Impact of Chemoradiotherapy on CSF Leak Repair after Skull Base Surgery

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J Neurol Surg B 2014;75:354–357.

Abstract

Keywords

- ▶ cerebrospinal fluid leak
- ▶ endonasal endoscopic surgery
- ▶ skull base tumors
- ▶ skull base reconstruction
- ▶ chemotherapy
- ▶ radiotherapy
- ▶ postoperative complications
- ▶ pedicled septal mucosal flap
- ▶ neurological sequelae
- ▶ neurosurgical patients

Background Transnasal endoscopic resection (TER) has become the treatment of choice for many skull base tumors. A major limitation of TER is the management of large dural defects and the need for repair of cerebrospinal fluid (CSF) leaks, particularly among patients who are treated with chemotherapy (CTX) or radiotherapy (RT). The objective of this study is to determine the impact of CTX and RT on the success of CSF leak repair after TER.

Methods We performed a retrospective chart review of a single-institution experience of TER from 1992 to 2011.

Results We identified 28 patients who had endoscopic CSF leak repair after resection of malignant skull base tumors. Preoperative RT was utilized in 18 patients, and 9 had undergone CTX. All patients required CSF leak repair with rotational flaps after cribriform and/or dural resection. CSF leak repair failed in three patients (11%). A history of RT or CTX was not associated with failed CSF leak repair.

Conclusion Adjuvant or neoadjuvant CTX or RT is not associated with failed CSF leak repair. Successful CSF leak repair can be performed in patients with malignant skull base tumors with an acceptable risk profile.

Introduction

Since 1981, when Wigand described the transnasal endoscopic closure of an iatrogenic cerebrospinal fluid (CSF) leak,¹ improvements to the technique have come about with the introduction of autologous and heterologous tissue grafts, synthetic biomaterials and bioadhesives, and absorbable and nonabsorbable packing materials.² However, for patients who have undergone presurgical chemotherapy (CTX) or radiotherapy (RT) and develop a CSF leak after resection of a skull

base tumor, the likelihood of a successful leak repair without a vascularized flap is low because of the compromised blood supply to the wound bed and skull base, extensive scarring, and tissue hypoxia.³ For patients requiring adjuvant therapy, the use of nonvascularized grafts to repair a CSF leak may delay healing⁴ and hence the initiation of postoperative RT and/or CTX.

Transnasal endoscopic resections (TER) have advanced the treatment of malignant skull base tumors, and the potential benefits of endoscopic approaches include decreased

received

January 23, 2014

accepted

February 19, 2014

published online

June 4, 2014

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Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0034-1373659>.
ISSN 2193-6331.

morbidity, improved cosmetic results, and enhanced visualization.^{5,6} However, one of the major complications associated with TER is the development of a CSF leak, which may result directly from resection of the cribriform plate and ethmoid roof, or it may be an unrecognized complication of cranial base surgery. Currently, the incidence of postoperative CSF leaks associated with the use of the nasoseptal flap is ~5%.⁷ Moreover, skull base lesions with intradural or juxta-dural involvement require dural resection and watertight reconstruction. For malignant lesions, unsuccessful CSF leak repair may result in devastating complications including meningitis, brain herniation, and a delay in the initiation of adjuvant therapies. With the increasingly important roles of CTX and RT for definitive and adjuvant therapy in the management of skull base cancers, surgical reconstruction of the skull base has become ever more complex.⁸

In the skull base literature, there is a paucity of data on the success of transnasal endoscopic CSF leak repair after resection of malignant skull base tumors, especially those treated with TER. Moreover, how nonsurgical therapies impact the success of these complex repairs is largely unknown. We previously reported our oncologic outcomes for patients managed with either TER or endoscopic-assisted craniofacial resection.⁴ The objective of this retrospective study was to determine the impact of CTX and RT on the success of CSF leak repair after TER of malignant skull base tumors and to determine risk factors associated with failed repair.

Materials and Methods

Subjects

After the study was approved by our institutional review board, we identified all patients who underwent endoscopic CSF leak repair after TER for a malignancy of the cranial base between 1992 and 2011 at the University of Texas MD Anderson Cancer Center. Medical records were reviewed for information regarding demographics, histopathologic findings, and treatment including initial surgery, CTX, RT, surgical repair, and repair-related complications.

Statistics

Descriptive statistics for scaled values and frequencies of study patients within the categories for each of the parameters of interest were enumerated with the assistance of commercial statistical software. Correlations between parameters and end points were assessed by the Pearson chi-squared test or, where there were < 10 subjects in any cell of a 2 × 2 grid, by the two-tailed Fisher exact test. These statistical tests were performed with the assistance of the Statistica (StatSoft, Inc., Tulsa, OK) and SPSS (IBM SPSS, IBM Corp., Armonk, NY) statistical software applications. Statistical tests were considered significant when $p < 0.05$.

Results

Demographics

We identified 28 patients who underwent transnasal endoscopic CSF leak repair after resection of malignant anterior

cranial base tumors. The patients' median age was 55.1 years (range: 29–76 years). Data on the patients, tumors, and prior treatments are summarized in ►Table 1.

Previous Treatment

Only four patients (15%) had a history of RT preoperatively (mean total dose: 45 Gy; range: 20–70 Gy), whereas 50% underwent RT postoperatively (mean total dose: 48.9 Gy; range: 5.4–60 Gy) 45.5 days after the leak repair (range: 30–90 days). Systemic CTX was utilized preoperatively in 14% of the patients and postoperatively in 18% of the patients; the most common agent used was cisplatin. Nineteen patients (68%) had at least one previous skull base surgery prior to CSF leak repair. Seven had a craniotomy as part of their initial tumor resection.

CSF Leak Repair

All CSF leak repairs were performed via an endoscopic approach. The sites of CSF leakage were identified and repaired with a multilayered technique.⁹ When CSF leaks were diagnosed postoperatively, intrathecal fluorescein dye was utilized to identify the leak site.¹⁰ All 28 defects were repaired with autologous tissue grafts and/or flaps (►Table 2). In all patients, a pedicled septal mucosal flap was used for reconstruction. A free tensor fascia lata flap, as an adjunct to a mucosal flap, was used in 32% of patients. In 46% of patients, a lumbar drain was utilized to augment the leak repair.

For the repair, 26 patients (93%) were treated with an exclusively endoscopic approach, and 2 patients (7%) were treated with a craniendoscopic surgical approach that also involved a craniotomy.

In 24 patients (86%), the CSF leak was diagnosed intraoperatively during tumor resection. In four patients (14%), CSF leaks were diagnosed after surgical tumor resection, and the repair was performed within a mean of 4 days of the CSF leak diagnosis (range: 2–6 days).

According to the operative reports, the leakage site was located in the cribriform plate in 29% of cases, the sphenoid sinus in 36%, the ethmoid roof in 25%, and the inferior clivus in 11% (►Table 2).

Postoperative Complications

A total of 21% of patients had one or more postoperative complications after leak repair (►Table 3). To better understand these complications, we divided them into two groups: early onset (occurring < 30 days postoperatively) and late onset (> 30 days). Early repair-related complications were uncommon. Meningitis and altered mental status were noted in two patients. Late complications, including meningitis, altered mental status, and seizures, were more likely than early complications to be related to failure in the CSF leak repair including meningitis, altered mental status, and seizures.

Three patients (11%) had a CSF leak recurrence. There was a statistically significant association between having at least one complication and having a recurrence of the CSF leak ($p = 0.017$). All 3 of the patients who had recurrence of CSF

Table 1 Characteristics of patients who underwent endoscopic CSF leak repair

Characteristic	n ^a	%
Sex		
Male	14	50.0
Female	14	50.0
Ethnicity		
White	21	75.0
African American	2	7.1
Latin American	2	7.1
Asian	2	7.1
Unknown	1	3.6
Site of CSF leak		
Cribriform plate	8	28.6
Sphenoid sinus	10	35.7
Ethmoid roof	7	25.0
Inferior clivus	3	10.7
Mean age, y, at time of CSF leak repair		55.1
Histopathology of resected tumor		
Squamous cell carcinoma	3	10.7
Adenoid cystic carcinoma	1	3.6
Mucoepidermoid carcinoma	1	3.6
Adenocarcinoma	3	10.7
Melanoma	4	14.3
Esthesioneuroblastoma	4	14.3
Other	12	42.9
Previous radiotherapy	4	14.3
Postoperative radiotherapy	14	50.0
Previous chemotherapy	4	14.3
Postoperative chemotherapy	5	17.9
Previous skull base surgery		
Open	6	21.4%
Endoscopic	13	46.4%

Abbreviation: CSF, cerebrospinal fluid.

^aData are number of patients (%) unless otherwise specified.

leaks also had at least one complication; only 5 (20%) of the 25 patients who did not have a leak recurrence had a complication. This was particularly pronounced in relation to meningitis.

CTX and RT (adjuvant or neoadjuvant) were not associated with an increased risk of CSF leak recurrence in comparison with nonradiated tumor resection patients at MD Anderson ($p = 0.45$).

Discussion

The increasing use of endoscopic techniques for the management of skull base malignancies has been associated with a

Table 2 Characteristics of CSF leak repairs

Characteristic	n	%
Reconstruction source		
Tensor fascia lata graft	9	32.1
Mucosal graft	4	14.3
Abdominal subcutaneous fat graft	4	14.3
Pedicled septal mucosal flap	28	100
Repair type		
Endoscopic and open	2	7.1
Endoscopic	26	92.9

Abbreviation: CSF, cerebrospinal fluid.

Table 3 Complications

Time of complication	n	%
Early onset (< 30 d)		
Meningitis	1	3.6
Altered mental status	2	7.1
CSF leak recurrence	2	7.1
Nasal oral bleeding	1	3.6
Late onset (> 30 d)		
Meningitis	3	10.7
Seizure	1	3.6
Altered mental status	2	7.1
CSF leak recurrence	1	3.6
Osteonecrosis related to RT	1	3.6

Abbreviations: CSF, cerebrospinal fluid; RT, radiotherapy.

substantial rate of CSF leakage, but the effectiveness of endoscopic repair of CSF leaks after TER craniotomy has not been assessed to date. Factors that theoretically should reduce the efficacy of endoscopic repair in this setting include neoadjuvant or adjuvant CTX and/or RT, previous surgery, and extensive dural involvement. The goals of this study were to review our experience in managing CSF leaks via an endoscopic approach and to identify factors that predict failed repair in the setting of adjuvant or neoadjuvant cancer treatments. In this study, we found that CSF leak repair with autologous local tissue flaps was associated with a low rate of leak recurrence in patients who had undergone TER of a malignant tumor of the anterior cranial base. These results further substantiate the safety of endoscopic resection and reconstruction for skull base cancers.

A variety of transnasal endoscopic techniques have been developed to repair small cranial base defects.² The technique chosen should be based on the clinical scenario,¹¹ the location of the fistula, and the need for additional therapy. For benign lesions, a simple mucosal graft may be sufficient for repair of small defects, but for malignant lesions that

necessitate large resections and adjuvant therapy, this may not be sufficient.

In a meta-analysis published by Harvey et al,¹² vascular flaps had a better outcome than free grafts for large dural defects. Previous reports have described some risk factors for postoperative CSF leak such as history of prior surgery, a large dural defect, opening of the cisterns or communication with the ventricles, large resection volume, incomplete tumor resection, obesity, and noncompliance with postoperative instructions.

When the arachnoid space is substantially disrupted during endoscopic tumor resection, persistent CSF leaks or postoperative ascending bacterial meningitis can occur. According to Horowitz et al,¹³ most cases of meningitis after skull base operations are probably associated with lumbar drainage infection or an unrecognized leak. This is particularly important when it recurs because, according to our study, those patients in our study with CSF leak recurrences all had at least one complication including meningitis. Our 11% incidence of CSF leak recurrence in this complex patient population is favorable compared with the incidences reported in the recent literature.^{2,5,14} Careful selection of candidates for TER can limit the devastating neurologic sequelae and delayed initiation of adjuvant therapies associated with persistent CSF leaks.

Adjuvant or neoadjuvant CTX or RT, based on our results, is not associated with an increased risk of failed CSF leak repair. This finding is supported by earlier studies in which RT was not associated with any intracranial complications after skull base surgery.^{15,16} Conversely, Zanation et al studied patients who had undergone a nasoseptal flap reconstruction for CSF leak during endoscopic skull base surgery and posited that proton RT may increase the risk of repair failure.³ Also, in a study of risk factors that could affect wound healing in neurosurgical patients, Krishnan et al found that the leading factors that impacted wound healing were underlying primary disease; RT, CTX, or both RT and CTX; prolonged cortisone administration; CSF leak; and, most strongly, multiple previous attempts at wound closure.¹⁷ However, these findings need to be carefully tempered by the highly selected patient sample.

Conclusion

Successful CSF leak repair can be performed in patients with malignant skull base tumors and an acceptable risk profile. Previous therapies such as CTX and RT were not associated with iatrogenic CSF leak repair failure. Transnasal endoscopic CSF leak repair after resection of skull base malignancies is safe in carefully selected patients.

Funding Source

The University of Texas MD Anderson Cancer Center is supported in part by the National Institutes of Health through core grant CA16672.

Notes

Presented at the XXII North American Skull Base Surgery Meeting, Las Vegas, Nevada, February 2012.

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