Impact of Dural Resection on Sinonasal Malignancies with Skull Base Encroachment or Erosion

Hedyeh Ziai¹ Eugene Yu² Terence Fu³ Nidal Muhanna⁴ Eric Monteiro⁴ Allan Vescan⁴
Gelareh Zadeh⁵ Ian J. Witterick⁴ David P. Goldstein⁴ Fred Gentili⁵ John R. de Almeida⁴

¹ Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

² Department of Medical Imaging, University of Toronto, Toronto, Ontario, Canada

³ Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

⁴ Department of Otolaryngology Head and Neck Surgery, University of Toronto, Toronto, Canada

⁵ Division of Neurosurgery, University of Toronto, Toronto, Canada

Address for correspondence John R. de Almeida, MD, MSc, Department of Otolaryngology Head and Neck Surgery, University of Toronto, University Health Network, Princess Margaret Hospital, 610 University Avenue, 3-955, Toronto, ON M5G 2C4, Canada (e-mail: john.dealmeida@uhn.ca).

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Abstract

Objectives (1) To determine the occult rate of dural invasion in patients with tumors extending to and/or eroding the bony anterior skull base but without evidence of dural invasion on preoperative imaging. (2) To determine the impact of dural resection and of skull base erosion on survival outcomes in this group of patients (without evidence of dural invasion upon preoperative imaging).

Study Design Retrospective study.

Setting Tertiary care academic center.

Participants Patients with sinonasal malignancies with anterior skull base encroachment/erosion without dural invasion on preoperative imaging treated surgically.

Main Outcome Measures (1) Histopathologic disease in the dura in patients who had dural resection and (2) Oncologic outcomes (5-year local recurrence, dural recurrence, disease-specific survival, and overall survival) in patients with and without dural resection, and patients with and without skull base erosion.

Results Thirty-seven patients were included. The occult rate of dural invasion was 54%. Patients with dural resection had improved margin control versus those without dural resection (90% vs 56%, $p = 0.02$). Dural resection improved 5-year overall survival only in patients with esthesioneuroblastoma compared with bony skull base resection alone (100% vs 75%, $p = 0.03$). Patients with skull base erosion had reduced local control versus those without erosion (63% vs 93%, $p = 0.047$).

Conclusion This study suggests a substantial rate of occult dural invasion despite no overt imaging findings. Dural resection may be associated with improved margin control, but no oncologic benefit except for esthesioneuroblastomas, although treatment heterogeneity and small sample size may limit conclusions.

Keywords

- ▶ nose and paranasal sinuses (head and neck)
- ▶ skull base (head and neck)
- ▶ radiology
- ▶ survival

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Introduction

Sinonasal malignancies with skull base encroachment are a rare and heterogeneous group of tumors. Malignancies of this area comprise ~3% of all head and neck tumors.^{1–4} Because of the rarity of these tumors, efforts to better understand their prognosis have generally grouped tumors into three histopathologic grades (low, intermediate, and high grade).⁵ In one study, 5-year survival rates range from as low as 0% for melanomas to as high as 71% for esthesioneuroblastomas.⁶

Treatment of these tumors varies by institution and surgeon with surgical resection playing an important role in many centers. Surgeons must balance the risk of microscopic residual disease with the added morbidity of dural resection and the possibility of incurring a postoperative cerebrospinal fluid (CSF) leak. Advances in instrumentation, the advent of image guided technology, and endoscopic endonasal approaches² have led to reductions in morbidity and mortality.⁷ Despite these advances, complications such as CSF leak remain a challenge. Because of the potential neurologic sequelae of this complication, the extent of resection and the need for dural resection must be justified.

It has previously been shown that as many as 31% of sinonasal tumors extended to or invaded the skull base.⁸ Preoperative imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI) may help predict skull base invasion, but may be associated with both false positives and false negatives with respect to occult invasion.^{9–15} The principal aim of this study was to determine the occult rate of dural invasion in patients with tumors extending to and/or eroding the bony skull base but without overt dural invasion. Furthermore, we explored the prognostic implications of bony skull base erosion and of resecting dura in this group of patients.

Methods

Patients and Treatment

Institutional Research Ethics Board approval was obtained prior to the commencement of the project. Patients were identified from the Ontario Cancer Registry. Patients 18 years or older with malignancies of the nasal cavity or paranasal sinuses with bony skull base (fovea ethmoidalis or cribriform plate) encroachment or erosion on preoperative imaging (CT and/or MRI) who underwent surgery at the University Health Network (UHN) in Toronto, Canada between 2000 and 2014 were eligible for the study. Patients with signs of overt dural or brain invasion on preoperative imaging as determined by a staff head and neck radiologist (EY) were excluded. All patients with distant metastatic disease, metastatic lesions of the skull base, or skin lesions with extension into the sinonasal cavity or skull base were further excluded. Operative and pathologic reports as well as clinical data were reviewed.

Data Collection

A retrospective chart and imaging review were performed to collect relevant patient information from the UHN health records. Information related to patient demographics, disease, treatment, and oncologic outcomes (i.e., recurrence patterns)

was collected. Patients were divided into three histopathologic groups (low, intermediate, and high grade) based on a previous histopathologic classification system.⁵ Low-grade tumors included esthesioneuroblastomas (olfactory neuroblastomas) and low-grade sarcomas. Intermediate-grade tumors included adenoid cystic carcinoma, mucoepidermoid carcinoma, epithelial myoepithelial carcinoma, adenocarcinoma, and squamous cell carcinomas. High-grade tumors included high-grade sarcomas, sinonasal melanoma, small cell carcinoma, and sinonasal undifferentiated carcinoma.⁵ Imaging was reviewed by a head and neck radiologist (EY) blinded to tumor histopathology and operative findings. Scans were initially reviewed to determine patient eligibility by excluding radiographic evidence of dural or brain invasion. Eligible patients' scans were evaluated for the extent of disease upon preoperative imaging. Pathology reports were also reviewed to determine microscopic tumor extension into the dura (in those who underwent dural resection).

Statistical Analysis

Statistical analysis was performed using SPSS statistical software, version 21.0 (SPSS Inc., Chicago, Illinois, United States) and Microsoft Excel. All *p*-values were two-tailed and a value of *p* < 0.05 was considered statistically significant. Comparison between categorical variables was performed using chi-squared analysis. Oncologic outcomes (5-year local control, dural control, disease specific survival, and overall survival) were measured using Kaplan–Meier methods. Multivariable analysis was performed using Cox proportional hazards models. Multivariable models included the following covariates: age, sex, histopathologic grade, TNM stage, radiotherapy, chemotherapy surgical approach, margin status, dural resection, and skull base erosion.

Results

Patients

Thirty-seven patients (mean age 55.5 years; SD 13.8; 51% male) met our inclusion criteria. Fifteen patients (41%) had low-grade tumors, 16 (43%) had intermediate-grade, and 6 (16%) had high-grade tumors. ► **Table 1** describes relevant demographic and clinical variables. Twelve patients (32%) had esthesioneuroblastoma, six patients (16%) had squamous cell carcinoma, and the remaining 19 patients (51%) had other malignancies (2 osteosarcoma, 2 adenoid cystic carcinoma, 2 mucoepidermoid carcinoma, 2 undifferentiated carcinoma, 2 adenocarcinoma, 2 melanoma, 1 basal cell carcinoma, 1 poorly differentiated basaloid squamous cell carcinoma, 1 leiomyosarcoma, 1 pleomorphic rhabdomyosarcoma, 1 large cell neuroendocrine carcinoma, 1 sarcoma, and 1 high-grade carcinoma with glandular, squamoid, and neuroendocrine differentiation).

Dural Resection

Twenty-one patients (57%) had dural resections. There was a higher proportion of skull base erosion in those with dural resection compared with those without dural resection (71% vs 38%, *p* = 0.04). There were no statistically significant differences in the method of surgical approach (i.e., endoscopic or open), histopathology grades, or TNM stage between patients

Table 1 Patient and tumor characteristics

Variables	No. of patients (%)			p-value
	Population n = 37	Dura resected n = 21	Dura not resected n = 16	
Age, year, mean (± SD)	55.5 (±13.8)	49.7 (±12.6)	63.1 (±11.4)	0.003
Sex, male	19 (51%)	12 (57%)	7 (44%)	0.4
T classification	T1–6 (16%)	T1–3 (14%)	T1–3 (19%)	0.6
	T2–8 (22%)	T2–4 (19%)	T2–4 (25%)	
	T3–7 (19%)	T3–3 (14%)	T3–4 (25%)	
	T4–16 (44%)	T4–11 (52%)	T4–5 (31%)	
N classification	N0–36 (97%)	N0–21 (100%)	N0–15 (94%)	0.3
	N1–1 (3%)	N1–0 (0%)	N1–1 (6%)	
Histopathology grade	Low–15 (41%)	Low–9 (43%)	Low–6 (38%)	0.7
	Intermediate–16 (43%)	Intermediate–9 (43%)	Intermediate–7 (44%)	
	High–6 (16%)	High–3 (14%)	High–3 (19%)	
Skull base erosion	21 (57%)	15 (71%)	6 (38%)	0.04
Surgical approach, endoscopic	12 (32%)	9 (43%)	3 (19%)	0.1
Margin status, positive	9 (24%)	2 (10%)	7 (44%)	0.02
Radiotherapy				
Neoadjuvant radiation	14 (38%)	10 (48%)	4 (25%)	0.5
Adjuvant radiation	12 (32%)	3 (14%)	9 (56%)	0.007
Chemotherapy				
Neoadjuvant chemotherapy	0 (0%)	0 (0%)	0 (0%)	N/A
Adjuvant chemotherapy	2 (5%)	1 (5%)	1 (6%)	0.8
Chemoradiation				
Neoadjuvant chemoradiation	6 (16%)	5 (24%)	1 (6%)	0.2
Adjuvant chemoradiation	2 (5%)	2 (10%)	0 (0%)	N/A

with dural resection and without. Compared with patients without dural resection, patients with dural resection had a lower rate of positive margins (10% vs 44%, $p = 0.02$), and were less likely to receive adjuvant radiotherapy (14% vs 56%, $p = 0.007$) (► **Table 1**). Although not statistically significant, patients with dural resection were more likely to experience surgical complications (53% vs 27%, $p = 0.09$). There was no difference in CSF leaks in patients who had dural resections compared with those who did not (5% vs 0%, $p = 0.3$). Complications in our cohort included CSF leaks ($n = 1$), infection ($n = 6$), meningitis ($n = 1$), abscess ($n = 1$), and pneumocephalus ($n = 1$).

Dural Invasion

Of the 21 patients who had a dural resection, reporting on pathologic invasion of the dura was available in 13 (62%) patients. Of these, seven (54%) had dural invasion. Patients with occult dural disease were stratified according to histopathology grade, skull base erosion status, and whether or not the malignancy was an esthesioneuroblastoma (► **Table 2**). Of

Table 2 Occult dural invasion

Variables	Positive dural invasion	Total dura resected (with known dural invasion status)	Proportion
Total population	7	13	54%
Grade			
Low	4	5	80%
Intermediate	2	6	33%
High	1	2	50%
Skull base erosion			
Yes	5	11	45%
No	2	2	100%
Histopathology			
Esthesioneuroblastoma	4	5	80%
Nonesthesioneuroblastoma	3	8	38%

Fig. 1 Kaplan-Meier survival curves for dural resection compared with no dural resection.

the 11 patients with skull base erosion, 5 (45%) had dural invasion and both (100%) of the patients without skull base erosion had occult dural invasion. Occult dural disease was more prevalent in esthesioneuroblastomas (80%) than in nonesthesioneuroblastoma (38%) malignancies ($p = 0.13$).

Fifteen (41%) patients developed recurrences. There were no statistical differences in dural recurrence patterns between patients with dural resections and those without (10% vs 19%; $p = 0.4$). There were differences in crude local, regional, or distant recurrence rates (19% vs 25%, $p = 0.7$; 10% vs 13%, $p = 0.7$; 10% vs 25%, $p = 0.2$). There were also no statistically significant differences in 5-year local control, dural/leptomeningeal control, overall survival, and disease-specific survival in the dural resection and no dural resection groups (81% vs 73%, $p = 0.5$; 92% vs 82%, $p = 0.4$, 86% vs 60%, $p = 0.6$, 86% vs 68%, $p = 0.9$) (►Fig. 1). There was, however, a significant improvement in 5-year overall survival in patients with esthesioneuroblastomas who had dural resection versus those who did not (100% vs 75%, $p = 0.03$) (►Fig. 2).

Fig. 2 Kaplan-Meier survival curves in patients with esthesioneuroblastoma with dural resection compared with no dural resection. Note: KM curve for dural/leptomeningeal Control N/A due to 0 recurrences in either group and one patient's cause of death was unknown.

Skull Base Erosion

Fifty-seven percent ($n = 21$) of patients had evidence of skull base erosion. Patients with skull base erosion were more likely to undergo dural resection compared with those without skull base erosion (71% vs 38%, $p = 0.04$). There were no differences between crude recurrence rates (local, dural, regional, and distant) in patients who had skull base erosion compared with those without (29% vs 13%, $p = 0.2$; 14% vs 13%, $p = 0.9$, 5% vs 19%, $p = 0.2$; 24% vs 6%, $p = 0.2$). On univariable analysis, skull base erosion was associated with reduced 5-year local control compared with those without skull base erosion (63% vs 93%, $p = 0.047$) (►Table 3). After controlling for skull base erosion and histopathologic grade on multivariable analysis, dural resection was not associated with an improvement in local control (HR = 0.49, 95% CI 0.12–2.13, $p = 0.3$). There were trends toward lower dural control, overall survival, and disease-specific survival in patients with skull base erosion compared with those without (79% vs 93%, $p = 0.2$; 61% vs 92%, $p = 0.1$; 69% vs 92%, $p = 0.2$) (►Fig. 3).

Discussion

In the present study, we observed that over half of patients (54%) with sinonasal malignancies with skull base encroachment or erosion who underwent dural resection had the presence of occult dural invasion. To the best of our knowledge, this is the largest study to document the occult dural invasion rate in patients with sinonasal malignancies in the absence of imaging findings of dural involvement. Interestingly, occult dural invasion was noted in patients regardless of whether they had skull base erosion, histopathologic grade, and whether or not they had esthesioneuroblastomas. Despite these findings, in this relatively small cohort, patients without dural resection had similar oncologic control to those with dural resection who had lower need for adjuvant radiation. The comparable outcomes are likely to be confounded by the fact that, in our cohort, patients without dural resections were more likely to receive adjuvant radiotherapy. This treatment heterogeneity may confer a survival advantage and contribute to the failure to demonstrate a surgical advantage with dural resection.

Preoperative imaging is instrumental in evaluating the extent of disease, in particular, dural invasion. While preoperative imaging may help predict the extent of invasion, few reports describe the accuracy of imaging in evaluating dural invasion. These studies associate radiographic markers of dural invasion with both false positives and false negatives.^{11–13} Linear dural enhancement and nodular thickening have been shown to have a positive predictive value (PPV) of 47% and 100%, respectively.⁹ One millimeter and ≥ 2 mm dural thickening had a PPV of 43% and 100%, respectively, while loss of hypointense zone had a PPV of 92%.⁹ Similarly, a recent study found that of those individuals who had normal MRI findings (intact bony skull base) and histologic analysis of dural involvement, 75% had tumor in the dura.¹³ However, this included only eight evaluable patients with normal MRI and histologic analysis of the dura of which six had histologically positive invasion into the dura. The same authors found that of those who had imaging evidence of breach of the bony skull

Table 3 Univariable and multivariable analysis for 5-year local control

Variables	No. patients	Log-rank	Cox regression	
			HR (95% CI)	p-value
Age				
Under 65	29	0.55		
65 and older	8			
Sex				
M	19	0.29		
F	18			
T category				
1–2	14	0.10		
3–4	23			
N category				
0	36	—		
1	1			
Grade				
Low	15	0.21	1.55 (0.29–8.30)	0.61
Intermediate or High	22			
Dural resection				
Yes	21	0.54	0.49 (0.12–2.13)	0.34
No	16			
Skull base erosion				
Yes	21	0.047	5.2 (0.84–32.2)	0.076
No	16			
Margins				
Positive	9	0.82		
Negative	28			
Radiotherapy				
Yes	34	0.39		
No	3			
Chemotherapy				
Yes	10	0.45		
No	27			
Surgical approach				
Open	25	0.40		
Endoscopic	12			

base and contrast-enhancing tumor abutting but not involving the dura, 68% had dural involvement. In another study, of the three patients with no dural enhancement, one of them had microscopic evidence of dural invasion.¹² Our results corroborate the findings of poor sensitivity of dural invasion.

The finding of occult dural invasion suggests that oncologic surgery for sinonasal malignancies encroaching or eroding the skull base should involve a dural resection. In the present study, preoperative skull base bony erosion did

Fig. 3 Kaplan-Meier survival curves for bony skull base erosion compared with no bony skull base erosion.

not seem to be a reliable predictor of dural invasion, although it was associated with more extensive surgery (i.e., dural resection), and also with poorer local control on univariable analysis. Interestingly, the absence of skull base erosion does not preclude the possibility of occult dural invasion, and, as such, patients with tumors either encroaching or eroding the skull base may require dural resection for margin control.

The goals of surgical resection of sinonasal malignancies include complete resection with negative margins. The intimacy of these tumors to critical structures such as the orbit, optic apparatus, dura mater of the skull base, brain, and cavernous sinus may in certain instances compromise the resectability of these tumors.^{4,13} The use of intraoperative frozen sections to obtain clear margins and preservation of normal surrounding structures when indicated remain an essential part of surgical treatment of paranasal sinus cancers.¹⁶ The most common failures of these tumors are locoregional, thus emphasizing the importance of complete resection and adjuvant therapy.^{5,7,16–18} Margin status has been shown to be the most significant histopathologic predictor of all outcome parameters, including local and regional

recurrences.^{7,19,20} In the present study, we demonstrate that patients with dural resections are more likely to achieve negative margins. This finding alone may suggest that patients with sinonasal malignancies that encroach and/or erode through the skull base should have dural resection to improve histologically complete resection of malignant tumors.

The rate of postoperative complications in most published series of patients undergoing sinonasal tumor resection ranges between 25% and 50%,^{6,17,21–27} with the most important factor associated with major complications being the extent of resection.^{6,22} Major complications include CSF leak, meningitis, abscess/infection, stroke, and pneumocephalus.^{6,22} Minor complications are defined as events which did not interfere with patient's hospital stay.²² Skull base and dural resections require reconstruction to separate the intracranial and extracranial compartments. Inadequate reconstruction may lead to CSF fistulae, meningitis, and tension pneumocephalus.^{28–30} In a recent study, all postoperative CSF leaks were encountered in cases where the dura was breached intraoperatively (either intentionally or not).¹³ In a previous study, the CSF leak rate in patients with dura resected was 23% compared with 6.5% in

patients without dural resection.²² As a consequence of the increased CSF leak rate, the incidence of meningitis was significantly higher in patients with dural resection versus no dural resection (23% vs 4.3%). In several published series, the prevalence of CSF leaks has been below 10%.^{8,13,30–32} However, even in experienced centers with tumors in the anterior cranial base, the leak rate has been reported to be above 20% and this may be attributable to several factors including tumor location as well as body mass index.³³ With the anterior skull base location in particular, tumors requiring resection of the posterior wall of the frontal sinus, for example, can be particularly challenging because of the difficulty in coverage of the defect with a local flap such as the nasoseptal flap.

CSF leaks could give rise to potentially life-threatening complications and in turn should not be underestimated. As such, the added morbidity of more extensive surgery must be carefully weighed in the surgical plan. For example, in patients who have skull base encroachment on imaging, but intraoperatively are noted not to have any extension to the skull base, may be treated with a more limited resection, particularly when the mucosal involvement spares the skull base and only the pedicled tumor reaches the skull base.

There were some limitations to this study. This study was a retrospective analysis and, therefore, susceptible to biases of such designs. Furthermore, the study involved a variety of histopathologies, all with unique biologic behaviors. Although there did not seem to be significant differences in the histopathologic grades, the variability of histopathology in the various groups may confound the oncologic results.^{3,6,17,18,21,34,35} In addition, the sample size of the present study was small, thus limiting the overall power to detect oncologic differences between groups. The power was further reduced by the incomplete reporting of pathologic evidence of dural invasion in those who had dural resections completed. Furthermore, our study groups were managed heterogeneously with differences in adjuvant treatment. For example, patients without dural resection were more likely to receive adjuvant radiotherapy than those patients with dural resection. This difference between groups may bias the results in favor of the group that did not undergo dural resection. Finally, the median follow-up time of 48 months may have been inadequate to identify all recurrences, particularly in histopathologies such as esthesioneuroblastoma where delayed recurrences are well known.³⁶ Despite these limitations, the current study should serve as a basis for future studies that may prospectively enroll a larger number of patients to yield more robust survival estimates.

Conclusion

To the best of our knowledge, the present study is the first attempt to ascertain the significance of dural resection in sinonasal tumors with no radiologic evidence of dural invasion. The absence of dural invasion upon preoperative imaging does not rule out the presence of microscopic dural disease. Dural resection was associated with a higher rate of negative margins, but did not result in statistically significant oncologic benefit except for patients with esthesioneuroblastoma. The small sample size and treatment heterogeneity may have

concealed a survival advantage. Consideration for dural resection should be given to patients with sinonasal malignancies encroaching and/or eroding the skull base.

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Conflicts of Interests/Financial Disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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