The Egyptian Journal of Radiology and Nuclear Medicine (2014) **45**, 841–847

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

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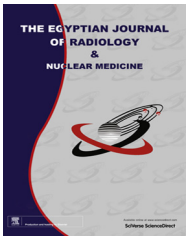

ORIGINAL ARTICLE

Cerebrospinal fluid rhinorrhea: Diagnostic role of gadolinium enhanced MR cisternography

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Received 15 April 2014; accepted 7 May 2014
Available online 15 June 2014

KEYWORDS

CSF;
Rhinorrhea;
MRI cisternography

Abstract *Background:* Accurate localization of the defect is crucial for successful surgical repair of CSF rhinorrhea. This could be achieved by MRI cisternography using T1 weighted sequences followed by intra-thecal injection of low dose of gadolinium for valuable localization and characterization of the defect.

Aim: The aim of this study was to evaluate the role of intrathecal gadolinium enhanced MR cisternography in localization of the defect in cases of CSF rhinorrhea to demonstrate how to utilize it as a roadmap to select the most appropriate approach for leak repair.

Patients and methods: This study included 24 patients (16 male and 8 females) with CSF rhinorrhea, referred from Otorhinolaryngology Department. Seventeen leaks were spontaneous, 5 cases were traumatic and two iatrogenic. All cases underwent MR gadolinium enhanced cisternography via lumbar puncture.

Results: Gadolinium enhanced MR cisternography accurately diagnosed and confirmed the site of CSF leak in 22/24 (91.7%) cases. The most common site was the ethmoidal roof in 18/24 cases. Our results were correlated with endoscopic surgery and repair with an accuracy rate of 100%.

Conclusions: Intra-thecal gadolinium enhanced MR cisternography is essential for accurate preoperative localization and characterization of the defect in cases of CSF rhinorrhea.

1. Introduction

The presence of CSF rhinorrhea indicates the existence of abnormal communication between the intra-cranial CSF spaces and the nasal cavity (1). It is potentially very serious because of the risk of an ascending infection which could produce fulminant meningitis (2).

CSF rhinorrhea may be traumatic, pathological, developmental or spontaneous (1,2). The leak may be located at the ethmoid roof, cribriform plate, posterior wall of frontal sinus, or the sphenoid sinus (2–4).

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Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

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The popularity of endoscopic closure of CSF leak has continually increased and endoscopic repair has almost completely replaced more traumatic transcranial and extracranial procedures (5–7) as the endoscopic technique offers a direct access, exact targeting of the site of the dural tear so precise placement of the graft with less operative time and high success rates and smell preservation (8,9). However successful repair of CSF leaks depends on accurate preoperative localization of the site of the defect (4).

The goals of imaging in CSF fistulae are to confirm the diagnosis, evaluate any underlying cause, localize the defect site and exclude associated lesions at the defect (2).

High-resolution computed tomography (HRCT) enables good definition of bony structures but CSF may appear as an opacification of a sinus that could not be distinguished from mucosal reaction, meningocele or percolated CSF from a distal breach (1,3,7). CT metrizamide cisternography is considered to be the gold standard for detecting CSF leaks. However its detection rate ranges between 40 and 92%, and the leak must be active (5,6,8). Furthermore, it is contraindicated in patients with high intracranial pressure and in those with spinal disorders beside the contraindications of CT. Its acceptability is low and accurate results are highly operator dependent (3).

Magnetic resonance imaging (MRI) cisternography depends on heavily T2-weighted sequences with fat suppression. CSF appears as a bright signal without the need to inject contrast media intrathecally. Furthermore, MRI details the intra-cranial anatomy and pathology in multiple planes within a relatively short time. The main disadvantage of MRI is poor spatial resolution and lack of bony details (5,6).

Intrathecal gadolinium-enhanced MR cisternography is a promising technique that may permit direct, sensitive visualization of the site of CSF leakage. It is also apparent that thin section CT is complementary to gadolinium-enhanced MR cisternography and therefore should be performed in all cases (7).

The aim of this study was to evaluate the role of gadolinium enhanced MR cisternography in localization of the defect in cases of CSF rhinorrhea to demonstrate how to utilize it as a roadmap to select the most appropriate approach for leak repair.

2. Patients and methods

From October 2010 to March 2014, 25 patients suspected clinically to have persistent CSF rhinorrhea were referred from Otorhinolaryngology departments to MRI unit, Radiodiagnosis department. Informed written consent was signed by all patients after discussing the risks and benefits. CSF leak stopped in one patient (4%) after the MR cisternography and is still under follow up over 18 months without surgery so, it is excluded. So the study subjects became 24 patients. The study has been approved by the institutional ethics board.

Cases with persistent leak for more than 3 months (refractory to conservative therapy) who were operated upon after MRI in Otorhinolaryngology Department were included. Cases of leak associated with meningoceles or meningoencephalocele, patients with CSF rhinorrhea of temporal bone, patients having contraindication to MRI examination (artificial heart valve, cardiac pacemaker, metallic stents or joint prosthesis except that made of titanium) and cases refusing surgical interference were excluded.

Preoperative diagnostic endoscopy was performed in all cases before surgery to assess the nasal cavity, follow the leak to the affected site, and to detect any associated pathology.

2.2. MR imaging

MRI studies were done using Philips medical system (01.5 Tesla). All patients were asked to get rid of any metallic subjects. The patients were informed about the duration of the examination, the position of the patient and the importance of being motionless.

The imaging protocol included sagittal, axial and coronal spin echo T1WI and fast spin echo (FSE) T2WI sequences (500/15) and (3500-4000/70) TR/TE using standard head coil in supine position, 3 mm sections 0 mm gap, 20 cm FOV and 512×220 matrix. Hyperintensity was detected in our patient outlining the site of defect to fill the ethmoid and/or the sphenoid sinus on T2WI FSE.

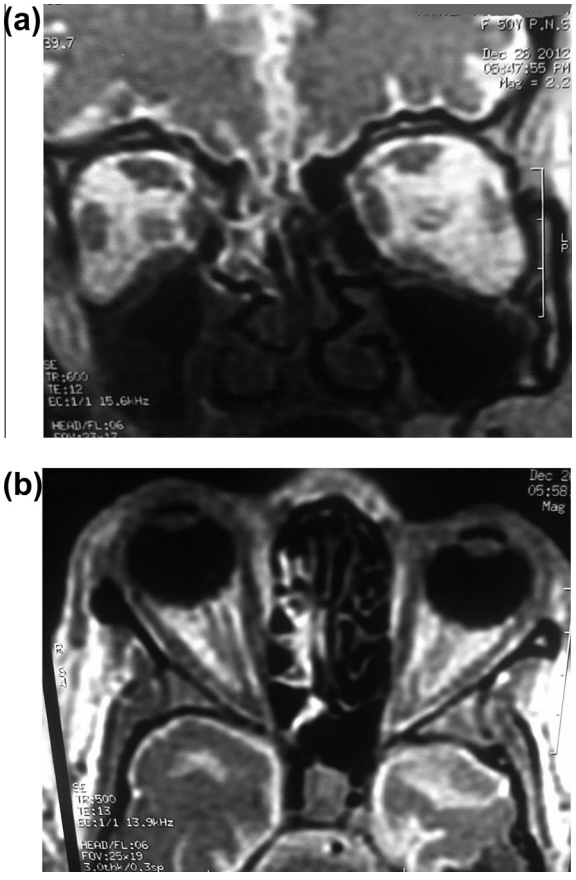

Fig. 1 CSF rhinorrhea following head trauma in a 50-year-old female. (a) Coronal T1-weighted intra-thecal gadolinium enhanced MR cisternogram shows contrast enhancement extending into the right ethmoidal air cells and to a lesser extent into the left side through defective cribriform plate of ethmoid bone. (b) Axial T1-weighted intra-thecal gadolinium enhanced MR cisternogram shows contrast leak into the right ethmoidal air cells from the cranial subarachnoid space.

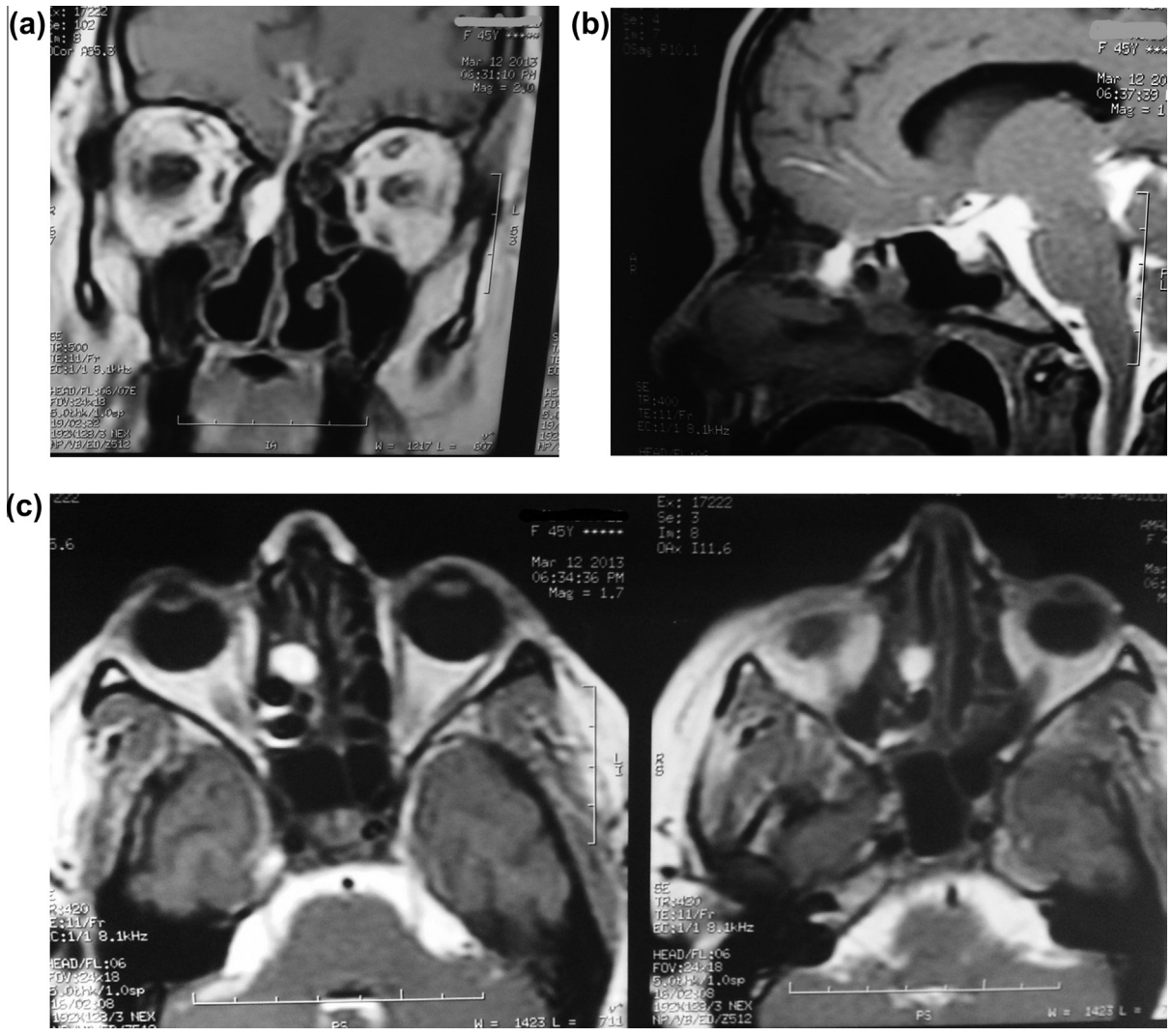

Fig. 2 Spontaneous CSF rhinorrhea in a 45-year-old female. (a) Coronal T1-weighted intra-thecal gadolinium enhanced cisternogram shows contrast leak into the right ethmoidal air-cells through a defect in the right aspect of cribriform plate. (b, c) Right para-sagittal and axial T1-weighted intra-thecal gadolinium enhanced cisternogram reveal focal right ethmoid contrast material leakage.

Table 1 Causes of CSF leak among the studied cases.

Etiology	Clinical CSF (24 cases)	HRCT (15 detected site)	MR cisternography (22 detected site)	Endoscopic diagnosis (23 detected site)
Spontaneous	17 (70.8%)	10 (66.7%)	15 (68.2%)	16 (69.6%)
Traumatic	5 (20.8%)	3 (20%)	5 (22.7%)	5 (21.7%)
Iatrogenic	2 (8.3%)	2 (13.3%)	2 (9.1)	2 (8.7%)

By mean of lumbar puncture, 3–5 mL of CSF was withdrawn and mixed with a single volume of 0.5 mL of gadopentate dimeglumine then injected into the subarachnoid space. After withdrawal of the needle, the patient was positioned prone in 30–40 degrees Trendelenburg position for 15–20 min for proper accumulation of the contrast agent in the intra-cranial basal subarachnoid CSF spaces. Immediate T1WIs were then obtained with the patient in prone position. For all patients, heart rate, blood pressure and neurological state were evaluated before, during and 60 and 120 min after injection.

2.3. Data interpretation

The MR cisternographic images were interpreted separately before surgery (blinded to surgical findings), who reached a consensus after combining the results from preoperative localization of the CSF fistula.

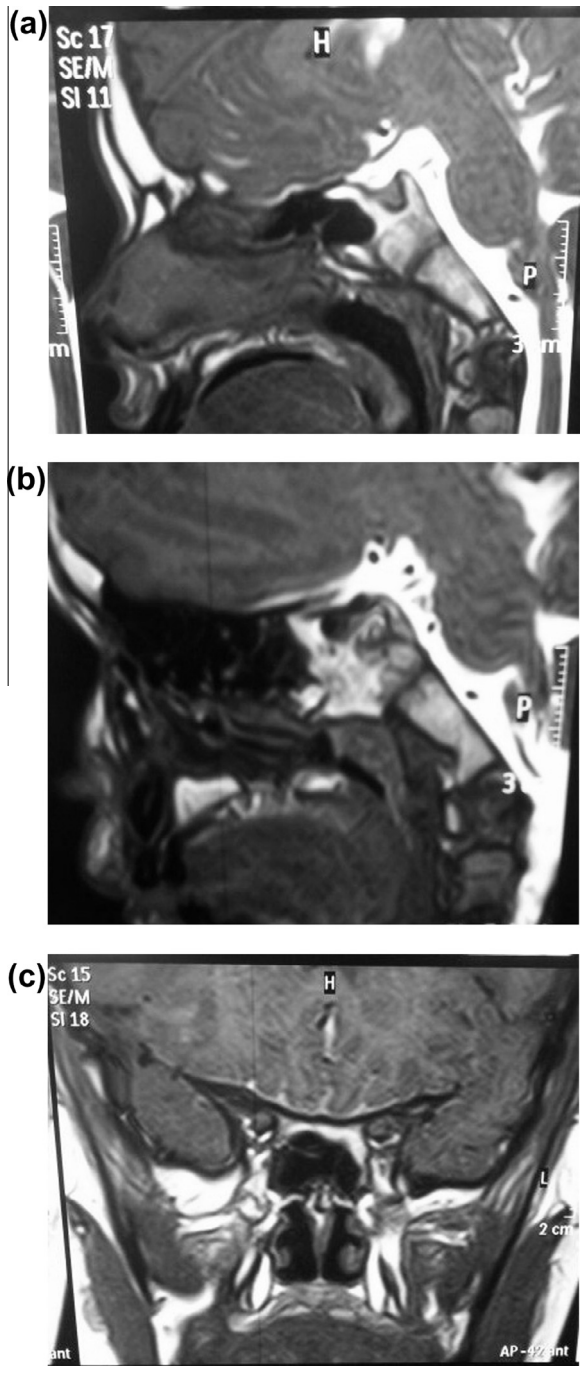

Fig. 3 CSF rhinorrhea in a 44-year-old female following traumatic insult. (a, b) Mid- and para-sagittalT1-weighted contrast enhanced MR cisternogram reveals focal contrast leak into the sphenoid sinus through a small defect detected and repaired on endoscopy. (c) Coronal T1-weighted contrast enhanced MR cisternogram shows partial opacification of the sphenoid sinus by contrast leak from the subarachnoid space through the bony defect.

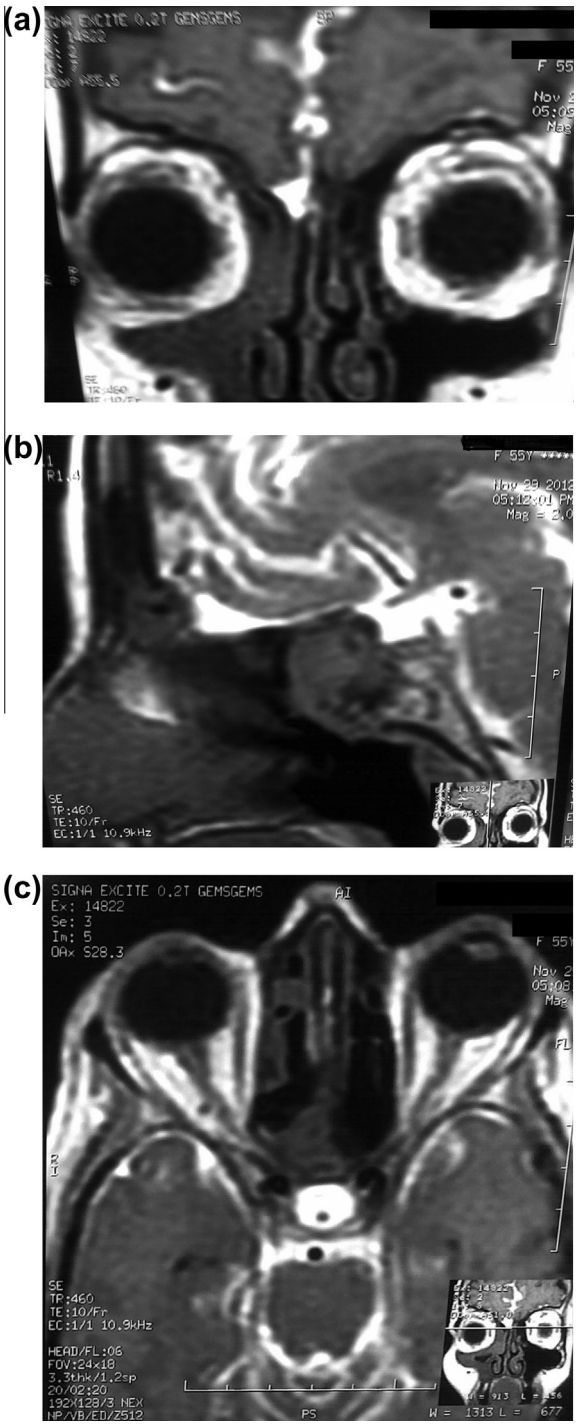

Fig. 4 CSF rhinorrhea following head trauma in a 55-year-old female. (a) Coronal T1-weighted intra-thecal gadolinium enhanced MR cisternogram reveals contrast leak into the right ethmoid air cells through a defect in the right aspect of cribriform plate. (b, c) Sagittal and axial T1 weighted contrast enhanced cisternogram reveal the site of the bony defect in the sagittal plane and contrast flow into the right ethmoid sinus from the enhanced subarachnoid space.

The site of the defect was confirmed intra-operatively by identification of the leak and washout sign. In case of failure to define the site of the leak intraoperatively, Valsalva-like maneuver, and intra-operative intrathecal fluorescein (2 cases) were performed. Intraoperative localization was then correlated with those of the imaging study.

Table 2 Site of the CSF leak.

Site	HRCT	MR cisternography localization; number (percent)	Endoscopic localization; number (percent)
Ethmoidal roof	13 (54.2%)*	16 (66.7%)	17 (70.8%)
Cribriform plate	2 (8.3%)	4 (16.7%)	4 (16.7%)
Sphenoid sinus	2 (8.3%)	2 (8.3%)	2 (8.3%)
Undetectable	7 (29.2%)	2 (8.3%)	1 (4.2%)

* Included 2 false defects found in posterior ethmoid by HRCT while detected in anterior ethmoid during endoscopic repair.

2.4. Statistical analysis

The results of MRI imaging and operative localization were compared. Specificity, sensitivity, negative predictive value (NPV) and positive predictive values (PPV) for the results of MR cisternography were calculated by using surgical results as a reference standard.

3. Results

Subjects ranged in age from 33 to 62 years; 16 (66.7%) were female and 8 were male (33.3%). All patients had active CSF leakage at the time of the study. Seventeen cases (70.8%) were spontaneous, five cases (20.8%) were traumatic and two cases (8.4%) were iatrogenic after endoscopic surgery. None of the patients with spontaneous CSF fistula had raised intracranial pressure.

No cases had a history of meningitis. The period of CSF leak prior to MRI and surgery ranged between 9 months and 8 years (average 26 months). Rhinorrhea was from the right side in 14 cases (58.4%) and left in 10 cases (41.7%) with no bilateral cases.

MR gadolinium enhanced cisternography confirmed the CSF leak and determined the site of the defect as a bright tract using T1WI in 22/24 (91.7%) cases (Figs. 1 and 2).

Two cases of spontaneous CSF rhinorrhea could not be detected by MR cisternography. In one of these cases, the defect was localized (small defect <1 cm) and treated on endoscopy while in the second case, no defect could be detected on endoscopic interference. So MR gadolinium enhanced cisternography could determine the site of the defect in 22 (95.7%) of the 23 endoscopy recognized cases (Table 1). No false positive CSF leak was detected by contrast enhanced MR cisternography.

According to the site of CSF leak, MR cisternography revealed that the most common site was the ethmoidal roof as detected in 16/24, followed by the cribriform plate in 4/24 and 2 cases were in the sphenoid sinus (Figs. 3 and 4). HRCT showed bone defect in 17 cases (70.8%) however 2 false defects (11.8% of detected defects) were found in posterior ethmoid by HRCT while detected in anterior ethmoid (small) during endoscopic repair (Table 2).

Bilateral defects were not encountered. Six (25%) patients had headache after lumbar puncture attributed to low pressure, headache was mild, self limited and stopped after the patient lay flat without analgesic. No neurological, cognitive, behavioral or hemodynamic changes were detected. Moreover no allergic reactions to gadopentetate dimeglumine were reported.

Specificity, sensitivity, PPV, NPV and accuracy were reported to be 100%, 95.65%, 100%, 50%, and 95.83% and for HRCT were 33.33%, 65.22%, 88.2%, 11.1%, 61.5%, respectively. MR cisternography localization was statistically significantly improved CSF leak localization ($P = 0.009$) (Table 3).

4. Discussion

Cerebrospinal fluid (CSF) rhinorrhea is a potentially dangerous problem (6). Persistent CSF leaks are usually repaired surgically (1,3) to prevent subsequent recurrent CSF leakage, pneumocephalus and infectious meningitis (10–12).

In this study, the presence of CSF leak was based on full history taking, clinical examination including, simple measures like asking the patients to bend down the head and strain beside endoscopic examination.

β2-Transferrin assay is the best laboratory investigation for detection of CSF as it is sensitive, specific and noninvasive (13). Since β2-transferrin assay was not available and not cost-effective, it had not been used in this study.

Accurate localization of the site of the CSF fistula is challenging for neuro-radiologists as well as surgeons.

Preoperative definition of leaking site is crucial as the approach for repair is tailored according to the preoperative defined detailed site of leak (4,7,8).

Precise preoperative identification of a CSF fistula helps in surgical planning and enhances the chances of a successful repair (5,6). Accurate diagnosis and localization of a dural defect often involve multiple imaging studies (1,3).

A greater proportion of the CSF leaks in the patients resolved spontaneously (2). Therefore, only the cases with persistent CSF leak more than 3 months were included in the current study to avoid unnecessary MRI in resolved cases.

The most common site of CSF leak was the ethmoidal roof cribriform plate (6 cases), in agreement with the results of Wakhloo et al. (9).

This may be attributed to that most of our cases were spontaneous CSF leak. This is in accordance with the published literatures that state the cribriform and ethmoid areas are particularly vulnerable to development of spontaneous leaks because of the presence of maldevelopments with extension

Table 3 Specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV) and accuracy of MR cisternography localization for CSF leak.

	Specificity (%)	Sensitivity (%)	PPV (%)	NPV (%)	Accuracy (%)	Chi-square	*p* value
MR cisternography localization	100	95.65	100	50	95.83	6.769	0.009*
HRCT localization	33.33	65.22	88.2	11.1	61.5		

* Significant.

of subarachnoid space through the foramina of the cribriform plate (9).

Most cases are spontaneous, and the most common site of CSF rhinorrhea is the anterior cranial fossa (anterior ethmoidal roof and cribriform plate), where the dura matter is particularly adherent to the thin overlying bone (9).

Jinkins et al. (7), stated that intrathecal gadopentetate dimeglumine administration was used to enhance CSF leakage through a putative dural defect in patients clinically suspected of having CSF rhinorrhea by means of lumbar puncture, and injection of a single dose of 0.5 mL of gadopentetate dimeglumine into the lumbar subarachnoid space.

The present study involved 24 cases (16 men and 8 women, aged 10–66 years) of CSF rhinorrhea, 17 spontaneous cases, 5 traumatic cases and 2 iatrogenic cases with preceding multislice CT for bone defect and T2WI positive findings in the form of hyperintensity CSF in the ethmoid sinuses. Gadolinium-enhanced MR cisternography was performed in all cases and showed positive contrast enhanced CSF leak in 22 cases, however, no false positive CSF leak was detected by contrast enhanced MR cisternography.

The main benefit of contrast enhanced MR cisternography is the significant contrast of the bright signal of the injected Gd-DPTA against the low signal para nasal sinuses and their mucosal linings at T1 w, consistent with Jinkins et al. (7), who found that MR contrast enhanced cisternography demonstrated positive findings in 13/15 cases of CSF rhinorrhea and negative findings in two.

MR contrast enhanced cisternogram showing accuracy rate of 95.83%.

Our findings were correlated surgically in 22 (95.7%) of the 23 diagnosed cases with repair of the defect. MR contrast enhanced cisternogram showed accuracy rate of 95.83% in the operated cases (22/24 cases).

Post technique headaches were detected in 6 (25%) cases which is explained by lumbar puncture exerted iatrogenic CSF space postural hypotension similar to explanation of Zeng et al. (14), however, no other hazards were detected immediately or after MRI owing to the use of low dose of gadolinium for diagnostic enhancement of the subarachnoid space as found by Zeng et al. (14), who stated that the results of initial human studies have shown that the low doses of intrathecal gadopentetate dimeglumine that are adequate for diagnostic enhancement of the subarachnoid space of humans at MR imaging do not manifest clinical evidence of gross physical or neurological abnormalities, CSF changes or electroencephalographic alterations after gadolinium-enhanced MR cisternography.

Besides, patients may be uncomfortable because of the invasion and the risk of intracranial infection cannot be neglected (2). The sensitivity of HRCT was 65.22% less than results of (2) while perfect sensitivity (100%) could be achieved with MR cisternography localization alone. That is better than previously reported sensitivity of fat-suppressed T2-weighted MRI (88.88%) even better than sensitivity reported after superimposing the CTs and MRIs to localize the CSF leakage site (89.74%). Beside that MRI details the intracranial anatomy and pathology in multiple planes (2). It was stated that CT and MRI seem to be complementary in the diagnosis of CSF leaks (2,4,6,7). However from our results we see that the main role of CT is detailed bony anatomy of the nose and paranasal sinuses needed for endoscopic approach. While localization with MR cisternography alone is perfectly sensitive and specific and highly accurate. This could be attributed to its high-contrast resolution, absence of bony artifacts, and direct multi-planar imaging (4). So we disagree with (4) in multiple basilar skull fracture. The combination of the HRCT and MR cisternography increases the diagnostic ratio of active CSF leak.

The specific site of a dural tear and therefore the active CSF leak cannot be confirmed with the HRCT (1,12) as it relies on the presence of indirect signs, such as fractures, bone defects, pneumocephalus, meningocele, cephalocele, mucous swelling, and air–fluid levels in the paranasal sinuses, to establish the presence of CSF leak without confirmation that the defect depicted is the actual cause of dural disruption (14).

4. Conclusions

Intrathecal low dose gadolinium-enhanced MR cisternography followed by T1w is a sensitive technique as it detects the high signal of Gd-DTPA against the low signal mucosal lining of PNS.

Intra-thecal gadolinium enhanced MR cisternography is highly reliable and accurate for pre-operative localization of the defect in cases of CSF rhinorrhea. Apart from self limited headache, no adverse effect occurred so it is relatively safe.

Conflict of interest

We have no conflict of interest to declare.

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