European Annals of Otorhinolaryngology, Head and Neck diseases (2012) 129, 77—81

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ORIGINAL ARTICLE

Endoscopic repair of anterior or middle skull base cerebrospinal fluid leaks after tumour resection

G. Mortuaire [a,*], S. Vandeville [a], R. Assaker [b], D. Chevalier [a]

[a] *Service d'ORL et de chirurgie cervico-faciale, hôpital Claude-Huriez, CHRU de Lille, place de Verdun, 59037 Lille cedex, France*
[b] *Clinique de neurochirurgie, hôpital Roger-Salengro, CHRU de Lille, rue du Pr-Émile-Laine, 59037 Lille cedex, France*

KEYWORDS
Endoscopy;
Skull base;
Cerebrospinal fluid leak

Summary
Objectives: This study analysed the factors influencing the risk of recurrence following endoscopic repair of CSF leaks of the anterior and middle skull base after endonasal skull base tumour resection.
Patients and methods: A retrospective review was conducted on 17 patients operated between May 2007 and December 2010 by endonasal endoscopic resection of anterior or middle skull base tumour who presented an intraoperative CSF leak. Epidemiological data (body mass index [BMI], age, gender) and type of leak (site, size) were studied.
Results: CSF leaks involved the roof of the ethmoid sinus (one patient), cribriform plate (three), posterolateral wall of the sphenoid sinus (six) or the sella turcica (seven). The CSF leak recurrence rate after the first endoscopic procedure was 29.4% (5/17). Failures were not influenced by gender, age, BMI or size of the leak. All recurrences involved the sella turcica or the lateral wall of the sphenoid sinus. The success rate after a second endoscopic procedure was 88.2%.
Conclusion: Endonasal endoscopic repair of anterior and middle skull base meningeal injuries after tumour resection is a minimally invasive and effective technique. The main challenge of this method consists of ensuring effective control of the postoperative defect after tumour resection in the sphenoidal region, as this region was the only potential risk factor for recurrence identified in this study.

Introduction

Cerebrospinal fluid (CSF) leaks of the anterior and middle skull base occurring during endonasal tumour resection can mostly now be repaired via the same endoscopic approach. Technical progress, the improved quality of endoscopes and the development of neurosurgical collaboration have facilitated the growth of this minimally invasive technique. Repair of CSF leaks is essential, as the risk of meningeal infectious complications is estimated to be 10% per year in the presence of an active CSF leak [1].

Many closure techniques (mucosal flaps, septal cartilage, septal and turbinate bone, fascia lata or fascia temporalis, abdominal fat) either intracranially (inlay) or extracranially (onlay) and fixation techniques (biological glue, silicone-coated sheet, resorbable mesh, balloon catheter) have been proposed, but no particular technique has been shown to

* Corresponding author. Tel.: +0320445672; fax: +0320445097.
E-mail address: g-mortuaire@chru-lille.fr (G. Mortuaire).

1879-7296/$ – see front matter © 2012 Published by Elsevier Masson SAS.
doi:10.1016/j.anorl.2011.10.003

be superior to another in terms of effective control of the leak [2]. Various modalities of perioperative care (lumbar drainage, osmotic diuretics such as mannitol) have also been proposed [3]. Regardless of the method, the efficacy of endonasal endoscopic repair is estimated to be 80 to 98% [2,4]. Identification of clinical and anatomical situations at risk of failure therefore constitutes an essential step in the repair procedure in order to adapt the closure technique.

The objective of this study was to identify these high-risk situations based on a review of failures of endonasal endoscopic anterior and middle skull base CSF leak repair following tumour resection.

Patients and methods

Population

A descriptive retrospective study was conducted on 17 consecutive patients treated between May 2007 and December 2010 by endonasal endoscopic resection of an anterior or middle skull base tumour involving the sphenoid sinus and presenting an intraoperative CSF leak.

This series comprised 11 men and six women with a median age of 47 years (range: 24 and 70 years). The tumour was situated in contact with the roof of the ethmoid sinus in four cases (23.5%) or the sella turcica or posterolateral wall of the sphenoid sinus in 13 cases (76.5%) (Table 1).

Surgical treatment

Endoscopic tumour resection and repair of the CSF leak were performed by the same otorhinolaryngologist or otorhinolaryngologist-neurosurgical team with the same neurosurgeon. For all patients, surgical equipment consisted of a video tower with a 150-Watt Xenon light source and a set of 4 mm, 0° and 30°, endoscopes equipped with an irrigation system. The patient was placed in 15° of reverse Trendelenburg position. The Digi-pointeur 6200 Collin® neuronavigation system was positioned by using the headlamp as reference point. Tumour resection was performed with a safety margin requiring skull base bone resection in 14 cases. An accidental tear was observed in one case (osteoma). In two cases (one oligodendroglioma and one chondrosarcoma), tumour-debulking surgery was performed prior to adjuvant therapy (Fig. 1).

The methods of closure of the CSF leak and maintenance of the duraplasty were defined according to the surgical protocol established by the operators on the basis of the data of the literature adapted to the site and size of the CSF leak. CSF leaks of the anterior skull base less than 1 cm in diameter were filled by a fat plug, followed by placing a fragment of turbinate mucosa or a fragment of fascia lata over the leak. CSF leaks of the anterior skull base larger than 1 cm in diameter after tumour resection were covered by a fascia lata inlay and onlay flap. CSF leaks of the middle skull base were closed by a fat plug covered by fascia lata. The sphenoid sinus was then filled with the remaining fat. One to 5 ml of Tissucol® biological glue (Baxter France, Maurepas, France) were deposited around the edges of the graft material. The duraplasty was maintained in place by Gélitaspon® (Gelita Medical B.V., Amsterdam, Netherlands) or Surgicel® resorbable mesh (Ethicon 360, Neuchâtel, Switzerland) for CSF leaks of the anterior skull base less than 1 cm in diameter or by carboxymethylcellulose-infused Rapid Rhino® balloon (ArthroCare ENT, Stockholm, Sweden) for CSF leaks of the anterior skull base more than 1 cm in diameter and for CSF leaks of the middle skull base. This balloon was left in place for 48 hours.

Postoperative bed rest was maintained for 48 hours. No lumbar drainage was performed and no osmotic diuretic was prescribed. Pneumococcal vaccination was planned at discharge.

Clinical follow-up comprised endoscopic assessment on D10 and at 1 month. Tumour follow-up was ensured by MRI 2 months after completing any adjuvant external beam radiotherapy, proton therapy or chemotherapy.

Statistical analysis

Data collected on an Excel® database (Microsoft France) were age, gender, body mass index (BMI), preoperative size and site of the CSF leak. Statistical analysis of these parameters was performed by MedCalc® software (MedCalc software, 9030 Mariakerke, Belgium). Frequencies were compared by Chi^2 test and means of non-paired independent series were compared by a Mann-Whitney non-parametric test. The limit of statistical significance for all tests was $p \leq 0.05$.

Results

Mean follow-up was 25 months (range: 12 months to 4 years). Five recurrences (29.4%) were observed after a median interval of 79 days (range: 15 days to 13 months). The

Table 1 Distribution of CSF leaks according to site and aetiology.

Anterior skull base (4)		Middle skull base (13)	
Anterior ethmoid (1)	Cribriform plate (3)	Roof of ethmoid sinus and sella turcica (7)	Posterolateral wall of sphenoid sinus (6)
Osteoma (1)	Esthesioneuroblastoma (1) Adenocarcinoma (1) Squamous cell carcinoma (1)	Pituitary macroadenoma (6) Chondrosarcoma (1)	Chondrosarcoma (1) Chordoma (2) Oligodendroglioma (1) Meningioma of clivus (1) Paraganglioma of clivus (1)

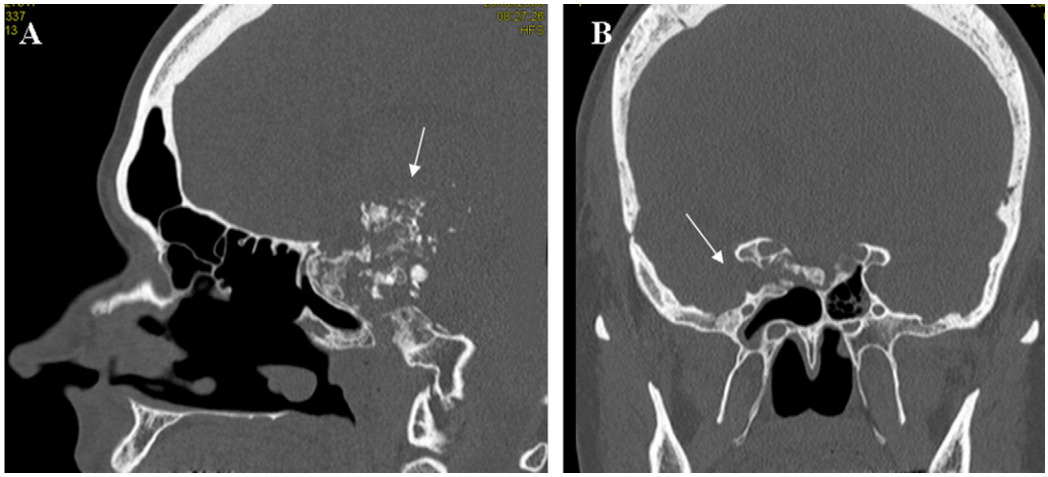

Figure 1 View of a chondrosarcoma of the middle skull base before endonasal tumour debulking surgery. Unenhanced computed tomography, bone window setting (sagittal [A] and coronal [B] sections). Calcified mass ($34 \times 37 \times 46$ mm) arising in the centre of the sella turcica with suprasellar extension and invasion of the right cavernous sinus. A transethmoidal incision had been performed for the initial histological diagnosis.

diagnosis was proposed on the presence of spontaneous clear rhinorrhoea and was confirmed by positive beta-2-transferrin assay on the collected nasal secretions. No case of spontaneous resolution of the CSF leak was observed after strict bed rest for 7 days. After a second endoscopic procedure, according to the same closure protocol depending on the site and size of the CSF leak, the CSF leak control rate was increased to 88.2%. A second recurrence was described for two patients initially treated for pituitary macroadenoma. One of these two patients required a transfacial paralateronasal procedure and the other patient required two complementary endoscopic procedures followed by a transfacial paralateronasal procedure to repair the CSF leak. Transfacial repair methods for these two patients were an iliac bone graft embedded in the sphenoid sinus after placement of the initial material (fat, fascia lata, bone paté). Closure of the sphenoidal orifice, before insertion of the carboxymethylcellulose-infused Rapid Rhino® balloon for 48 hours, was completed by a muscle flap in one case and a nasoseptal mucosal flap pedicled on the sphenopalatine artery in the other case. Lumbar drainage was ensured for 72 hours for the patient who was finally controlled after four operations. No meningeal infectious complications were observed.

Onset of the first recurrence was not related to age ($p = 0.39$) or gender ($p = 0.76$). The mean BMI was 29.6 kg/m^2 (range: 20.2 to 40.2). BMI was not statistically higher among patients with recurrent CSF leak (29.6 vs. 29.5, $p = 0.67$). All recurrences of CSF leak after a first endoscopic procedure involved the sphenoid sinus (sella turcica in three cases, posterolateral wall in two cases) (Table 2). The risk of recurrence was not related to the size of the CSF leak ($p = 0.83$).

Three of the five recurrences concerned patients treated for pituitary macroadenoma. Two recurrences were observed after treatment of a grade II chondrosarcoma of the sphenoid sinus and a grade B oligodendroglioma extending to the sphenoid sinus, treated by proton therapy and chemotherapy after endoscopic tumour debulking surgery, respectively.

Discussion

Endonasal endoscopic repair of CSF leaks of the anterior or middle skull base is a widely used method. This approach ensures primary repair of the leak in 80 to 90% of cases with limited morbidity and rapid postoperative recovery [4—8]. Precise identification of the site of the CSF leak is an essential factor ensuring successful surgery, especially in redo situations after failure of a first attempt of endoscopic closure. Some authors use intrathecal fluorescein injection to facilitate identification of the CSF leak, but a negative fluorescein test does not formally exclude the diagnosis of CSF leak. Based on a retrospective series of 47 patients in whom fluorescein injection was performed, Seth et al. reported that fluorescein was present at the operative site in 31 cases, but the false-negative rate was 26.2% [9]. In our study, the diagnosis of CSF leak was clearly confirmed intraoperatively, including in the case of fronto-ethmoidal osteoma, in which resection induced a limited CSF leak involving the roof of the ethmoid sinus at the junction between the root of the middle nasal turbinate and the anterior ethmoidal canal. This fluorescein test was not used in the five recurrent cases.

A very large number of closure techniques have been described in the literature. They are based on each surgical team's experience and allow a wide range of technical possibilities depending on the size and site of the CSF leak and local conditions (inflammatory diseases, redo surgery, tumour resection). It is difficult to compare the various closure techniques in terms of efficacy due to their diversity and the lack of definition of standard practices according to the aetiology and site of the CSF leak. Furthermore, most publications present a descriptive analysis of retrospective series that are not statistically comparable. In a retrospective analysis of 126 cases of endonasal repair of CSF leaks of the anterior skull base, Schick et al. obtained control of the CSF leak in 94.9% of cases after the first procedure with no significant differences according to the technique used [10]. Local grafts (turbinate and septal mucosa, septal cartilage, turbinate and septal bone) or regional grafts (fat, fascia temporalis or fascia lata) are the basic materials

Table 2 Aetiologies and sites of recurrences.

	Site	
	Middle skull base (5)	
	Roof of ethmoid sinus and sella turcica (3)	Posterolateral wall of sphenoid sinus (2)
Aetiologies	Pituitary macroadenoma (2)Oligodendroglioma (1)	Pituitary macroadenoma (1)Chondrosarcoma (1)

classically used. These materials can be placed either above (inlay) or underneath (onlay) the site of the leak. In a meta-analysis based on 14 series of patients treated between 1990 and 1999, Hegazy et al. did not reveal any significant difference between inlays and onlays in terms of the efficacy of the repair. Inlays are often proposed as first-line procedure to stabilize the duraplasty in contact with cerebral structures [2]. The onlay technique is used when dissection of the dura mater in contact with the leak is likely to cause a vascular or nerve lesion [2]. In the present series, the inlay technique was used when the defect was sufficiently large to allow introduction of the instruments and the graft, i.e. about 1 cm.

Analysis of failures of first-line endonasal endoscopic closure of CSF leaks is an essential element to improve endoscopic techniques in difficult situations. Intracranial hypertension, especially described in the context of spontaneous CSF leak attributed to a defect of CSF resorption inducing a pulsatile hydrostatic force on weak points of the skull base (cribriform plate, wing of the sphenoid), is considered to be a risk factor for recurrence [10,11]. In a retrospective study of 193 patients undergoing endoscopic repair of CSF leak, Banks et al. reported a significantly higher mean BMI in patients with spontaneous CSF leak [12]. Obesity has also been incriminated by some authors as a risk factor for recurrence, as it appears to be associated with higher CSF pressure [12,13]. In our study based on a small sample size, BMI was not statistically higher in the case of recurrence. Nevertheless, the presence of obesity must be taken into account when repairing CSF leaks, especially spontaneous leaks. The size of the defect has also been proposed as a possible risk factor for recurrence [10]. In his series of 127 endoscopically treated patients, Tabaee et al. considered that defects larger than 3 cm were associated with more difficult repair of the CSF leak [14]. Size was not a discriminant factor in our study. The small sample size and the larger size of defects of the anterior skull base during tumour resections, while recurrences occurred exclusively in the middle skull base, could account for this result.

The site of CSF leak, in terms of its accessibility and the nature of adjacent cerebromeningeal and vascular structures, is an important technical element. CSF leaks of the middle skull base involving the sella turcica and posterolateral wall of the sphenoid sinus are difficult to control. They also constitute zones of weakness in relation to CSF hydrostatic pressure [11]. In the present study, five recurrences concerned CSF leaks of this region. The sellar region is essentially the site of pituitary tumours and resection of these lesions can induce intraoperative CSF leak in 18.1 to 53.2% of cases [15]. In a review of 216 patients treated for a sellar lesion, Shiley et al. reported a higher risk of recurrence of CSF leak in the presence of intraoperative CSF leak [15]. In the present study, three of the five cases of recurrent CSF leak concerned patients with pituitary adenoma in whom a CSF leak was observed intraoperatively. When wide resection is required, the anatomical proximity of the internal carotid artery, optic nerve and cavernous sinus can make it difficult to ensure a bony support around the leak to stabilize the graft. CSF leaks of the posterolateral wall of the sphenoid sinus, lateral to the cavernous sinus, are at greater risk of recurrence due to the difficulties of endoscopic access [16]. This region is also a frequent site of spontaneous CSF leak occurring in a context of an overexpanded sphenoid sinus with an overdeveloped lateral extension into the greater wing [17].

CSF leak related to resection of a skull base tumour constitutes a risk factor for recurrence. Several factors are involved: satisfactory support for the graft may sometimes be difficult to achieve due to the size of the defect, surgery in a context of tumour recurrence may be associated with inflammatory changes and scarring that may alter the stability of the repair, and preoperative radiotherapy can alter tissue viability [18]. Two patients in the present study simply underwent tumour debulking surgery prior to adjuvant proton therapy or chemotherapy, which may account for the relatively unstable initial repair and the presence of scar tissue after adjuvant therapy, leading to failure of the repair.

Various treatment strategies can be proposed in these situations at high risk of recurrence. Exposure of the bony margins of the leak with resection of all adjacent mucosa is essential to obtain a stable support, facilitate detachment of the dura mater in the case of an inlay graft and prevent the risk of secondary mucocele [10]. For large defects, Tabaee et al. have proposed reconstruction in several layers according to a flow diagram comprising adipose tissue to fill any intracranial defects related to the tumour resection, fascia lata inlay graft, a septal bone inlay graft and then biological glue to stabilize the repair [14]. Kassam et al. proposed a similar procedure with a collagen matrix inlay graft [19]. For CSF leaks of the sphenoidal region, filling the sphenoid sinus with adipose tissue is recommended to maintain the graft in place over the leak [8]. A single or double nasoseptal mucosa flap with a pedicle based on sphenopalatine arteries can be used to reinforce the duraplasty from the os planum to the clivus according to a simple and reliable technique [12,20]. For CSF leaks of the posterolateral wall of the sphenoid sinus, a transpterygoid trans-sphenoid endoscopic approach can be used to obtain complete control of this region [16]. In the present study, two patients presenting with a second recurrence were controlled by the final operation comprising a small bone graft wedged in the sphenoid bone to maintain the fat graft. The nasoseptal pedicle flap was used in one case to provide vascularized tissue, but this flap could not be used in the other cases. A muscle graft was used to reinforce the repair after three initial failures.

Compression of the site of repair of complex CSF leaks by a balloon left in place for 48 to 72 hours helps to maintain the graft in place over the ethmoid sinus and as far as the clivus and allows minimally traumatic removal without dislodging the graft [19]. The value of first-line complementary lumbar drainage has not been clearly established [12,14], but a reduction of CSF pressure could help to maintain the graft in place and could facilitate its adhesion [2]. On the basis of a meta-analysis of 289 cases of endoscopic repair of CSF leak, Hegazy recommended the use of lumbar drainage for 3 to 5 days in situations at high risk of recurrences: spontaneous CSF leak, posttraumatic or postoperative CSF leak with hydrocephalus, CSF leak associated with meningocele and CSF leak with a large defect [2], but this strategy was not used in the present study. Nevertheless, as recurrences exclusively concerned CSF leak of the middle skull base, we now use lumbar drainage for large CSF leaks of this region following tumour resection.

Conclusion

Endonasal endoscopic repair of CSF leaks of the anterior and middle skull base following tumour resection is a minimally invasive and reliable method. Situations at high risk of recurrence concern CSF leaks of the sphenoidal region where local anatomical support and CSF hydrostatic pressure make control of the leak more difficult. Identification of these clinical situations allows improvement of the reconstruction technique comprising closure in two or three adipose and fibrous layers, maintenance of the repair by use of a balloon and postoperative lumbar drainage.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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