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Closure of cerebrospinal fluid leaks prevents ascending bacterial meningitis*

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SUMMARY

***Introduction**: Endoscopic surgery of the anterior skull base has become the standard procedure for the repair of cerebrospinal fluid (CSF) leaks of various origins. Closure of the leaks is believed to prevent ascending meningitis, although no report has specifically shown this.*
***Material and methods**: Retrospective chart study of 39 patients who underwent endoscopic skull base surgery from 1/1993 to 11/2002.*
***Setting**: Tertiary University Hospitals.*
***Outcome measurement:** Incidence of ascending meningitis after endoscopic skull base repair in patients with anterior skull base defects associated or not with meningitis and CSF leak.*
***Results**: Forty-one endoscopic repairs of anterior skull base defects of various origins were performed in 39 patients. Fifteen (36.5%) had suffered bacterial meningitis before surgery. Mean follow-up was 65 months (range 22-120). The defect was repaired using an "underlay" technique with lyophilized dura (n=11) or fascia lata (n=30), and covered with free mucosal grafts from either the middle or the inferior turbinates. Closure was achieved in 40/41 cases at first attempt. No recurrence of ascending bacterial meningitis was observed during follow-up in any of the fifteen patients who had previously presented with a CSF leak or skull base defect with meningitis. Also, no new bacterial meningitis occurred in all other patients. One case of meningoencephalocele of the lateral sphenoid wall developed a recurrent CSF fistula associated with bacterial meningitis two years after endoscopic repair, requiring endoscopic revision surgery. No patient received vaccination in this series.*
***Discussion**: Closure of active CSF leaks and reconstruction of skull base defects without CSF-leak in patients with prior ascending bacterial meningitis seem to provide excellent long-term results with neither recurrence of ascending meningitis nor incidence of meningitis in the other patients, unless a CSF leak re-appears. Conservative treatment of CSF leaks may lead to bacterial meningitis, therefore surgical closure of leaks or defects at the skull base should be considered treatment of choice to prevent ascending meningitis.*

Key words: CSF fistula, skull base, bacterial meningitis, meningocele, meningoencepaholocele, FESS, endoscopic sinus surgery, iatrogenic CSF-leak

INTRODUCTION

Endoscopic repair of defects of the anterior skull base was introduced many years ago in ENT departments in preference to a more aggressive external approach. Several techniques have been proposed, and overall results of between 75% and 100% for closure of the CSF-leak have been achieved [1-6]. Thus, endoscopic repair of anterior skull base defects is an established technique with a negligible morbidity.

Ascending bacterial meningitis has repeatedly been reported as a consequence of these skull base defects and may in fact occur years after trauma or in the absence of active leakage [7].

In a previous study the incidence of ascending bacterial meningitis was found to be relatively high when conservative treatment alone (rest with or without lumbar drainage) of posttraumatic cerebrospinal fluid leaks was selected [8]. However, no report on the long-term prevention of ascending meningitis after endoscopic closure of defects of the anterior skull base has been published to date. We decided to study the incidence of ascending meningitis before and after closure of CSF leaks or skull base defects without active CSF leaks, especially in patients who had developed meningitis prior to surgery, but also in patients without prior meningitis.

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MATERIAL AND METHODS

Patients

This retrospective study included 39 patients who had undergone endoscopic skull base surgery from 1/1993 to 11/2002. Patients operated on from January 1993 to December 1997 (Palma de Mallorca) were assessed endoscopically until December 2000 and then by phone calls. Patients operated on from February 1998 until September 2002 (Barcelona) were reviewed endoscopically until March 2005.

Analysis

Skull base defects and CSF leaks were assessed with CAT scans, MRI and β2-transferrin testing. Active leaks were all submitted for β2-transferrin analysis. In cases where the leak had stopped we relied on high resolution CAT scan to show minor or mayor defects of the skull base. In cases with an ascending bacterial meningitis clinical history showed either active CSF leaks, or radiological anterior skull base defects. Only in one patient with normal radiological findings and no history of CSF leakage but an episode of meningitis an anterior skull base defect was assumed and found at the insertion of the middle turbinate. MRI was used additionally in cases with suspition of meningoceles or meningoencephaloceles.

Surgery

Preoperatively, patients from the second period (Barcelona) were checked for intracranial hypertension by ophthalmologic study of the ocular fundus.

All surgical procedures were performed under general anaesthesia. Sterile 5% sodium fluorescein was used intrathecally (0.5-1 ml) in all patients to identify the CSF leak or the skull base defect with exposed dura.

Surgical exposure of the skull base defect included mucosal denudation and complete visualization of the bony edges. For closure of leaks of the cribiform plate the anterior ethmoidal artery was regularly exposed in order to avoid its damage extra- and intracranially.

Closure of the leakage was achieved by means of an "underlay" reconstruction with lyophilized dura (period 1993 to 1996) or with lyophilized fascia lata (since 1996), positioned between the bone of the skull base and the dura. For defects of the cribiform plate, where it is almost impossible to achieve an "underlay" medially due to the lack of bony support, dura or fascia were positioned on the dura and bent towards the Crista galli. Two or three pieces of dura or fascia lata were used in a tile-shaped fashion in order to achieve a watertight closure of the leakage already with the "underlay" material, and so as not to rely on the mucosal graft for the definitive closure. A free mucosal graft from the middle or the inferior turbinate surrounded by Oxycel® covered this reconstruction, which then was fixed with a loose packing of gauze embedded in terramycin ointment. In cases of anterior skull base defects with no active leak the same procedure (underlay plus mucosal graft) was performed to cover the dura.

No obliteration was performed after repair of defects in the sphenoid sinus. In these cases, the sinus was filled with absorbable material, which was suctioned after 2-3 weeks.

Fibrin glue to secure the mucosal graft was used in two cases.

Patients remained in bed for 72 hours with the head elevated by about 30°-35° to reduce intracranial pressure. Subcutaneous heparin treatment was provided during this period. No lumbar drainage was used. Patients received prophylactic, intravenous treatment with a 3rd generation cephalosporin for 6 to 8 days until the packing was removed. They were forbidden to blow their nose or to sneeze with their mouth closed for 10 days, and to perform any type of physical exercise for about 4 weeks. In order to avoid peaks of increased abdominal pressure laxative drugs were given during the first week.

No vaccination was performed in any patient.

Follow-up

Follow-up was performed regularly once every week until the defect was covered with mucosal epithelium. Pre- and postoperative assessment of sense of smell was not regularly performed.

RESULTS

Thirty-nine patients had 41 endoscopic repairs of various anterior skull base defects: idiopathic (n=10), benign tumors (n=12), posttraumatic (n=14), and iatrogenic (n=4). All idiopathic cases occurred in women. One of them had three idiopathic CSF fistulas, on both cribiform plates and another at the posterior wall of the sphenoid sinus. No signs of intracranial pressure were found in these patients. Benign tumors comprised acquired or congenital meningoceles or encephaloceles, osteomas arising from the skull base or fibrous dysplasia involving the anterior skull base.

Sodium fluorescein was applied intrathecally in all patients to identify the defect and to assess the watertight closure of the CSF-leak. This was helpful in 41/41 cases. In one case of a CSF leak at the skull base attachment of the middle turbinate there was a need to enhance the fluorescein with orange light and to visualize it with blue light. No major or minor complications were observed secondary to the intrathecal application of sodium fluorescein.

Defects were located at the cribiform plate (n=21), the ethmoidal roof (n=12) or the sphenoid sinus (posterior wall n=3; lateral wall n=5). The size of the defects ranged from millimeters to the entirety of one side of the skull base in one case with a fibrous dysplasia.

Lyophilized dura (n=11) or lyophilized fascia lata (n=30) was used to reconstruct the defects. Closure was achieved in 40/41 cases at the first attempt and after a second endoscopic approach in the remaining patient.

Fifteen patients had suffered bacterial meningitis before surgery (Table 1). With a mean follow-up of 65 months (range 22 - 120) for all patients neither a recurrent bacterial meningitis nor a new meningitis was observed, excepting one case with a

Name	Age / gender	Diagnosis or origin of CSF-leak / skull base defect	Previous meningitis	Date of surgery	Disease free period in months
C.S.S.	45 y / w	Spontaneous CSF leak 1/97. Loss of > 600 ml per day	1984 lymphocitic meningitis	3/1997	96
S.V.M.	63 y / w	Meningoencephalocele 9/98	Twice: 4/97 and 9/98	11/1998	65
A.G.L.	26 y / m	Traumatic CSF-leak	3/1998	6/1998	62
M.G.G.	56 y / m	Iatrogenic CSF at rigth skull base leak after FESS. Severe bacterial meningitis needing intensive care unit	8/1998	10/1998	60
A.D.M	49 y / m	Meningoencephalocele + CSF leak left sphenoid	12/1998	3/1999	60
A.R.A	50 y / w	Iatrogenic complication after FESS	5/1999	6/1999	63
H.A	29 y / w	Spontaneous CSF-leak probably since 1/1999, at lateral lamella of middle turbinate. Loss of 400 ml per day	7/1999	11/1999	60
R.S.G.	49 y / w	Encephalocele + CSF leak at cribiform plate	3/2000	5/2000	50
D.D.M.	66 y / w	Spontaneous CSF leak from meningocele at cribiform plate	1/2000	5/2000	49
A.A.P.	60 y / w	Spontaneous CSF leak from sphenoid sinus		11/2000	48
L.M.O.	30 y / w	Iatrogenic CSF leak after Septorhinoplasty 1995, located at Lamina perpendicularis of the septum.	7/2000	8/2001	39
A.-M.M.M.	24 y / w	Iatrogenic CSF after frontal osteoma endoscopic surgery 6/2001	6/2001	8/2001	40
B.G.S.	53 y / w	Three spontaneous CSF-leaks At both cribriform plates and posterior wall of sphenoid sinus.	7/2001. Unknown which of the CSF-leaks was the origin.	10/2001	37
S.R.N.	31 y / w	Iatrogenic CSF-leak after Septorhinoplasty with meningitis 2 days after septorhinoplasty	2/2002	4/2002	29
J.M.G.	61y / m	CSF leak (lateral wall of right sphenoid sinus) operated on 21-6-2000. Recurrent CSF-leak 2 years later with meningitis.	10/2002	11/2002	28

meningoencephalocele of the lateral sphenoid wall, who developed a recurrent CSF fistula associated with bacterial meningitis needing revision surgery. Two and a half years after the revision no CSF leakage was observed and no further meningits occurred.

Two patients developed symptoms compatible with meningitis two and three days after surgery, with negative cultures of the lumbar puncture. They were treated with moxifloxacin intravenously for seven days.

Another patient with a meningocele of the anterior cribiform plate had a frontal mucocele, which resolved after two further Draf type IIb endoscopic procedures

No intracranial complication was observed.

DISCUSSION

Retrospective analysis of patients with CSF-leaks or anterior skull base defects reveal abscense of recurrent bacterial ascending meningitis. Patients with no prior meningitis showed no incidence of meningitis either. One patient with recurrent CSF-leak of the lateral sphenoid sinus developed a bacterial meningitis but did not repeat after secondary closure of the leak.

Benign intracranial hypertension has been cited as a potential cause of idiopathic CSF leaks. In our series, most CSF leaks appeared in female patients with a tendency to obesity. No indications of benign intracranial hypertension were found. However, we did not perform intrathecal measurements postoperatively, as proposed elsewhere [9], because invasive diagnostic procedures are difficult to be accepted by asymptomatic patients.

Useful algorithms have been proposed for the management of CSF leaks [10]. Beta2-transferrin assessment of active leaks has nowadays been substituted by beta-trace determination [11], which can be performed by any laboratory.

Many materials have been proposed for the anterior skull base reconstruction [5]. Interestingly, they all seem to work relatively well [6]. The reported overall percentages of closure by means of the endonasal procedure (microscope and endoscope) range between 75% and 76% [1,2] and 100% [3,4] after a first attempt, which rises to 95% - 100% after a second procedure [12,13]. In our hands, primary and revision surgery achieved 97.6% and 100% closure, respectively.

Free mucosal grafts seem to be better for closing minor defects than pedicled grafts or flaps [2], which may arch or retract during the healing process. Moreover, fistulas treated with local nasal mucosa advancement flaps had a higher rate of failures in the long-term [14].

According to Mattox and Kennedy, defects larger than 10 mm must be provided with a bony scaffold [15]. In our hands, the tile-shaped reconstruction of larger defects with lyophilized dura and later on with fascia lata provided stable reinforcement for the dura. However, time alone will tell if this is enough to prevent encephaloceles or meningoencephaloceles in the long-term. Since lyophilized dura was described to potentially transmit viral disease we have introduced fascia lata for the reconstruction.

Fibrin glue is frequently recommended to improve the attachment of the free mucosal graft [15-17]. Fibrin glue was used in only two cases in our series. In all other cases we felt that, with little blood in the operative site, the free mucosal flap positioned well and remained attached to the skull base supported by oxicel®. However, this can only be achieved if the CSF loss has been terminated previously, because the CSF would certainly detach the mucosa. In cases in which the leakage could not be halted with only the underlay reconstruction the use of fibrin glue was indicated.

The endonasal approach for CSF leaks of various origins proved to be reliable. In our hands, 40 / 41 cases (97.6%) could be closed after a first operation and only one recurrence was operated on for a second time. Our results suggest that the origin of the skull base defect with a CSF leak does not influence the outcome as long as the reconstruction is performed thoroughly.

Intrathecally applied sodium fluorescein helped to identify all active leaks; in cases with skull defects dyed CSF could be recognized through the dura or weakend skull base. During surgery it was of crucial help to assess the watertight closure of the leak.

Although some authors recommend lumbar drainage [13,15], our results suggest, that there is no need for it if no underlaying endocranial hypertension has been found.

The rate of complications after endonasal skull base surgery seems to be low in the literature, considering the number of procedures which have been performed. Two cases of meningitis [13], one intracerebral abscess [2], one case with infection of the thigh [1], two frontal mucoceles [18], and one intracranial mucoceles [19] have been reported. In our series, two cases with clinical meningitis and one frontal mucocele were successfully treated with antibiotics and endoscopic surgery, respectively.

Weber et al. [20] reported loss of olfaction disturbances in 17% of cases. This figure seems acceptable, especially bearing in mind the risk of bilateral olfaction loss associated with craniotomy, as the alternative surgical approach.

In addition, we strongly believe in the positive influence on the final outcome of collateral measures, some of which have been recommended elsewhere [21-23], such as avoiding peaks of intraabdominal pressure, reducing intracranial pressure with orthostatic positions, prescribing relaxant medication, prohibiting nose blowing sneezing with the mouth closed, as well as avoiding physical exercise for a certain period of time.

Conservative management of dural defects had a 50% success rate only [24]. Moreover, after conservative management of CSF fistulas the rate of ascending bacterial meningitis may rise to 18.5% [8]. In the light of these findings and the excellent results and low complication rate reported after minimally invasive endonasal surgery, we strongly recommend an endoscopic skull base revision for patients with a CSF leak and especially in those with a prior ascending bacterial meningitis, even if the CSF leak is not active.

Although it seems obvious that closure of the CSF leak or skull base defects where the leak is no longer active prevents ascending bacterial meningitis, to our knowledge no studies of this association have been reported to date.

Our results show that a minimally invasive endoscopic reconstruction of the skull base with a watertight closure of the CSF-leak also provides long-term protection against ascending bacterial meningitis in patients who had and in others who had not previously suffered such meningitis.

Patients with meningitis were usually referred for endoscopic surgery from the Department of Infectious Diseases, where vaccination was not part of their routine treatment protocol. After closure of the CSF leak and a two or three layer reconstruction of the skull base defects, we considered these patients to be cured; therefore vaccination was not considered either.

CONCLUSIONS

Intrathecal sodium fluorescein application helps to identify the CSF leak and to confirm its watertight closure. No complications were observed secondary to the use of fluorescein.

Lyophilized transplants in an “underlay” position together with free mucosal grafts seem to provide excellent long-term results in the reconstruction of defects of the anterior skull base associated with CSF leakage. Furthermore, the closure of the CSF leaks prevents recurrent episodes of ascending meningitis in the long-term, unless a new CSF leak appears. In patients with no previous record of meningitis reconstruction of anterior skull base defects and / or the CSF-leaks prevented from infection in all cases. Therefore, closure of CSF-leaks and repair of skull base defects, even without an active CSF leak, should be considered standard of care to prevent ascending bacterial meningitis and thus, be included in management algorithms for CSF rhinorrea / anterior skull base defects. Conservative leak management, even when the active leaks stops, seems to be risky.

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