence. The advantages of this sequence include high spatial resolution, increase in image contrast between the CSF and other structures, high signal to noise ratio, multiplanar capability, lack of bony artifacts, and lack of requirement of an intrathecal contrast material.

Our present review article is based on our experience on 128 patients who underwent MR cisternography from June 2009 to July 2016. The age of the patients ranged from 42 year old male presented with Non Traumatic CSF rhinorrhoea .(A) Coronal CT image demonstrating thin bony defect on left side. (B and C) Coronal T2 DRIVE MR images demonstrating the CSF leak on both sides which is seen in continuity with subarachnoid space. (D) Axial T2 weighted image showing posterior fossa mass lesion causing raised intracranial pressure

Figure 5 (A-D): 42 year old male presented with Non Traumatic CSF rhinorrhoea .(A) Coronal CT image demonstrating thin bony defect on left side. (B and C) Coronal T2 DRIVE MR images demonstrating the CSF leak on both sides which is seen in continuity with subarachnoid space. (D) Axial T2 weighted image showing posterior fossa mass lesion causing raised intracranial pressure

Figure 6 (A and B): 52 year old man with spontaneous CSF rhinorrhoea, coronal and axial T2 DRIVE MR images demonstrating CSF fistula into right sphenoid sinus thru osseous defect of inferolateral wall of sphenoid sinus

Figure 6 (A and B): 52 year old man with spontaneous CSF rhinorrhoea, coronal and axial T2 DRIVE MR images demonstrating CSF fistula into right sphenoid sinus thru osseous defect of inferolateral wall of sphenoid sinus
5 years to 78 years and included 92 males and 36 females. Out of 128 patients, in 16 patients CT cisternography was also performed to confirm the equivocal findings of MRI and the same were confirmed on CT cisternography. Twenty eight cases were nontraumatic in origin [Figure 5], six were spontaneous [Figure 6] and the rest (n = 94) were traumatic. The commonest site of leak was cribiform plate (n = 73) followed by frontal sinus (n = 26), lateral lamella (n = 18), and sphenoid sinus (n = 9). Multiple sites of leak were noted in 41 patients. Two patients presented with otorrhoea [Figure 7] only. Of the 126 cases presented with rhinorrhoea, MR cisternography alone confidently identified CSF leaks in 112 patients [Figures 8 and 9]. Sixty-eight of 112 patients underwent endoscopic surgery. CSF leak was confirmed on surgery in 60 patients [Figures 10 and 11]. Eight patients did not show demonstrable leak during surgery, could be due to very thin leak which might be spontaneously sealed by the time of surgery. Overall, the 3D DRIVE sequence showed a sensitivity of 100% and a positive predictive value of 80% in detecting a CSF leak. Unlike CT cisternography, MR cisternography does not require an active CSF leak to demonstrate the site of leak. Inactive leaks are often under-diagnosed on CT cisternography. Both active and inactive leaks can be diagnosed on MR cisternography. Another important and
The robust advantage of MR cisternography is the detection of spontaneous leaks. Many of the spontaneous leaks might be associated with cephaloceles and encephaloceles. Cephaloceles are easier to be missed on CT but can be confidently diagnosed on MRI. The major disadvantage of MR cisternography is the lack of bony detail. The gradient-echo images greatly improved the detail of the osseous anatomy in the skull base, but still the osseous anatomy is better appreciated with CT imaging rather than with MRI. A diagnostic algorithm has been postulated to carry out sequential imaging for accurate diagnosis.

**Conclusion**

Accurate diagnosis of CSF rhinorrhea and otorrhea and precise localization of CSF leak helps in surgical planning and enhances chances of successful dural repair. The emphasis and onus of CSF repair has shifted towards endoscopic surgery. This requires accurate localization of the dural and osseous defects with imaging. This can be accomplished by HRCT imaging of the skull base. However, the utility of HRCT is limited in the presence of multiple osseous defects. The combination of 3DT2 DRIVE MR cisternography and HRCT imaging of the skull base allows accurate identification of the leak and the osseous defect necessary for planning of the endoscopic surgery. CT cisternography can be reserved for equivocal cases.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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