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Clinical Study

Endoscopic resection of esthesioneuroblastoma

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ABSTRACT

Esthesioneuroblastoma, or olfactory neuroblastoma, is an uncommon malignant tumor arising in the upper nasal cavity. Surgical approaches to this and other sinonasal malignancies involving the anterior skull base have traditionally involved craniofacial resections. Over the past 10 years to 15 years, there have been advances in endoscopic approaches to skull base pathologies, including malignant tumors. In this study, we review our experience with purely endoscopic approaches to esthesioneuroblastomas. Between January 2005 and February 2012, 11 patients (seven men and four women, average age 53.3 years) with esthesioneuroblastoma were treated endoscopically. Nine patients presented with newly diagnosed disease and two were treated for tumor recurrence. The modified Kadish staging was: A, two patients (18.2%); B, two patients (18.2%); C, five patients (45.5%); and D, two patients (18.2%). All patients had a complete resection with negative intraoperative margins. Three patients had 2-deoxy-2-(^{18}F)fluoro-D-glucose avid neck nodes on their preoperative positron emission tomography–CT scan. These patients underwent neck dissections; two had positive neck nodes. Perioperative complications included an intraoperative hypertensive urgency and pneumocephalus in two different patients. Mean follow-up was over 28 months and all patients were free of disease. This series adds to the growing experience of purely endoscopic surgical approaches in the treatment of skull base tumors including esthesioneuroblastoma. Longer follow-up on larger numbers of patients is required to clarify the utility of purely endoscopic approaches in the management of this malignant tumor.

1. Introduction

Esthesioneuroblastoma, or olfactory neuroblastoma, is a malignant tumor arising in the superior aspect of the nasal cavity. It is an uncommon neoplasm, first described in 1924 by Burger and Luc.[1] A review of internationally indexed literature and its citations from 1924 to 1994 revealed that only 945 cases had been reported during that time.[2] Given the rarity of this tumor, there is some variability in treatment strategies. In the meta-analysis reported by Dulguerov et al., the best survival rates were observed in patients treated with the combination of surgical resection and postoperative radiotherapy[3] and thus this has become the standard treatment algorithm in many institutions.

The surgical approach to esthesioneuroblastomas has changed over time. Initially, extracranial procedures were employed,[4] and then later, beginning in the 1970s, craniofacial resections became the preferred technique.[5,6] Over the past 10 years to 15 years, there has been tremendous development in endoscopic approaches to skull base pathologies, including malignancies involving the anterior cranial fossa. Due to the rarity of this disease and the limited literature on endoscopic approaches in patients with esthesioneuroblastoma, however, there remains debate as to whether a purely endoscopic technique is an appropriate therapeutic modality for this tumor. In this report, we update our experience, which lends further support to the feasibility and effectiveness of purely endoscopic approaches in well selected patients with esthesioneuroblastomas.

2. Methods

We retrospectively reviewed patients treated at Johns Hopkins Hospital with a diagnosis of esthesioneuroblastoma between January 2005 and February 2012. Patients treated solely with an endonasal endoscopic approach were included; patients undergoing an endoscopic-assisted resection or endoscopic biopsy without a surgical resection were excluded. Patient records were reviewed for demographic information, Kadish staging, complications, pathology, postoperative treatment, length of follow-up, and disease status at last follow-up. Modified Kadish staging was used: A = confined to the nasal cavity; B = confined to the nasal cavity and paranasal sinuses; C = extension beyond the nasal cavity and paranasal sinuses including involvement of the cribriform plate, base of the skull, orbit or intracranial cavity; D = metastasis to

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cervical lymph nodes or distant sites.[7] This study was approved by the Johns Hopkins Hospital Institutional Review Board.

Our preoperative evaluation, surgical approach and postoperative care have been previously described.[8] Briefly, patients are evaluated preoperatively by high resolution CT and MRI skull base imaging and a whole body positron emission tomography (PET)-CT scan. Cases are discussed at our Neuro-oncology and Head and Neck Tumor Boards. There are several distinct surgical stages. Initial tumor debulking is followed by assessment of intranasal margins. Once negative circumferential nasal margins are achieved, tissue is ablated up to the skull base and extracranial skull base margins are analyzed. Once these margins are confirmed negative, the cribriform plate with tumor attached, underlying dura, and olfactory bulbs and distal tracts are resected *en bloc*. Contiguous dural and falcine margins are then analyzed and tissue removed until negative margins are achieved. Several methods are utilized for the reconstruction of the skull base, including use of the autologous tissue such as a nasoseptal flap, synthetic materials, as well as cadaveric tissue.

3. Results

A total of 11 patients (seven men and four women; mean age at presentation, 53.3 years; age range 40–72 years) underwent a purely endoscopic resection of an esthesioneuroblastoma between January 2005 and February 2012 (Table 1, Fig. 1). Nine patients presented with newly diagnosed disease and two patients presented with recurrent disease (Patients 7 and 8). All patients had previous surgical intervention, either partial resection or biopsy, and the pathology slides for all cases were reviewed at the Johns Hopkins Department of Pathology and interpreted as esthesioneuroblastoma. The modified Kadish staging results were: A, two patients (18.2%); B, two patients (18.2%); C, five patients (45.5%); and D, two patients (18.2%). Three patients had 2-deoxy-2-(^{18}F)fluoro-D-glucose (FDG) avid neck nodes on their preoperative PET–CT scan (Patients 5, 9, and 11).

All patients underwent surgery with the intention of cure. In Patients 5 and 6, the surgery was performed in a staged fashion; all others were performed in a single stage. Three patients also underwent a neck dissection based on the preoperative PET-CT findings (Patients 5, 9 and 11). In all patients except the two with Kadish stage A, a formal cribriform resection was performed. Negative intraoperative margins were obtained in all 11 patients. Two of the three patients undergoing a neck dissection were found to have tumor in the removed lymph nodes (Patients 5 and 11). Final histopathological analysis confirmed the diagnosis of esthesioneuroblastoma in all patients.

Two patients developed perioperative complications (Table 2). One patient developed intraoperative hypertension (Patient 5). One patient developed more than expected postoperative pneumocephalus (Patient 9), which was managed conservatively and with early removal of his lumbar drain. There were no postoperative CSF leaks or episodes of meningitis.

All patients received postoperative radiotherapy and three patients also received chemotherapy (Table 2). Chemotherapy was indicated in two patients for metastatic neck disease (Patients 5 and 11) and in a third patient for submucosal spread noted at significant distances from the tumor origin (Patient 4). The mean follow-up was 28.5 months with a range from 10 months to 57 months. At the time of writing, no patients had evidence of disease.

Three patients developed late complications (Table 2). Two patients developed nasolacrimal duct dysfunction following radiotherapy requiring bilateral lacrimal duct dilation (Patients 2 and 11). Patient 2 also developed symptomatic frontal sinusitis requiring an endoscopic frontal sinusotomy. Patient 3 developed worsening dysosmia following radiotherapy requiring numerous medical regimens including carbamazepine, valproic acid, gabapentin, and alpha-lipoic acid, with modest improvement.

4. Discussion

Craniofacial resection has been the standard surgical approach to malignant tumors involving the anterior skull base for many decades. Over the past 10 years to 15 years, and with advances in endoscopic approaches to skull base pathologies including malignancies, there has been a shift in the surgical treatment of these tumors. Given the rarity of esthesioneuroblastoma, however, there are no single center large series on this topic. In the current study, we update our initial experience[8] and now report 11 patients with esthesioneuroblastoma treated with a purely endoscopic approach. We were able to achieve negative intraoperative margins in all patients, and at the time of writing, all patients are without evidence of disease.

There are increasing reports of endoscopic resections of esthesioneuroblastoma.[9–27] To our knowledge, Folbe et al. is the largest series reported.[16] This was a combined series from the University of Pittsburgh Medical Center and the University of Miami Miller School of Medicine and builds on the authors' previous experience.[10,11,14] In this study, 23 patients were reported: 19 were treated for primary disease and four were treated for recurrent tumors. The modified Kadish staging for the 19 patients with primary disease was: A, two patients; B, 11 patients; C, five patients; and D, one patient. A complete resection and negative intraoperative mar-

Table 1
Preoperative, intraoperative and postoperative characteristics of patients with esthesioneuroblastoma treated purely endoscopically

Pt	Age/sex	Kadesh[A]	Negative margins	Neck dissection[B]	Skull base reconstruction[D]	CSF leak	Meningitis
1	72/F	A	Yes	No	None	No	No
2	46/M	B	Yes	No	DuraGen, Alloderm	No	No
3	57/F	C	Yes	No	DuraGen, Alloderm, NSF	No	No
4	44/M	B	Yes	No	DuraGen, NSF	No	No
5	56/M	D	Yes	Yes/+	DuraGen, Alloderm	No	No
6	55/M	C	Yes	No	DuraGen, Alloderm, NSF	No	No
7	58/M	C[C]	Yes	No	DuraGen, DuraMatrix, Alloderm	No	No
8	67/F	C[C]	Yes	No	DuraGen, DuraMatrix, Alloderm, NSF	No	No
9	51/M	C	Yes	Yes/−	DuraGen, NSF	No	No
10	40/F	A	Yes	No	None	No	No
11	40/M	D	Yes	Yes/+	DuraMatrix, Alloderm	No	No

CSF = cerebrospinal fluid; NSF = nasoseptal flap; Pt = patient.
[A] Modified Kadish staging according to Morita et al.[7]
[B] "+" and "−" refer to the final histopathological analysis of resected lymph nodes for esthesioneuroblastoma.
[C] Stage at recurrence.
[D] AlloDerm (LifeCell, Branchburg, NJ, USA), DuraGen (Integra LifeSciences, Plainsboro, NJ, USA), DuraMatrix (Stryker, Kalamazoo, MI, USA).