Esthesioneuroblastoma: An Update on the UCLA Experience, 2002–2013

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Abstract

Objectives To profile the clinical presentation and treatment results of esthesioneuroblastomas at the University of California, Los Angeles (UCLA), from 2002 to 2013.

Design Retrospective review.

Setting Tertiary academic institution.

Participants Forty-one patients with esthesioneuroblastomas treated at UCLA.

Main Outcome Measures Overall survival (OS) and recurrence-free survival (RFS).

Results Thirty-six patients were included with a mean age of 50.1 years and a median duration of follow-up of 33 months. The 5-year RFS and OS were 54% and 82%, respectively. Modified Kadish stage was the only factor identified to affect OS. Multivariate analysis demonstrated that tumor grade was the only factor that had an independent impact on RFS. There was no statistical difference in survival among the surgical approaches chosen.

Conclusions The updated data on the UCLA experience reveals that all three surgical approaches chosen provide comparable survival, although longer follow-up will be needed to ascertain if these findings hold true. The endoscopic approach had a statistically significant decrease in length of hospital stay and a trend toward reduced blood loss, intensive care unit admission, and complications. The modified Kadish staging was the only factor identified to predict OS. Multivariate analysis revealed that tumor grade was an independent predictor of recurrence; therefore, its importance should be emphasized in future staging systems.

Keywords

- esthesioneuroblastoma
- olfactory neuroblastoma
- sinonasal tumors
- expanded endoscopic sinus surgery
- anterior skull base surgery

Introduction

Esthesioneuroblastoma, also known as olfactory neuroblastoma (ONB), is a rare tumor thought to arise from the olfactory

epithelium in the superior nasal vault. Despite its rarity, there has been considerable interest and debate over optimal treatment protocols. This debate stems from variability in staging, histopathology, treatment, and surgical approach.

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The first staging system for ONB was described by Kadish et al in 1976 in his review of 30 patients treated over a 30-year period.¹ They proposed a staging system based on extent of tumor in the nasal cavity. An initial concern of the Kadish system is that it did not adequately account for tumors with distant or regional spread. A modified Kadish system was proposed by Morita and colleagues to account for these tumors with distinct biologic behavior (►Table 1).² Biller et al proposed another staging scheme; however, it did not receive widespread use because the staging system required craniotomy for staging and assumed the cribriform plate is involved in all stages of disease.³

Dulguerov and Calcaterra performed the next pioneering work in the staging of esthesioneuroblastomas at the University of California, Los Angeles (UCLA) in 1992.⁴ Their proposed staging used the familiar TNM type of classification (►Table 2). This staging had the added benefit of accounting for regional and distant metastasis and utilizing imaging modalities such as computed tomography and magnetic resonance imaging. In their series of patients treated from 1970 to 1990, the authors concluded that surgery and adjuvant radiation therapy provided the best local control. The authors also proposed that surgery is best performed by an en bloc resection by craniofacial resection that requires a craniotomy and transfacial approach. The classic craniofacial resection is considered by many to be the gold standard treatment of esthesioneuroblastoma to date.⁵

Despite the successful outcomes of craniofacial resection, postoperative morbidity (~ 35%) and mortality (2–5%) with this procedure remains relatively high.⁶ Further original work was performed at UCLA to address this issue. Nabili and colleagues proposed a fully transnasal transfacial approach for en bloc resection of ONB obviating the need for frontal craniotomy. Using a lateral rhinotomy approach along with anterior skull base resection via a two-team approach with neurosurgery, they showed that an en bloc resection with negative margins could be achieved with decreased complications and a well-camouflaged scar. They also showed comparable survival with patients who underwent conventional craniofacial resection.⁷

In the current era of expanded endoscopic endonasal surgery, it has been shown that anterior skull base tumors can be endoscopically controlled within the limits of oncologic principles.⁸ Indeed, current literature supports that this may be true of ONB. There are now numerous accounts

Table 1 Modified-Kadish stage of esthesioneuroblastoma

Stage	Extent
A	Tumor limited to the nasal cavity
B	Tumor in the nasal cavity and extending to the paranasal sinuses
C	Tumor extends beyond the nasal cavity and paranasal sinuses involving the cribriform lamina, the skull base, the orbit, or the intracranial cavity
D	Tumor with neck or distant metastases

Table 2 Dulguerov-Calcaterra staging of esthesioneuroblastoma

Stage	Characteristics
T1	Tumor involving the nasal cavity and/or paranasal sinuses (excluding sphenoid), sparing the most superior ethmoidal cells
T2	Tumor involving the nasal cavity and/or paranasal sinuses (including the sphenoid) with extension to or erosion of the cribriform plate
T3	Tumor extending into the orbit or protruding into the anterior cranial fossa
T4	Tumor involving the brain
N0	No cervical lymph node metastasis
N1	Any form of cervical lymph node metastasis
M0	No metastasis
M1	Distant metastasis present

in the literature of ONB resected by a fully endoscopic approach.^{6,9,10} More institutional accounts are needed, however, to assess outcomes using this approach.

Here, we seek to add to the growing body of literature regarding treatment and outcomes of ONB and offer an update on the UCLA experience. We aim to update our outcomes with the transnasal transfacial approach and to provide our more recent experience with the expanded endoscopic endonasal approach.

Methods

Patient Data

The study was approved by the UCLA institutional review board. Patients with ONB were identified from the pathology specimens received between 2002 and 2013 at the UCLA Ronald Reagan Medical Center through a computer-assisted search by the UCLA Tumor Registry in the Department of Pathology. Forty-one patients were identified, and their clinical records were accessed for chart review. Five patients were excluded because they only received biopsies or underwent debulking procedures without intent for cure, leaving 36 patients for analysis.

Pathologic Review

All pathologic diagnoses were determined by head and neck pathologists at UCLA. Tumor histopathology including grade and margin status were obtained. Tumors were graded as low or high if diagnosed as such by the pathologist based on microscopic features including architecture, pleomorphism, the number of mitoses, the prominence of the neurofibrillary matrix, the presence of rosettes, calcifications, and necrosis. Alternatively, if Hyams grade only was reported, tumors were classified as low grade for Hyams grade I/II or high grade for Hyams grade III/IV. Margin analysis was determined by intraoperative frozen section analysis as well as final pathology.

Statistical Analysis

Primary outcome was recurrence-free survival (RFS) and overall survival (OS). RFS was defined as the time from initial treatment to diagnosis of a local, regional, or distant recurrence. OS was defined as the time from initial treatment to death from any cause. RFS and OS were calculated using the Kaplan-Meier method, and univariate comparisons between groups were performed using the log-rank test. Significant factors were entered into multivariate analysis using the Cox proportion hazards model. The one-way analysis of variance test was used to compare means between groups. Nonparametric qualitative variables were cross-classified into contingency tables and compared using chi-square tests. The Fisher exact test was used when expected value was < 5 . A p value ≤ 0.05 was considered significant for all statistical tests. Statistical analyses were performed with SPSS v. 21 (IBM Corp., Armonk, New York, United States).

Results

Patient Demographics

Thirty-six patients were included in the study. The mean age of the study population was 50.1 ± 16.9 years (range: 12–84 years). Males and females were evenly distributed (► **Table 3**). All patients had some follow-up, with median duration of follow-up of 33 months. Four patients only had a 1-month follow-up and thus were removed from the survival analysis but were included in the perioperative analysis.

Clinical Presentation

Patients most frequently presented with unilateral nasal obstruction and congestion (61%). Unilateral epistaxis was the next most common presenting symptom (39%). Initial presentation with a neck mass was uncommon (8%).

Primary Tumor

Eight patients (22%) presented with recurrent disease after being treated at an outside institution. Modified Kadish and Dulguerov-Calcaterra stagings are listed in ► **Table 3**. Overall, 16.7% showed intraorbital extension and 55.6% had intracranial extension. Nine of the 20 patients with intracranial extension had invasion through the dura. Most of the tumors (28 of 36) were low grade (78%).

Treatment

Eight patients had prior treatment (► **Table 3**). All 36 patients in the study population underwent surgical resection via transnasal transfacial craniofacial resection with craniotomy (CFR), transnasal transfacial craniofacial resection without craniotomy (TFR), or expanded endoscopic endonasal craniofacial resection (ECR). Twenty-six patients received adjuvant radiation. Five patients had adjuvant chemotherapy and radiation. Three patients had no adjuvant therapy due to limited-stage disease and low-grade pathology. Adjuvant radiation dose was not available for most patients but ranged from 5000 to 6000 cGy when reported.

Table 3 Patient demographics, tumor characteristics, and treatment modality

Characteristic	Number (%)
Sex	
Female	18 (50)
Male	18 (50)
Presenting symptoms at diagnosis	
Nasal obstruction/congestion	22 (61)
Epistaxis	14 (39)
Hyposmia/anosmia	4 (11)
Headache/Pain	4 (11)
Neck mass	3 (8.3)
Prior treatment	
Surgery	2 (5.6)
Surgery and XRT	1 (2.8)
Surgery, chemotherapy, and XRT	2 (5.6)
Chemotherapy and XRT	3 (8.3)
No treatment	28 (77.8)
Tumor grade	
Low	28 (78)
High	6 (16.7)
Unable to be determined	2 (5.6)
Margin status	
Negative	30 (83.3)
Positive or < 5 mm from margin	6 (16.7)
Kadish staging	
A	2 (5.6)
B	15 (42)
C	20 (56)
D	4 (11)
Dulguerov-Calcaterra T staging	
T1	2 (5.6)
T2	16 (44)
T3	9 (25)
T4	9 (25)
Intraorbital extension	
Yes	6 (16.7)
No	30 (83.3)
Intracranial extension	
Yes	16 (44)
No	20 (56)
Surgical approach	
CFR	8 (22.2)
TFR	20 (55.6)
ECR	8 (22.2)

Abbreviations: CFR, traditional craniofacial resection with craniotomy; ECR, expanded-endoscopic, endonasal approach; TFR, transnasal, transfacial resection without craniotomy; XRT, radiation.

In choosing the surgical approach, a conventional craniotomy with craniofacial resection was used due to possible brain invasion in three cases. For the remainder of cases, when choosing a CFR, TFR, or ECR approach, surgeon preference and expertise were the sole reason for choosing each approach. In general, cases earlier in the series were performed by a more aggressive open approach and more minimally invasive approaches were used later in the series. This reflects the change in our institution with regard to expertise in endoscopic surgery.

In the CFR group, seven patients required a resection of the anterior skull base. In the remaining patient in the CFR group, a craniotomy was only required due to isolated recurrence intracranially. In the TFR group, 13 patients required resection of the anterior skull base with reconstruction. Six patients did not undergo skull base resection because the

cribriform was not involved and confirmed to be free of disease on frozen section analysis. In the final patient in the TFR group, the procedure was aborted before skull base resection due to significant intraoperative bleeding. In the ECR group, seven patients required skull base resection and only one patient did not due to noninvolvement of the cribriform plate confirmed on frozen section analysis. In general, skull base reconstruction was performed in a multilayered fashion buttressed by nasal packing inferiorly. ► **Table 4** depicts the method of skull base reconstruction for all cases that required resection of the anterior skull base.

Overall, negative margins were achieved in 83.3% of patients. Mean estimated blood loss was 839.7 mL. A lumbar drain was required in 58.3% of patients. Mean hospitalization was 5.11 days. A total of 55.6% of patients required intensive

Table 4 Patients requiring anterior skull base reconstruction and method of reconstruction

Age, y	Sex	Kadish stage	Surgical approach	Intracranial extension?	Type of reconstruction
26	M	C	CFR	Yes	Pericranial flap
62	F	C	CFR	Yes	Pericranial flap
63	F	C	CFR	Yes	Pericranial flap
41	M	C	CFR	No	Pericranial flap
51	F	B	CFR	No	Pericranial flap
42	F	C	CFR	Yes	Pericranial flap
33	M	C	CFR	Yes	Pericranial flap
39	M	C	TFR	Yes	Abdominal fat, titanium mesh
56	F	C	TFR	No	Abdominal fat, titanium mesh
75	M	B	TFR	No	Periorbital fat, titanium mesh
27	F	B	TFR	No	Abdominal fat, titanium mesh
58	F	B	TFR	No	Abdominal fat, titanium mesh, nasoseptal bone graft
43	F	D	TFR	Yes	Abdominal fat, titanium mesh
48	F	B	TFR	No	Abdominal fat, titanium mesh
46	M	B	TFR	No	Periorbital fat, titanium mesh
40	M	C	TFR	Yes	Abdominal fat, titanium mesh
44	F	D	TFR	No	Abdominal fat, titanium mesh
30	M	C	TFR	Yes	Abdominal fat, titanium mesh
69	M	C	TFR	Yes	Abdominal fat, titanium mesh
70	F	B	TFR	No	Periorbital fat, titanium mesh
49	F	B	ECR	No	Abdominal fat, fascia lata graft
50	M	A	ECR	No	Fascia lata graft
70	M	C	ECR	Yes	Acellular dermal matrix free tissue graft
72	M	B	ECR	No	Acellular dermal matrix free tissue graft
55	M	D	ECR	Yes	Dura matrix graft, nasoseptal flap
40	F	C	ECR	Yes	Abdominal fat, fascia lata graft, absorbable plate, nasoseptal flap
12	F	C	ECR	No	Fascia lata graft, septal bone, free mucosal graft

Abbreviations: CFR, traditional craniofacial resection with craniotomy; ECR, expanded-endoscopic, endonasal approach; TFR, transnasal, transfacial resection without craniotomy.

care unit (ICU) admission postoperatively with an average of 2.8 days (range: 1–6 days) in the ICU. Complications occurred in 42% of patients and were most commonly cerebrospinal fluid leaks that occurred in 13.8%. The distribution of complications is shown in ►Table 5.

Overall Survival and Recurrence-Free Survival

Seven patients (19%) developed neck metastases of which four were isolated and three were in the setting of multifocal recurrence. Time to recurrence of isolated regional neck disease ranged from 7 to 24 months. Three patients (8.3%) developed spinal cord and multifocal dural metastases in the setting of local recurrence. No other sites of metastasis were identified. Time to any recurrence ranged from 7 to 38 months. The 5-year RFS and OS were 54% and 82%, respectively, for the entire cohort of patients with > 1-month follow-up (►Fig. 1). Median OS and RFS was 132 and 120 months, respectively. Of patients with isolated neck recurrence, two underwent neck dissection and the remaining two underwent neck dissection followed by radiation therapy. The three patients who developed multifocal spinal cord and dural metastasis were treated with palliative chemotherapy. One patient who developed local and regional neck recurrence underwent open craniofacial resection and neck dissection followed by chemoradiation after having undergone TFR initially.

Surgical Approach

Data were grouped according to surgical approach (►Table 6). There was a statistical difference in mean hospital stay ($p = 0.006$) between the three treatment groups. This finding

Fig. 1 Kaplan-Meier curves for (A) recurrence-free survival and (B) overall survival.

Table 5 Complications by surgical approach

CFR	TFR	ECR
CSF leak (3)	CSF leak (2)	Preseptal cellulitis
Pneumocephalus (2)	Meningitis (2)	Pneumonia
Meningitis (2)	Anemia requiring transfusion (2)	
Epidural hematoma	Nasocutaneous fistula	
Brain herniation	Subarachnoid hemorrhage	
Nasocutaneous fistula	Hyponatremia	
Hyponatremia	Wound infection	
	Intraoperative coagulopathy	
	UTI	
	Pneumocephalus	
	Nasal deformity	

Abbreviations: CFR, traditional craniofacial resection with craniotomy; CSF, cerebrospinal fluid; ECR, expanded endoscopic endonasal approach; TFR, transnasal transfacial resection without craniotomy; UTI, urinary tract infection.

Table 6 Outcome by surgical approach

Outcome	CFR	TFR	ECR	<i>p</i> value
Estimated blood loss, mL	600	1107	411.25	0.103
Hospital stay, d	8.63	4.47	3.13	0.006
Patients with complications, <i>n</i> (%)	5 (62.5)	8 (40)	2 (25)	0.306
Mean no. of complications per patient	1.375	0.75	0.25	0.267
Intensive care unit admission, <i>n</i> (%)	6 (75)	7 (35)	2 (25)	0.095
Lumbar drain placement, <i>n</i> (%)	6 (75)	7 (35)	2 (25)	0.085
Positive margins, <i>n</i> (%)	2 (25)	4 (20)	0 (0)	0.348
Mean follow-up, mo	47.9	39	12.25	0.352

Abbreviations: CFR, traditional craniofacial resection with craniotomy; ECR, expanded endoscopic endonasal approach; TFR, transnasal transfacial resection without craniotomy.

held true when excluding those patients who did not require skull base resection ($p = 0.037$). In addition, there was a trend toward decreased complications, lumbar drain placement rate, and ICU admission rate for the ECR group, although this did not reach a statistical difference. Interestingly, there was a trend toward increased blood loss in the TFR group. There was no statistical difference between OS and RFS (log rank $p = 0.669$ and 0.223 , respectively) among the three groups.

Factors Predicting Recurrence and Overall Survival

Patient and tumor factors were evaluated with respect to RFS and OS by univariate analysis. Analysis revealed that grade (log-rank $p = 0.04$), intracranial extension with dural invasion (Log rank $p = 0.009$), presentation with recurrent disease (Log rank $p = 0.002$), and Dulguerov-Calcaterra staging (log-rank $p = 0.014$) affected RFS. Modified Kadish stage was the only factor identified to affect OS (log-rank $p = 0.015$). Intracranial extension with dural invasion and presenting with recurrent disease were near significant (log-rank $p = 0.051$ for both factors). Multivariate analysis based on the three factors significant by univariate analysis showed that grade (12.132; 95% confidence interval [CI], 1.699–86.626; $p = 0.013$) was the only factor that had an independent impact on RFS.

Discussion

ONB is a rare malignant tumor of the superior nasal vault postulated to be derived from the olfactory epithelium. Previous reports vary, but it has been shown to have a unimodal age distribution with a peak at 53 years of age.¹¹ Other studies have shown a bimodal age distribution with peaks in the third to fifth decade of life and another peak in the seventh decade.⁶ Age distribution was uniform in this study with a mean of 50.1 ± 16.9 years. There was an equal distribution of males and females, corroborating prior reports on sex distribution.^{2,6,11} Most patients presented with nasal obstruction (61%) and epistaxis (39%).

In this study, most of the patients had surgery followed by postoperative radiation (72%). Chemotherapy was considered if the patient presented with high-grade pathology, had positive margins, regional or metastatic disease, or was being treated for a recurrent tumor. Surgical resection was performed via CFR, TFR, or ECR in all patients with the goal of negative margins.

Complication rates were not statistically different between the three surgical approaches; however, the breadth of complications depicted in **Table 5** exemplifies the morbidity of the traditional open approaches, especially with the addition of craniotomy. This is in agreement with prior reports of endoscopic versus open approaches to anterior skull base tumors that report significant increased morbidity for open approaches.¹² Furthermore, two patients developed nasocutaneous fistulas following radiation, and one patient developed significant nasal deformity requiring multiple revision nasal surgeries as a consequence of using a transfacial approach. Adoption of an endoscopic approach may obviate these complications in the future.

Length of hospitalization was reduced as the procedure became more minimally invasive, and this finding was statistically significant ($p = 0.006$) and held true when excluding those patients who did not require skull base resection ($p = 0.037$). In addition, there was a trend toward decreased ICU admission rate and lumbar drain placement rate. Interestingly, there was a trend toward increased blood loss in the TFR group, possibly due to increased difficulty controlling bleeding deep in the sinonasal cavity without the exposure provided by a traditional CFR or with the endoscope.

The endoscopic approach is not without its own inherent limitations. Traditional open approaches still need to be utilized for tumors with far lateral or superior extension, orbital invasion necessitating exenteration or removal of prior orbita, and tumors invading the facial soft tissues. Additionally, many oncologic surgeons still defend an en bloc resection, and there are significant concerns regarding piecemeal resection of tumors. Wellman et al attempted to address this question in their series of 30 patients with malignant midline anterior skull base tumors, of whom 53.3% received an en bloc resection and 46.7% were resected in a piecemeal fashion. Survival was comparable between the groups and depended on margin status, independent of approach used.¹³ More research is needed regarding long-term outcomes from fully endoscopic approaches for malignant tumors of the skull base.

The 5-year RFS and OS were 54% and 82%, respectively, among all patients in this study, in line with prior published data.⁵ Perhaps the most extensive study of survival was by Kane et al in their systematic review of 956 patients from 205 studies reporting ONB outcome. In their study, OS was ~76% at 5 years and 64% at 10 years.¹⁴ There was no statistical difference in RFS and OS by surgical approach (log-rank $p = 0.223$ and 0.669 , respectively); however, the endoscopic group had 0% recurrence and 100% survival. Follow-up was too short for this cohort of patients (median follow-up: 8 months) to statistically detect a difference. Song et al performed one of the largest studies investigating surgical approach for ONB. In their study, they showed that 5-year disease-free survival was higher in patients treated with endoscopic approaches versus traditional open approaches (100% and 80.8% for endoscopic and endoscopic assisted versus 41.7% for traditional CFR). This finding held true on multivariate analysis that excluded the bias of stage.⁶ Longer follow-up will be needed to make more definitive statements because ONB has been known to recur > 10 years from presentation.⁵ In addition, one must take into account the bias of stage because earlier staged tumors are more likely to be resected by an endoscopic approach as opposed to late-stage tumors, which may have indications for an open approach.

Multiple studies have attempted to identify prognostic factors for survival among patients with ONB. One of the largest series was an international collaborative study involving 151 patients investigating outcomes after craniofacial surgery for ONB. On multivariate analysis, intracranial extension and positive surgical margins were identified to be independent predictors of worse overall disease-specific

survival and RFS.⁵ Other studies have identified the Kadish system, T staging of the Dulguerov-Calcaterra staging, grade, nodal involvement, and radiation dose.^{5,15,16} In this study, univariate analysis revealed that grade (log-rank $p = 0.04$), intracranial extension with dural invasion (log-rank $p = 0.009$), presenting with recurrent disease (log-rank $p = 0.002$), Dulguerov-Calcaterra staging (log-rank $p = 0.014$) all affected RFS. However, on multivariate analysis, only grade (12.132; 95% CI, 1.699–86.626; $p = 0.013$) was an independent predictor of RFS. Interestingly, intracranial extension without dural invasion did not affect RFS (log-rank $p = 0.309$). Modified Kadish stage was the only factor identified to affect OS (log-rank $p = 0.015$). Intracranial extension with dural invasion and presenting with recurrent disease were near significant predictors of OS (log-rank $p = 0.051$ for both factors). Intraorbital extension did not affect RFS or OS (log-rank $p = 0.852$ and 0.5 , respectively).

Intriguingly, the breadth of data supporting grade as a prognostic factor for survival in ONB has been growing. A recent study from UCSF investigated Kadish stage C ONB for outcome with regard to grade. They report that in patients with low-grade ONB (Hyams grade 1–2), the 2-year progression-free survival (PFS) was 86% and the 5-year PFS was 65% in comparison with 73% and 49% in patients with high-grade ONB (Hyams grade 3–4), respectively.¹⁷ In addition, Malouf et al recently reported that when compared with patients with low-grade ONB (Hyams grade $\leq$ III), patients with high-grade ONB (Hyams grade $>$ III) have higher T4 staging ($p = 0.02$), have frequent lymph node involvement ($p = 0.009$), and are more often unresectable ($p = 0.005$). They also report reduced disease-free survival and OS for high-grade ONB.¹⁵ The study previously mentioned by Kane et al also showed on univariate analysis worse survival in patients with Kadish C tumors, Hyams grade 3 or 4 tumors, and in patients $>$ 65 years of age. Multivariate analysis demonstrated that Hyams grade 3 or 4 tumors carried significant risk (hazard ratio = 4.83; $p < 0.001$).¹⁴ Van Gompel et al performed one of the largest single-institution experiences including 109 patients and also concluded a distinct natural history of low- and high-grade ONB. In addition to reporting worse OS survival for high-grade pathology, they showed that high-grade tumors correlated with more advanced localized disease as well as regional neck metastasis.¹⁸ The growing evidence supports that grade may have a larger influence than previously described. This study supports by multivariate analysis that grade is an independent predictor of recurrence.

Conclusion

This update on the UCLA experience on ONB confirms prior findings that a transnasal transfacial approach offers comparable survival, obviating the need for craniotomy. In addition, we share our new experience with a fully endoscopic approach that preliminarily has yielded positive results with respect to blood loss, length of hospitalization, ICU admission rate, and complications. Finally, we show through multivariate analysis that tumor grade is an independent predictor of

survival and its importance may need more emphasis in future staging systems.

Notes

This study was selected for oral presentation at the 24th Annual North American Skull Base Society meeting in San Diego, CA.

References

- Kadish S, Goodman M, Wang CC. Olfactory neuroblastoma. A clinical analysis of 17 cases. *Cancer* 1976;37(3):1571–1576
- Morita A, Ebersold MJ, Olsen KD, Foote RL, Lewis JE, Quast LM. Esthesioneuroblastoma: prognosis and management. *Neurosurgery* 1993;32(5):706–714; discussion 714–715
- Billier HF, Lawson W, Sachdev VP, Som P. Esthesioneuroblastoma: surgical treatment without radiation. *Laryngoscope* 1990; 100(11):1199–1201
- Dulguerov P, Calcaterra T. Esthesioneuroblastoma: the UCLA experience 1970–1990. *Laryngoscope* 1992;102(8):843–849
- Patel SG, Singh B, Stambuk HE, et al. Craniofacial surgery for esthesioneuroblastoma: report of an international collaborative study. *J Neurol Surg B Skull Base* 2012;73(3):208–220
- Song CM, Won TB, Lee CH, Kim DY, Rhee CS. Treatment modalities and outcomes of olfactory neuroblastoma. *Laryngoscope* 2012; 122(11):2389–2395
- Nabili V, Kelly DF, Fatemi N, St John M, Calcaterra TC, Abemayor E. Transnasal, transfacial, anterior skull base resection of olfactory neuroblastoma. *Am J Otolaryngol* 2011;32(4):279–285
- Snyderman CH, Carrau RL, Kassam AB, et al. Endoscopic skull base surgery: principles of endonasal oncological surgery. *J Surg Oncol* 2008;97(8):658–664
- Gallia GL, Reh DD, Salmasi V, Blitz AM, Koch W, Ishii M. Endonasal endoscopic resection of esthesioneuroblastoma: the Johns Hopkins Hospital experience and review of the literature. *Neurosurg Rev* 2011;34(4):465–475
- Monteiro EM, Lopes MG, Santos ER, et al. Endoscopic treatment of esthesioneuroblastoma. *Braz J Otorhinolaryngol* 2011;77(2): 171–177
- Jethanamest D, Morris LG, Sikora AG, Kutler DL. Esthesioneuroblastoma: a population-based analysis of survival and prognostic factors. *Arch Otolaryngol Head Neck Surg* 2007;133(3):276–280
- Eloy JA, Vivero RJ, Hoang K, et al. Comparison of transnasal endoscopic and open craniofacial resection for malignant tumors of the anterior skull base. *Laryngoscope* 2009;119(5):834–840
- Wellman BJ, Traynelis VC, McCulloch TM, Funk GF, Menezes AH, Hoffman HT. Midline anterior craniofacial approach for malignancy: results of en bloc versus piecemeal resections. *Skull Base Surg* 1999;9(1):41–46
- Kane AJ, Sughrue ME, Rutkowski MJ, et al. Posttreatment prognosis of patients with esthesioneuroblastoma. *J Neurosurg* 2010;113(2): 340–351
- Malouf GG, Casiraghi O, Deutsch E, Guigay J, Temam S, Bourhis J. Low- and high-grade esthesioneuroblastomas display a distinct natural history and outcome. *Eur J Cancer* 2013;49(6):1324–1334
- Ozsahin M, Gruber G, Olszyk O, et al. Outcome and prognostic factors in olfactory neuroblastoma: a rare cancer network study. *Int J Radiat Oncol Biol Phys* 2010;78(4):992–997
- Kaur G, Kane AJ, Sughrue ME, et al. The prognostic implications of Hyam's subtype for patients with Kadish stage C esthesioneuroblastoma. *J Clin Neurosci* 2013;20(2):281–286
- Van Gompel JJ, Giannini C, Olsen KD, et al. Long-term outcome of esthesioneuroblastoma: Hyams grade predicts patient survival. *J Neurol Surg B Skull Base* 2012;73(5):331–336