Intrathecal Gadolinium-Enhanced MR Cisternography in the Evaluation of CSF Leakage


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Cerebrospinal fluid (CSF) leakage implies abnormal communication between the subarachnoid space and the nasal or middle ear cavity. It is generally classified as traumatic, nontraumatic (ie, spontaneous), or postsurgical in origin, and most cases are traumatic. Approximately 70% of traumatic CSF fistulas close spontaneously within 1 week after injury without surgical intervention. However, even in cases of mild CSF rhinorrhea or early spontaneous closure, patients remain at risk of recurrent CSF leakage, pneumocephalus, and infectious meningitis. Precise identification of the location of the CSF fistula allows proper surgical planning, increases the chance of dural repair, and can prevent complications.

Numerous techniques, including plain skull radiography, intraoperative injection of fluorescein dye, positive contrast (iophendylate) studies, and radionuclide cisternography, are all helpful in limited ways. MR imaging with T2-weighted sequences has been used to localize CSF fistulas. The demonstration of high-signal-intensity fluid extending from the subarachnoid space directly into the adjacent paranasal sinuses or herniation of the brain into a sinus through a bone defect has been the principal diagnostic criterion. However, some or all of these findings can occasionally be observed in the absence of fistula formation on MR images obtained for reasons other than CSF leakage. The most common method for evaluating a patient with suspected CSF rhinorrhea is a combination of thin-section CT and subsequent CT cisternography (CTC). Although high-resolution CT (HRCT) is sufficient to show bony defects in the skull base, the site of the dural tear and active CSF leak can be difficult or impossible to confirm by using this technique. In addition, the combination of CT and CTC results in additional radiation exposure. Thus, a safer and less invasive method is necessary to detect CSF leakage.

This article describes our experience in analyzing clinically suspected cranial CSF fistulas by using MR imaging combined with the intrathecal administration of a gadolinium-based contrast agent.

**Materials and Methods**

A total of 85 consecutive patients with suspected CSF fistulas who presented with persistent or intermittent rhinorrhea or otorrhea lasting for more than 1 month between 2003 and 2007 were included in this study. The patients ranged from 15 to 72 years of age (mean, 35.3 ± 14.7 years) and included 45 males and 40 females. The study protocol was reviewed and approved by the ethics committee of Istanbul University Cerrahpasa Medical School. Consent was obtained from all of the patients, who were informed before the study that intrathecal Gd is an off-label use.

Regarding the cause of suspected CSF leakage, 14 patients (16%) had skull base surgery, 65 (77%) experienced cranial trauma, and 6 (7%) had spontaneous CSF rhinorrhea. The time between trauma and imaging ranged from 1 month to 3 years. Rhinorrhea was evaluated due to detection by both the patient and physician. The patients were divided into several groups as follows: group 1 consisted of 12 patients with at least 1 case of bacterial meningitis combined with rhinorrhea, group 2 consisted of 16 cases of continuous rhinorrhea detected by both the patient and physician, group 3 consisted of 17 cases of intermittent rhinorrhea detected by both the patient and the physician, and group 4 consisted of 40 cases of suspected rhinorrhea. None of the patients had signs of meningitis at the time of intrathecal injection. Previous HRCT studies showed evidence of skull base fractures, defects, or erosions in each patient. The β2 transferrin test was performed in 40 patients with active rhinorrhea, and the results were positive in 30 (75%).

We performed Gd-enhanced MR cisternography (Gd-MRC) to confirm and localize CSF leaks in all patients. All lumbar puncture procedures were performed by using a 22-gauge needle at the L4-L5 level.
level under sterile conditions with the patient sitting in an upright position. Saline (4 mL) was mixed with 0.5 mL of gadopentetate dimeglumine (Gd-DTPA or Magnevist; Schering, Berlin, Germany) to produce a solution of 469.01 mg/mL. This solution was injected into the subarachnoid space, and the needle was removed. The patients remained in the knee-to-elbow position for 15 minutes after injection to maximize accumulation of the contrast medium in the basal cisterns and to facilitate its passage into the CSF fistula. One hour after injection, the patient was moved into a prone position and fat-saturated T1-weighted images were obtained in 3 orthogonal planes. Coronal and sagittal T1-weighted images (TR/TE, 500/17 ms; 2 signals acquired) and axial T1-weighted images (TR/TE, 600/17 ms; 2 signals acquired) were obtained by using a 1.5T MR imaging unit (Symphony; Siemens Medical Systems, Erlangen, Germany). In cases in which the CSF leak could not be accurately visualized on MR images, additional scans were obtained in the third and fifth hours. The authors (H.S. and S.A.) reviewed all images. In the evaluation, the extension of hyperintense Gd-enhanced CSF from the cerebral cisterns into the paranasal sinuses, the nasal cavity, or middle ear cavity and/or axial sections has a sensitivity of 84%–95%12,21; however, this technique relies on indirect signs (eg, fractures of the skull base, bony lesions or defects, mucosa swelling, fluid levels in the paranasal sinus, pneumoencephalos, and meningoencephalocele) to detect the site of the leak. Therefore, the question arises as to whether a defect depicted by HRCT is truly correlated with the site of the CSF fistula. Wenzel and Leppien22 reported a case of CSF rhinorrhea following posterior fossa surgery due to an acoustic schwannoma; in this patient, HRCT suggested a CSF leak laterally into the mastoid, whereas Gd-MRC clearly showed communication into the petrous pyramid adjacent to the internal auditory canal. In cases with multiple defects or fractures of the skull base, it may not be possible to determine the precise localization of the leak via HRCT.

MR imaging provides excellent anatomic depiction of the CSF spaces and surrounding tissues. However, in cases of suspected CSF leakage, further imaging evaluation may be required. Previous studies have indicated that unenhanced coronal T2-weighted MR imaging has the capability of demonstrating CSF fistulas; however, there is a relatively high incidence of false-positive findings (42%), especially in the presence of paranasal sinus disease.21,23,24 False-negative findings have also been reported on nonenhanced MR images from patients who subsequently exhibited skull base fractures and frank CSF leaks during surgery.23 Therefore, T2-weighted im-
CTC is accepted as the most accurate method for the investigation of active cranial CSF leakage, but it has a number of disadvantages. The sensitivity of CTC ranges between 72% and 81%, and CTC may have problems in detecting low-flow fistulas or fistulas with only hairlike communications. This is because iodinated contrast media do not distribute freely in the CSF spaces due to their tendency to form sediment or because the tiny amount of dilute contrast medium that leaks through a fistula cannot be distinguished from the surrounding bone. Wenzel and Leppien presented a case in which a CSF fistula was detected only by contrast-enhanced MR cisternography, whereas CTC did not show abnormal CSF communication. In these cases, Gd-DTPA may have certain advantages because it is distributed freely in the subarachnoid space and MR imaging offers much higher contrast resolution.

To further increase sensitivity, one could examine patients in the prone position or apply the Valsalva maneuver; however, the Valsalva maneuver remains controversial and is not widely used. Additional delayed scans are frequently required in slow-flow fistulas, and CT fluoroscopy is required to construct cine images for high-volume fistulas. Considering the high doses of radiation and the lack of criterion-standard sensitivity of the CTC, it is logical that safer and more reliable techniques are required to detect CSF leakage.
Many studies have supported the safety of intravenously administered Gd-DTPA. Although some potential adverse systemic effects have been reported, the incidences of these side effects are low.\(^{28-33}\) Nausea or vomiting and headache are the most common side effects, with frequencies ranging from 0.26% to 0.42%.\(^{28}\) Other rare reactions reported after the intravenous administration of Gd products include paresthesia, dizziness, focal convulsions, urticaria, cardiovascular reactions (eg, tachycardia and arrhythmia), laryngospasm, and anaphylactic shock.\(^{26-31}\) In addition, nephrogenic systemic fibrosis characterized by skin thickening resembling scleroderma has been recently described as one of the adverse effects following Gd administration in patients with renal failure.\(^{32}\)

Animal studies have demonstrated the practical applicability of Gd-MRC in detecting the sites of surgically induced nasoethmoidal CSF fistulas.\(^{34-36}\)

In 2 previous reports, the behavioral and neurologic alterations were observed only after the intraventricular injection of relatively high doses of Gd; no such behavioral or morphologic changes were observed in the same studies when the total dose was limited to <3.3 \(\mu\)mol/g brain in 15 \(\mu\)L.\(^{37,38}\) However, several recent studies reported intrathecal Gd-induced encephalopathy in humans after the accidental intrathecal injection of a high dose of Gd.\(^{39,40}\) In these cases, the patients developed severe neurologic symptoms, such as dysarthria, blurred vision, nystagmus, ataxia, and somnolence, followed by behavioral disturbances and psychotic symptoms.

Intrathecal Gd-DTPA is currently used to identify potential CSF fistulas in patients with rhinorrhea. In the first prospective human trial, no significant gross neurologic abnormalities, CSF changes, electroencephalographic alterations, MR morphologic evidence, or MR signal intensity changes were observed during the initial examination or during follow-up clinicoradiologic studies.\(^{44}\) With a total volume of 0.5–1.0 mL, the estimated intrathecal dose per gram of brain in this trial was much lower than the dose used in animal experiments (0.07–0.36 versus 2.5–15 \(\mu\)mol/g brain).\(^{37,38,42,43}\) Reiche et al\(^{44}\) and Aydin et al\(^{45}\) used the same technique to evaluate CSF fistulas, and a multicenter human study performed by Tali et al\(^{43}\) evaluated the safety and clinical response to Gd-DTPA in 95 patients who presented clinically with a variety of cranial or spinal signs and symptoms. A recent study demonstrated the safety of low-dose intrathecal Gd application in pediatric patients.\(^{46}\) In addition, a large case series published by Aydin et al\(^{47}\) demonstrated the relative safety and tolerability of low-dose (0.5 mL) intrathecal Gd administration in the evaluation of CSF fistulas. However, the long-term effects of intrathecal Gd in large numbers of patients are not known.

In our series, CSF fistulas were not observed in 21 patients (25%), mostly in groups 3 and 4. One possible explanation is that the patients included in the study were clinically suspected of having CSF leakage, but their symptoms were, in fact, related to other causes. In addition, 10 of these patients showed no rhinorrhea during imaging, so there was probably no leakage during that period. Negative findings may also have been related to slow-flow fistulas. Thus, rhinorrhea must be present at the time of imaging to obtain good results. The patients without demonstrable CSF fistulas showed no persistent symptoms, and during the follow-up period, they showed no fistula complications.

Furthermore, we encountered an interesting case in which the patient developed a leak from a defect in the medial wall of the middle cranial fossa into the infratemporal fossa following trauma; to our knowledge, no such case has been reported in previous series. In addition, leakage into the middle ear cavity from a defect in the mastoid bone was detected in 6 patients with otorrhrea following trauma. Finally, leakage into the sphenoid sinus was demonstrated in 8 patients who had undergone sellar surgery.

Dural repair was performed in 64 patients diagnosed with CSF leakage. Probable rhinorrhea occurred in only 1 patient approximately 1 week after treatment. Control MR cisternog-
raphy was performed in this patient, and images obtained in the first hour showed probable leakage, which became obvious in images from the third and fifth hours. These observations emphasize the importance of late control images. In patients with strongly suspected leakage, combining early images with the late images increases the diagnostic value of the procedure.

As in previous studies, no early or late complications due to the intrathecal administration of Gd were observed in the present study. However, 5 patients experiencing postprocedural postural headache lasting <24 hours were treated with conservative measures. The mean incidence for postural head-ache reported here (8%) falls within the lower range of values observed for either water-soluble iodinated contrast material—enhanced myelo-graphic procedures or simple diagnostic lumbar puncture. Thus, this subjective complaint is likely due to the lumbar tap (ie, iatrogenic CSF space postural hypotension associated with needle puncture–related transient CSF leakage) and not Gd-MRC.

In conclusion, MRC after the intrathecal administration of Gd-DTPA represents an effective and minimally invasive method for evaluating suspected CSF fistulas along the skull base. It provides multiplanar capabilities without risk of radiation exposure and an excellent approach to depict the anatomy of CSF spaces and CSF fistulas.

References
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