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# The contribution of 3D-CISS and contrast-enhanced MR cisternography in detecting cerebrospinal fluid leak in patients with rhinorrhoea

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**ABSTRACT.** The aim of this prospective study was to evaluate the value of unenhanced (three-dimensional constructive interference in steady state (3D-CISS)) and contrast-enhanced MR cisternography (CE-MRC) in detecting the localisation of cerebrospinal fluid (CSF) leak in patients with rhinorrhoea. 17 patients with active or suspected CSF rhinorrhoea were included in the study. 3D-CISS sequences in coronal and sagittal planes and fat-suppressed $T_1$-weighted spin-echo sequences in three planes before and after intrathecal contrast media adminstration were obtained. Images were obtained of the cribriform plate and sphenoid sinus. In addition, high-resolution CT (HRCT) was performed in order to evaluate the bony elements. The leak was present in 9/17 patients with 3D-CISS and 10/17 patients with CE-MRC. The leak from the cribriform plate to the nasal cavity in six patients and from the sphenoid sinus in four patients was nicely shown by CE-MRC. Eight of those patients were surgically treated, but spontaneous regression of the symptoms in two precluded any intervention. The leak localisations shown with CE-MRC were fully compatible with surgical results. The sensitivities of HRCT, 3D-CISS and CE-MRC for showing CSF leakage were 88%, 76% and 100%, respectively. In conclusion, 3D-CISS is a non-invasive and reliable technique, and should be the first-choice method to localise CSF leak. CE-MRC is helpful in conditions when there is no leak or in complicated cases with a positive $\beta$2-transferrin measurement.

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Cerebrospinal fluid (CSF) leaks generally occur following trauma and can cause serious complications, *e.g.* meningitis, unless treated properly [1]. A CSF fistula can cause rhinorrhoea if it causes a communication between the subarachnoid space and sinonasal cavity. It was shown 50–60 years ago that correct localisation of the defect is the mainstay of surgical treatment [2].

In patients with a suspected CSF fistula, it is difficult to detect the leak localisation with routine cranial CT, MRI or radionuclide cisternography (RC) [3], even though it is necessary to detect the localisation before surgical treatment. High-resolution CT (HRCT) is helpful for detecting defects in the bony elements, but direct evaluation of the leak is not possible, which is the major limitation of the technique [4, 5]. CT cisternography (CTC) can also show the leak localisation, but ionising radiation and the application of iodine-based contrast material are the major disadvantages of this technique [3].

In the literature, there are a limited number of articles concerning the value of unenhanced MR cisternography (three-dimensional constructive interference in steady state (3D-CISS)) and contrast-enhanced MR cisternography (CE-MRC) obtained with fat-suppressed (FS) $T_1$ weighted sequences for demonstrating CSF leak [3–8]. The aim of this prospective study was to explore the value of unenhanced and enhanced MRC in patients with rhinorrhoea.

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## Methods and materials

17 patients who were referred to our clinic between January 2003 and July 2008 with active or suspected CSF rhinorrhoea were included into the study. None of the patients had epilepsy, neoplasm or additional neurodegenerative diseases. The patients comprised 13 males and four females aged between 11 years and 70 years (mean age, 32 years). $\beta$2-transferrin levels were obtained in eight patients in order to validate the diagnosis of rhinorrhoea. In the other patients, $\beta$2-transferrin levels were not obtained, either because of the lack of symptoms at the time of consultation or because the patient underwent an emergency operation owing to trauma. CSF leak occurred as a result of trauma in 11 patients and following endoscopic sinus surgery in two patients. The rest of the patients had no history of trauma or surgery, but three were undergoing follow-up because of recurrent meningitis (suspected spontaneous rhinorrhoea) and one had active spontaneous rhinorrhoea. All of the patients were examined by an experienced neurosurgeon (blinded to the study) before the MRC examination; no signs and symptoms of meningitis were

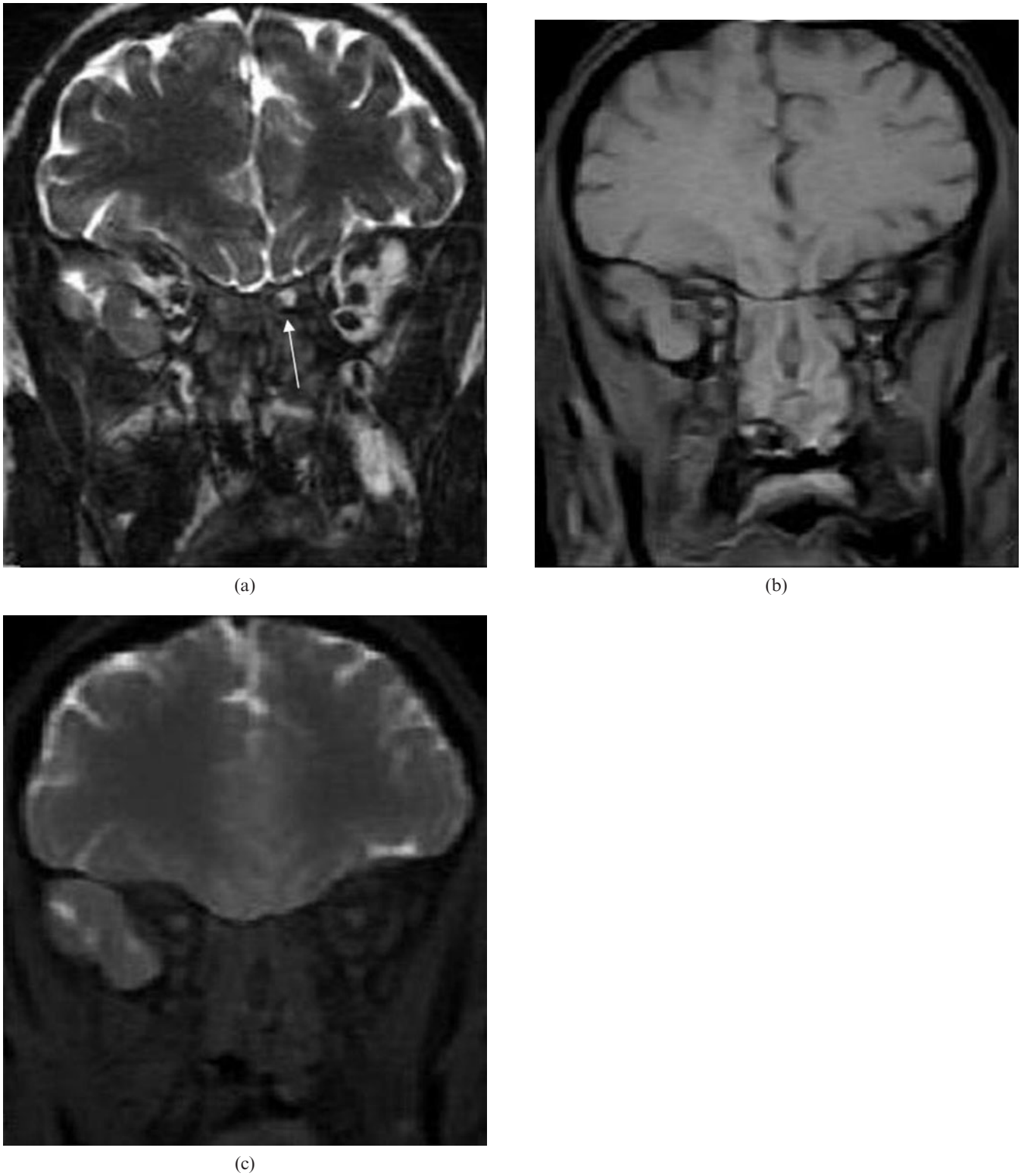

**Figure 1.** A 24-year-old male patient with rhinorrhoea after trauma (Case 2). (a) Coronal three-dimensional constructive interference in steady state (3D-CISS) image showing vague hyperintensity at the left ethmoidal cells suspicious for cerebrospinal fluid leak (arrow). (b,c) Coronal contrast-enhanced MR cisternography (CE-MRC) images showing that the cribriform plate is intact and there is no leak.

detected. Two paediatric patients with clinical signs of meningitis were excluded from the study. The study protocol was approved by the institutional ethics committee. Informed consent was obtained from every patient.

The examinations were performed on a 1.5 T MR scanner (Magnetom Vision Plus; Erlangen Siemens). The patients were placed in the prone position during the examinations. $T_1$-weighted (T1W) FS Spin-echo images were obtained in three planes (repetition time/echo time

**Table 1.** The findings detected on HRCT, 3D-CISS and CE-MRC

| No. | Age/ sex | History | β2 transferrin | HRCT | 3D-CISS | Gd-enhanced MR cisternography | Side-effects | Progress |
|---|---|---|---|---|---|---|---|---|
| 1 | 11/M | Trauma | Positive | Right cribriform plate defect | Leak from right cribriform plate | Leak from right cribriform plate | Headache | Operated and improved clinically |
| 2 | 24/F | Trauma | Not measured | No defect | Leak from left cribriform plate | No leak | None | Follow-up |
| 3 | 11/M | Trauma | Not measured | Temporal bone defect | No leak | No leak | None | Follow-up |
| 4 | 30/M | Trauma | Positive | No defect | No leak | Right sphenoidal leak | Headache | Operated and improved clinically |
| 5 | 54/M | Meningitis | Positive | Right sphenoidal sinus defect | Right sphenoidal leak | Right sphenoidal leak | None | Operated and improved clinically |
| 6 | 12/M | Trauma | Not measured | No defect | No leak | No leak | Fever | Follow-up |
| 7 | 49/M | Trauma | Not measured | Right frontal sinus and right cribriform plate defect | Leak from right cribriform plate | Leak from right cribriform plate | None | Spontaneous resolution |
| 8 | 29/M | Meningitis | Positive | Left cribriform plate defect | No leak | Leak from left cribriform plate | Headache | Operated and improved clinically |
| 9 | 19/F | Spontaneous | Not measured | No defect | No leak | No leak | Headache | Follow-up |
| 10 | 35/M | Trauma | Positive | Right cribriform plate to planum sphenoidale | Right sphenoidal leak | Right sphenoidal leak | None | Operated and improved clinically |
| 11 | 39/M | Trauma | Not measured | No defect | No leak | No leak | None | Follow-up |
| 12 | 70/M | Endoscopic surgery | Not measured | No defect | No leak | No leak | None | Follow-up |
| 13 | 34/M | Trauma | Positive | Planum sphenoidale defect | Leak from planum sphenoidale | Leak from planum sphenoidale | Headache | Operated and improved clinically |
| 14 | 53/F | Endoscopic surgery | Not measured | No defect | Leak from right cribriform plate | Leak from right cribriform plate | None | Spontaneous resolution |
| 15 | 18/M | Trauma | Positive | Left cribriform plate defect | Leak from left cribriform plate | Leak from left cribriform plate | None | Operated and improved clinically |
| 16 | 18/F | Meningitis | Not measured | No defect | No defect | No defect | None | Follow-up |
| 17 | 33/M | Trauma | Positive | Right cribriform plate defect | Leak from right cribriform plate | Leak from right cribriform plate | None | Operated and improved clinically |

M, male; F, female; HRCT, high-resolution CT; 3D-CISS, three-dimensional constructive interference in steady state; CE-MRC, contrast-enhanced MR cisternography.

(TR/TE) 539/12 ms, flip angle 90°, matrix 192 × 256, number of excitations (NEX) 2, slice thickness 3 mm, field of view (FOV) 25 × 25 cm, number of slices 14) before contrast medium administration. 3D-CISS sequences were obtained in sagittal and coronal sections. Parameters of this sequence were as follows: TR/TE 12.3/5.90 ms, flip angle 70°, matrix 230 × 512, NEX 2, effective thickness 0.7 mm, FOV 26 × 26 cm, slab thickness 48 mm. The sections included anterior cranial fossa and paranasal sinuses. The acquisition time of pre-contrast MRC and 3D-CISS sequences was approximately 15 min. Intrathecal gadopentetate dimeglumine (1 ml of 0.5 mmol) (Magnevist; Schering, Germany) was administrated with a 26-gauge needle (via lumbar puncture) and the patient was allowed to rest in the prone position in an observation room. T1W FS images were obtained in three planes in the prone position 1–2 h after contrast material administration. The duration of post-contrast MRC was approximately 10 min. The patients were then clinically followed up for 24 h after the MR examination.

The criteria for a CSF fistula on a 3D-CISS sequence were as follows [5–7]: (i) the presence of a defect between the bone–dura interface and (ii) hyperintense CSF or continuation of CSF towards paranasal sinuses. In addition to this, extracranial extension of brain tissue or meninges or soft-tissue intensity at the paranasal sinuses, representing a sinus tract, were also accepted as signs of a fistula. 3D-CISS images were accepted as negative for fistula if the border between the hyperintense CSF signal and paranasal sinuses–lamina cribrosa was clearly depicted. The most significant positive sign on CE-MRC was the extravasation of contrast agent to the paranasal sinuses or nasal cavity. Enhanced and non-enhanced images were analysed together in order to avoid false-positive results. During surgical intervention, a bone–dura defect or parenchymal–meningeal herniation was sought and accepted as a positive finding for leak localisation when found. The patients were followed during regression of the symptoms after surgical treatment in order to verify that the leak localisations were correctly demonstrated and treated.

All patients were subjected to HRCT imaging of the paranasal sinuses in the coronal plane before MRC examinations. One patient had an RC performed in an outside hospital before an MRI examination. Those images were evaluated before the MRC images by an experienced neuroradiologist (M.P.). 3D-CISS images, as well as MRC images, were evaluated alongside HRCT images in a different session by two experienced radiologists (O.A; B.H), and the decision was made in consensus. Sensitivity values of HRCT, 3D-CISS and CE-MRC were calculated according to Nilsson et al [9].

## Results

Active CSF leak was validated with $\beta$2 transferrin level measurements in eight patients. The findings detected on HRCT, 3D-CISS and CE-MRC images are listed in Table 1. During the 24-h follow-up period after CE-MRC examination, none of the patients suffered seizures or allergic reactions or showed neurological symptoms. Five patients (30%) had a postural headache, which responded well to conventional painkillers or spontaneously resolved within 48 h. One paediatric patient had fever that resolved with antihistaminics, which was accepted as drug-related fever owing to contrast agent.

CSF leak from the cribriform plate to the nasal cavity was demonstrated on 3D-CISS images in six (30%) patients and to the sphenoid sinus in three (18%) patients. No leak was detected in eight (52%) patients. Uniform filling of the basal cisterns with gadopentetate dimeglumine (Gd-DTPA) was depicted in all of the patients on images obtained 1 h after intrathecal contrast media administration. In CE-MRC images, CSF leak from the cribriform plate towards the nasal cavity was demonstrated in seven (41%) patients and towards the sphenoid sinus in three (7%) cases. No leak was detected in seven (42%) patients.

Eight out of 10 CSF leak localisations demonstrated on CE-MRC were confirmed during surgical exploration and treated with dural graft implantation. None of these patients showed signs of recurrence of symptoms. Two patients whose symptoms resolved spontaneously with bed rest before surgical exploration were subjected to follow-up. During follow-up, the symptoms resolved totally and surgical intervention was cancelled. One patient had suspicious findings at the left side of the cribriform plate on 3D-CISS images, although no leak was detected on CE-MRC (Figure 1). In seven patients, leak localisation was not detected on CE-MRC and these patients were treated conservatively. Those patients were then subjected to follow-up after resolution of their symptoms with medical treatment; they were not operated on, as their symptoms resolved totally within one year.

In eight out of 10 patients with a CSF leak detected on CE-MRC images, defects in bony elements on HRCT images were also detected (Figure 2). The HRCT findings of those eight patients were consistent with both CE-MRC findings and surgical results (Figure 3), whereas, in the other two patients, HRCT images were unable to show the defect. In addition, in one patient whose symptoms resolved during follow-up, no leak was detected on CE-MRC images but a defect in the temporal bone was seen on coronal HRCT images (false-negative). The sensitivities of HRCT, 3D-CISS and CE-MRC showed 88%, 76% and 100% CSF leakage respectively.

## Discussion

Rhinorrhoea can be described as the leakage of CSF to the nasal cavity from a defect in the subarachnoid space [1, 10]. This abnormal drainage route can cause serious complications, such as meningitis or abscesses [9]. Most of them occur because of defects in the anterior cranial fossa [5, 6]. The aetiology consists of trauma, endoscopic surgery, congenital defects (meningocele, meningoencephalocele and skull base malformations), hydrocephalus and erosions (the last two owing to tumour or infection) [10]. It can also occur spontaneously [1, 11]. The leak after trauma usually resolves spontaneously without any intervention [4]. The differential diagnosis of serous rhinorrhoea includes allergic and hyperactive rhinopathy, sinusitis, paranasal cyst, polyps of the nasal or paranasal sinus, foreign body or tumour [8, 11].

In patients with rhinorrhoea, the diagnosis should first be confirmed by measurement of $\beta$2-transferrin levels. This protein is specific for CSF, and a small amount of rhinal discharge (0.4 ml) is adequate for the evaluation [1]. Glucose and protein level measurements made in the past are no longer carried out in many institutions [11]. In a patient suffering from rhinorrhoea, the correct demonstration of the leak localisation is of the utmost importance while planning the surgical intervention [1]. Many imaging methods, including conventional cranial radiography–polytomography, RC, intra-operative dye injection and CTC, have been used in order to detect the correct localisation of CSF leakage, but the diagnostic yield of these methods is limited [4]. RC is also unsuccessful at showing the leak localisation owing to its low resolution [1]. The presence of ionising radiation is another limitation [3]. In our study, in one patient with suspected leak to the right nasal cavity on RC images, leak into the right frontal sinus and the correct localisation of the defect was demonstrated by CE-MRC. CTC also involves ionising radiation, and the amount of iodinated contrast material used is much more than that for CE-MRC (8–10 ml). The high viscosity of the contrast material used for CTC poses application difficulties, and larger needles (18–22 gauge) have to be used [3]. According to our experience, high headache frequency after CTC can be attributed to this.

In patients with rhinorrhoea, HRCT can indicate the leak localisation by detecting the bone defect [1]. However, CSF leakage may not be present at the congenital or traumatic defect localisation [3]. In one of our patients, no leak was detected even though there was a bone defect on HRCT images. Because of cases such as this, HRCT is used in combination with other modalities such as RC, CTC and unenhanced MRC for surgical intervention in many institutions [1–3]. The sensitivity and specificity of HRCT are reported as 84–95% and 57–100%, respectively [1, 4, 12–16]. The sensitivity of HRCT increases significantly when combined with MRC [1, 13–17]. The sensitivity of HRCT is 88% according to our study.

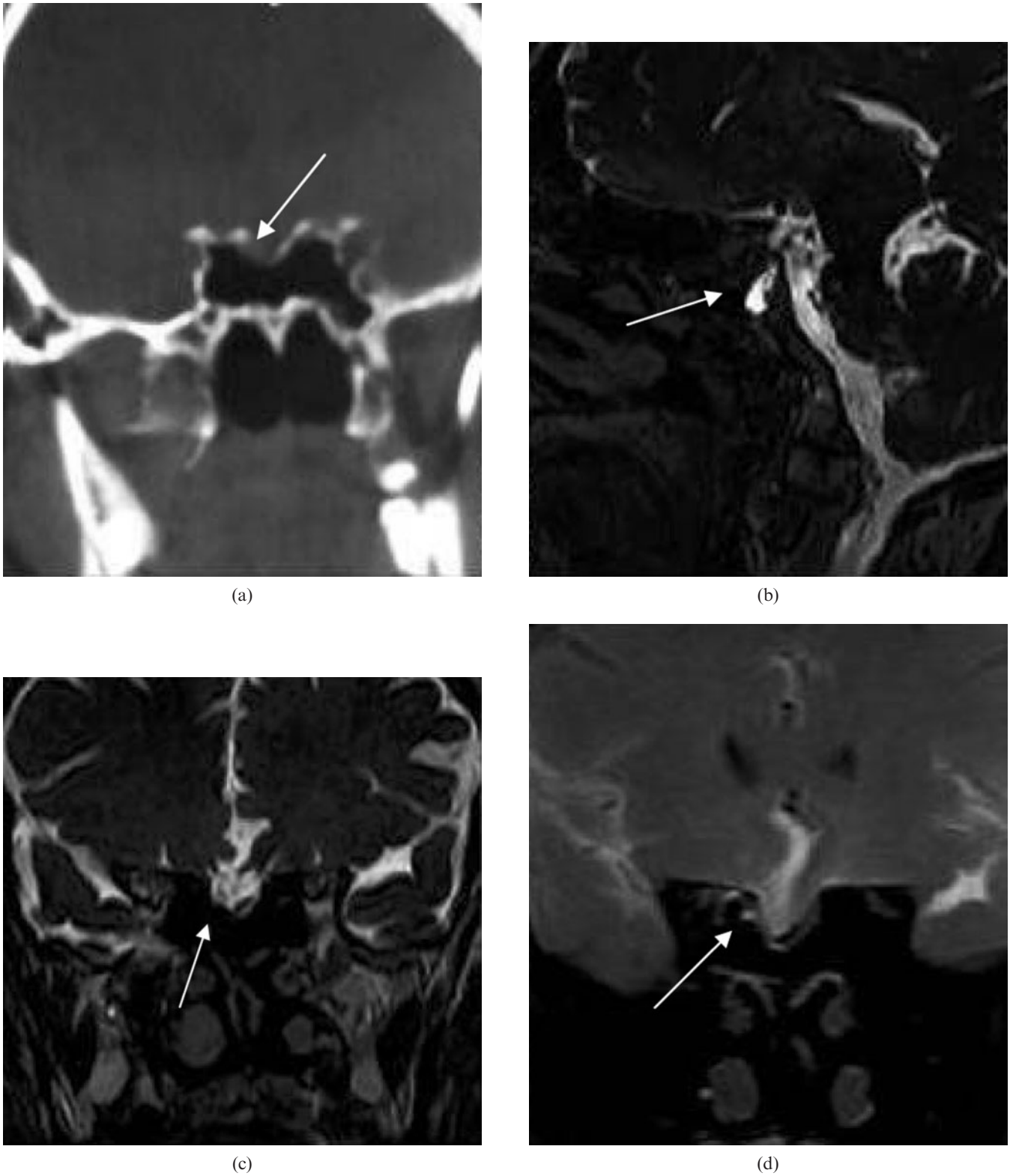


**Figure 2.** A 54-year-old man with recurrent meningitis (Case 5). Coronal high-resolution CT images demonstrate a fracture at the roof of the right sphenoid sinus (arrow in (a)). Leak towards the sphenoid sinus (arrows) is seen in (b,c) sagittal coronal three-dimensional constructive interference in steady state (3D-CISS) images and (d) a coronal contrast-enhanced MR cisternography (CE-MRC) image. Leak was confirmed via surgery.

CE-MRC was first performed by Di Chiro et al in 1986 [18] (see also [6]). In this study, CSF leak in two dogs was detected after intrathecal contrast medium administration. Gd-DTPA shortens the $T_1$ relaxation time of hydrogen protons in CSF, and CSF becomes hyperintense [15–19]. After intrathecal contrast medium administration, significant contrast difference occurs between CSF and the bone–brain parenchyma. In the literature, it is

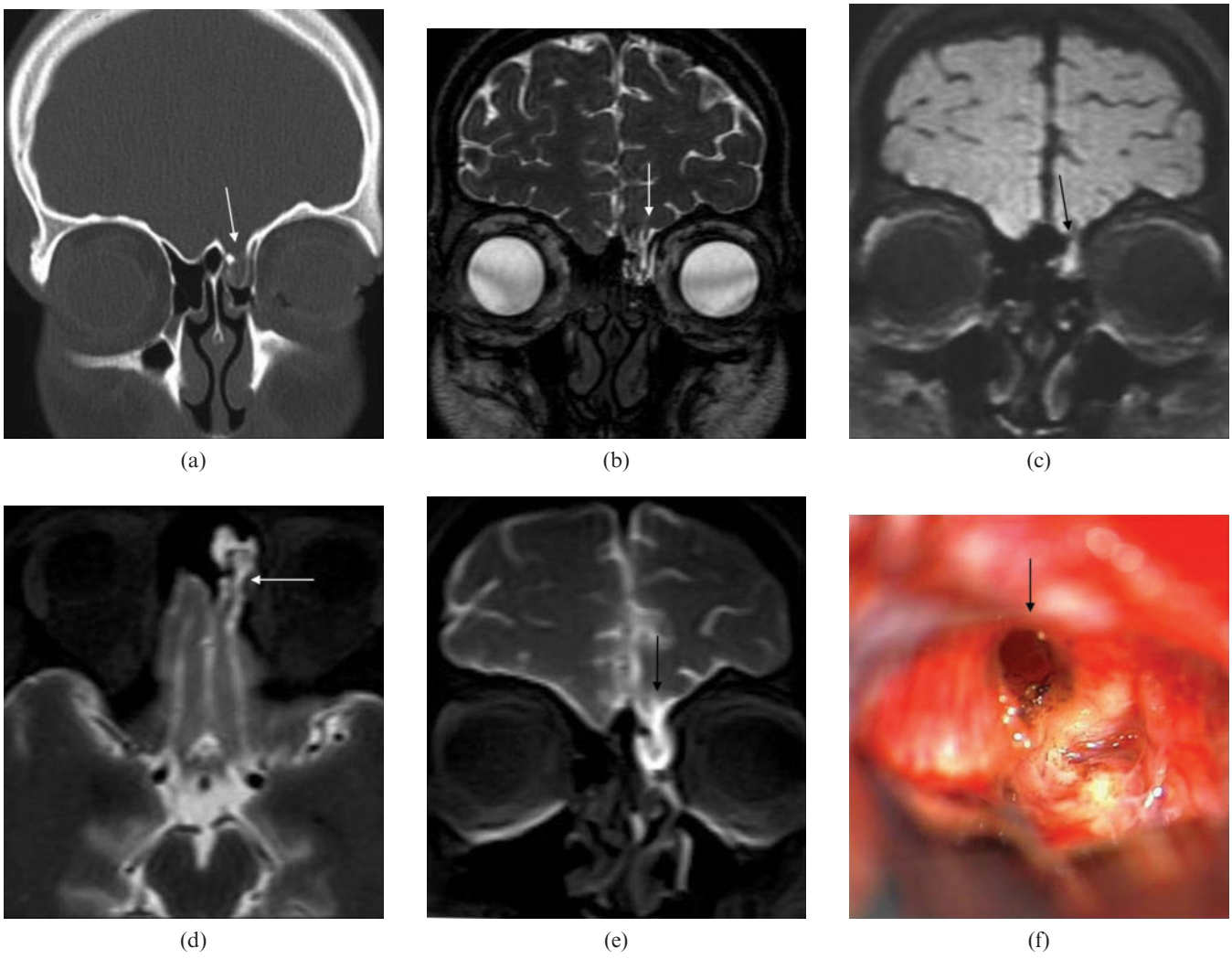


**Figure 3.** An 18-year-old man with recurrent meningitis after trauma (Case 15). Coronal high-resolution CT images demonstrate the bone defect in the left cribriform plate (arrow in (a)). (b) Cerebrospinal fluid (CSF) leak from the left cribriform plate is nicely seen on the coronal three-dimensional constructive interference in steady state (3D-CISS) image (arrow). The size and relationship of the defect with neighbouring structures and CSF leak (arrows) is clearly depicted on (b) non-enhanced coronal, (d) axial and (e) coronal contrast-enhanced MR cisternography (CE-MRC) images. (f) The defect of the cribriform plate (arrow) was proven surgically.

reported that intrathecal adminstration of 1 ml (0.5 mmol) Gd-DTPA causes neither neurological or behavioural abnormalities nor early or late complications [3, 15–20]. It is also still used for evaluating CSF dynamics and arachnoid cysts, and the safety of this dose was verified in all of the studies [19, 20]. However, intrathecal administration of Gd-DTPA is not accepted worldwide [17, 19].

In our study, contrast medium diffused in the subarachnoid space and details of the structures containing CSF became visible. Depiction of hyperintense CSF and the leak was easy owing to the hypointense signal of fat tissue and structures adjacent to the subarachnoid space in T1W with FS images. Inflammatory areas, which are seen as hyperintense regions on 3D-CISS images and cause false-negative results, do not cause these problems on CE-MRC. In our study, no significant adverse reaction occurred after CE-MRC except postural headache, which was resolved with painkillers. Headache after the procedure was attributed to lumbar puncture, as in the literature [3, 17]. Headache of a similar pattern was also seen after CTC in our patients. No neurological or behavioural abnormalities occurred after CE-MRC in our patients. Intrathecal administration of Gd-DTPA was safe, parallelling recent literature [3, 15–19].

During the past 10 years, studies emphasising the value of CE-MRC in rhinorrhoea and showing leak localisations have been published [1, 3, 11–13, 15–17, 21]. Jinkins et al [17] detected CSF leak in 13 of 15 patients. Seven of those underwent surgery and CE-MRC results correlated well with the surgical information. Reiche et al [15], in their study of 10 patients, detected five CSF fistulae, four of which correlated with surgery. In another study [12], leak was detected in nine out of 10 patients; in one patient, leak localisation was found and repaired during the surgery (false-negative). In our study, the leak was detected correctly in 10 of 17 patients with CE-MRC; eight patients were treated surgically and their leak localisations correlated well with CE-MRC images. The sensitivity of CE-MRC is reported as 84% [3]. The sensitivity of CE-MRC is 100%, according to our study.

The literature concerning the utility of heavily $T_2$-weighted thin-slice 3D-CISS images in rhinorrhoea is limited, as well as the numbers of patients included in those studies [5, 6, 8, 12]. Brain parenchyma and fat are suppressed with this sequence, and CSF is hyperintense. It can demonstrate that CSF fistulae, as with the paranasal sinuses and the bones, indirectly form a dark background [1]. The criteria for depicting CSF fistulae in 3D-CISS sequences are the continuation of a hyperintense CSF signal towards the extracranial area and extracranial herniation of the meninges or brain. These criteria are also non-specific, as for HRCT. Hyperintense inflammatory processes, such as sinusitis or mastoiditis, and viscous secretions can cause false-positive results in 42% of patients [11, 15, 18]. In different studies, the sensitivity and specificity of FS heavily $T_2$-weighted unenhanced MRC is reported to be 80–90% [1, 4, 6, 11, 15]. The sensitivity of 3D-CISS is 76%, according to our study. Increasing the contrast between CSF and the adjacent structures and obtaining thin slices with a high spatial resolution and signal-to-noise ratio are the advantages of this sequence [5]. In addition to these, it is superior to CTC, as images in three planes are available, ionising radiation and contrast medium administration is not used, it is non-invasive and images at skull base level without artefacts are available [1, 2, 4–6, 12].

Goel et al [12] compared the 3D-CISS, CE-MRC and CTC imaging findings of nine patients with rhinorrhoea with surgical results. In this study, leak localisation could be seen on CISS sequences in six of the nine patients whose leak was surgically confirmed. Conversely, CTC depicted the leak in only three patients. In our study, CSF leak was depicted on CE-MRC and confirmed with surgery in eight patients. 3D-CISS was able to show the leak in six of these patients. 3D-CISS could not detect the leak in two patients. Furthermore, one patient had suspicious findings at the left side of the cribriform plate on 3D-CISS images, but no leak was detected on CE-MRC.

The fundamental limitation of our study is the lack of a standard reliable diagnostic modality other than surgical confirmation of pathology. Therefore, false-negative rates and specificity of HRCT, 3D-CISS and CE-MRC cannot be evaluated statistically. Confirmation of the diagnosis with $\beta$2-transferrin measurements was not possible in nine patients, which is another limitation. This measurement was not accomplished in trauma patients, owing either to their need for emergency procedures or technical insufficiency in our emergency department. In the rest of the patients, rhinorrhoea was confirmed with $\beta$2-transferrin measurements. All cases with a positive result in the $\beta$2-transferrin test had CSF leak that was determined by CE-MRC. We suggest the use of this test in all patients with suspected CSF leak.

False positivity on 3D-CISS images may be caused by the high frequency of susceptibility artefacts on 3D-CISS sequences, as in one of our cases. Another limitation of our study was a lack of comparison between 3D-CISS sequences and 3D-turbo-spin echo (TSE) sequences, which are less sensitive to susceptibility artefacts. We could not add 3D-TSE sequences to our study protocol because of the possible increase in examination time.

Intrathecal administration of Gd-DTPA is not approved in many countries and is therefore difficult to implement in clinical practice. The number of patients in our study is limited, but the results look promising. New studies with a follow-up of patients looking at the long-term complications of contrast medium administration are warranted.

## Conclusions

In patients with rhinorrhoea, 3D-CISS sequences should be the method of choice owing to their lack of ionising radiation and contrast medium administration, high soft-tissue contrast, non-invasiveness, lack of artefacts from bony elements and multiplanar image capacity. CE-MRC may be useful in more complicated situations, *e.g.* in cases with a positive $\beta$2-transferrin test and no CSF leak or suspicious leak on 3D-CISS images. FS T1W images before intrathecal contrast medium administration are suggested in order to avoid false-positive results.

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