S169 PREDICTORS OF REGIONAL AND DISTANT METASTASIS IN ESTHESIONEUROBLASTOMA PATIENTS TREATED OVER 30 YEARS AT MEMORIAL SLOAN-KETTERING CANCER CENTER

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Purpose:

Esthesioneuroblastoma (ENB) is a malignant neuroendocrine tumor originating from the olfactory neuroepithelium in the cribriform plate. To date, the precise incidence of metastases has not been well defined. We report our experience with ENB over the last 30 years.

Methods:

Retrospective analysis of 57 patients presenting to Memorial Sloan Kettering Cancer Center (MSKCC) with esthesioneuroblastoma from 1979 through 2009. Median follow up was 68 months.

Results:

Of the 57 patients, 23% (13/57) were Kadish A at presentation, 35% (20/57) Kadish B, 33% (19/57) Kadish C and 9% (5/57) were Kadish Stage D (with neck or distant metastases at presentation). At time of diagnosis, 37% (21/57) had intracranial extension. Presenting symptoms of nasal obstruction and epistaxis were the most common (73% and 45% respectively).

Overall survival for all Kadish Stages was 85% at 5 years and 75% at 10 years. Intracranial extension, positive resection margins, and neck metastasis were significant independent predictors of worse mortality (p<0.001, p=0.05, and p=0.017 respectively). Five patients had neck disease at presentation and of the patients originally N0, 17% (11/57) patients developed subsequent neck failure at median time 60 months. Kadish stage was not associated with risk of neck failure (p=0.5). After neck failure, 82% underwent surgical salvage and 78% (7/9) had successful locoregional control. However, of patients developing neck failure, more than half developed distant metastases. The cumulative incidence of distant metastasis was (39%) at a median time of 40 months. Patients who presented with Kadish stage C or D had a significantly increased risk of distant failure (p<0.001).

Conclusion:

Regional and distant failure in patients with esthesioneuroblastoma generally occurs in a delayed fashion and negatively impacts survival. The 17% rate of delayed neck metastasis was not associated with Kadish stage. Neck recurrences were usually able to be surgically salvaged, but may be a harbinger of distant metastases.
EARLY STAGE ESTHESIONEUROBLASTOMA: IS RESECTION OF THE BONY SKULL BASE, DURA AND OLFACTORY BULB NECESSARY?

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Background

Esthesioneuroblastoma is a rare sinonasal malignancy. The exact origin of the tumor is unclear but the most likely site is the basal neural cell of the olfactory mucosa. In a previous large series from our institution, a significant proportion of patients (41%) were identified to have Kadish A or B stage disease. Resection of the cribriform plate, dura and olfactory bulb remains controversial in patients with tumor confined to the sinonasal cavity. We report the outcomes of patients with Kadish A and B esthesioneuroblastoma treated at MD Anderson Cancer Center.

Methods

We retrospectively reviewed all patients undergoing treatment for Kadish A and B esthesioneuroblastoma from 2002 to 2013. Demographic, clinical, pathological data and oncological outcomes were collected. Kaplan-Meier methods were used for survival analysis.

Results

Thirty-five patients were identified to have Kadish A or B tumors on initial evaluation. There were 18 males and 17 females, median age 44 years (range 13 to 71). The median follow up was 66 months. The majority of patients had tumors of low or medium histological grade (80%). One patient had a Hyams grade 3/4 tumor, the rest were grade 2 or grade 2/3. The majority of patients had unilateral sinonasal involvement (91.4%). Fifty-four percent of patients had tumors arising from the nasal cavity, the rest originated from the ethmoid sinuses. Forty percent of patients had tumor involvement of the skull base mucosa and one patient had minor erosion of the bony skull base. Twenty-three patients (65.7%) received surgery with post-operative radiation therapy and the rest were treated with surgery alone. The proportion of patients treated with resection of the bony skull base, dura and olfactory bulb were 34.3%, 22.9% and 20% respectively. One patient was unexpectedly found to have an intracranial dural nodule during surgery. 6.6% of margins were reported as grossly positive and 6.6% as microscopically positive. The 5-year overall survival (OS) and disease free survival (DFS) was 92.6% and 88.4% respectively. Regional recurrence was 2.9%. Local and distant recurrence was 2.9% and 2.9% respectively and occurred in the same patient with Hyams Grade 3/4 tumor who refused post-operative radiation therapy. There was no significant difference in survival or recurrence between patients who were treated with resection of the bony skull base, dura and olfactory bulbs and those who were not.

Conclusion

The majority of patients with Kadish A and B esthesioneuroblastomas have low histological and Hyams grade tumors with unilateral involvement. They have favorable survival outcomes and oncological control. Resection of the skull base, dura and olfactory bulb does not have a positive impact on survival in appropriately selected patients who are treated with complete surgical resection and post-operative radiation therapy.
Squamous Cell Carcinoma Arising from Sinonasal Inverted Papilloma: Survival Outcomes of 27 Patients Treated with Endoscopic Endonasal Resection

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Background

Inverted papillomas are rare benign, epithelial tumors of the sinonasal tract that can be associated with malignancy (5-10% of cases). Invasive squamous cell carcinoma is the most frequently reported tumor and its diagnosis usually occurs synchronously with inverted papilloma. Less commonly, however, metachronous squamous cell carcinoma may arise after previous resections of inverted papilloma. The mortality rate has been reported to be around 40%. The aim of the present study is to add our experience to the small amount of data currently available on this topic, analyzing the clinical features, treatment modalities (focusing on the endoscopic endonasal approach) and survival outcomes in this specific subgroup of patients.

Methods

The medical records of all patients diagnosed with inverted papilloma between November 1991 and August 2013 at two university centres following a uniform policy were retrospectively reviewed. 27 of these patients had also presented association to squamous cell carcinoma. To the best of our knowledge this is the largest series presented to date.

Results

The age of the enrolled patients ranged from 34 to 78 years (mean: 58.7 years); 17 patients were male, whereas 10 were female. Squamous cell carcinoma metachronous to the initial diagnosis of inverted papilloma in three cases and synchronous in 24. The tumors were staged as T1 (5/27), T2 (7/27), T3 (8/27), T4a (2/27) and T4b (5/27). Eight patients were treated previously while 19 patients have never been treated before. All patients underwent surgery with an exclusive endoscopic endonasal resection (23 cases), a cranio-endoscopic resection (3 cases), a combined endoscopic-osteoplastic flap procedure (1 case). Subsequently, 11 patients underwent adjuvant radiotherapy, 1 adjuvant chemotherapy, 2 concomitant radio-chemotherapy while the rest of the patients were not submitted to any adjuvant treatment. After the first line treatment, 2 and 7 patients respectively presented persistent and recurrent disease (mean: 22 month). The follow-up ranged from 130 to 5 months (mean: 46.9 months). 21 patients had no evidence of disease, 1 patient was alive with disease, while 5 patients developed distant metastases and died of disease (1 with previous persistent disease and 4 with previous recurrent disease). The 5-years overall survival in our series was 66.8% (22/27).

Conclusions

In correctly selected patients, the endoscopic endonasal approach offers a less invasive alternative than resection by an open approach, with acceptable morbidity. Adjuvant radiotherapy with or without
chemotherapy should be indicated in advanced disease or in presence of close or positive margins. Recurrent disease can develop after prolonged period of time, thus long term follow-up by means of endoscopic examination and radiological studies, is recommended.
ENDOSCOPIC ENDONASAL RESECTION OF ADENOID CYSTIC CARCINOMA: OUR EXPERIENCE FROM A SERIES OF 28 CASES
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Background: The increasing expertise in the field of transnasal endoscopic surgery has recently expanded its indications to include the sinonasal malignancies. We report our experience in the management of sinonasal adenoid cystic carcinoma through an endoscopic endonasal approach.

Materials and Methods: Retrospective analysis of patients treated through an endoscopic endonasal approach from 1998 to 2012, managed by two surgical team at the Departments of Otorhinolaryngology of the University of Varese and Brescia.

Results: The patients considered eligible for the present analysis were 28. The nasal fossa (46%), maxillary sinus (32%), nasal septum (15%), and sphenoid sinus (7%) were the primary tumor sites encountered. The majority of patients presented with locally advanced disease, without a systemic spreading. In 5 cases, the involvement of anterior skull base required a transnasal endoscopic craniectomy. Overall, 14/28 (50%) patients received some form of adjuvant radiotherapy. The follow-up ranges from 6 to 168 months (mean of 56 months). The 5-year overall, disease-specific, disease-free and recurrence-free survival were 87.5% ± 8.98%, 87.5% ± 8.98%, 67.9% ± 11.6% and 69% ± 11.5%, respectively.

Conclusions: These results combined with short hospitalization time, due to a very limited morbidity typical of mini-invasive procedures, seem to indicate that endoscopic surgery, when properly planned and in expert hands, may be a valid alternative to standard surgical approaches for the management of this subset of sinonasal cancers.
S173 SKULL BASE DEFECTS AND RELATED COMPLICATIONS AFTER CRANIOFACIAL TUMORS REMOVAL

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Skull base defects of the anterior fossa or middle fossa take place during the surgery on intra-extracranial tumors. Such tumors invade or destroy the anterior fossa or middle fossa. Having prognosed the defect and having planned the closure in advance would avoid complications in early and later periods.

Materials and Method: We investigated 87 anterior skull base defects (ASBD) and 44 defects to the floor of the middle fossa. Skull base meningiomas (17 cases), angiofibromas (20), osteomas, osseous, and cartilaginous tumors (17 cases), sino-paranasal malignancies (43 cases), esthesioneuroblastoma (7 cases), adenocarcinoma (9 cases), neurofibromas, schwannomas (18 cases). ASBD were median (square equals 10-15 cm2) in 22 patients, median widened (square equals 16-32 cm2) in 35 patients, median-lateral (square equals 32-54 cm2) - in 30 patients. Middle fossa defects (MFD) were present in 44 cases: moderate (square equals 12-20 cm2) - in 37 patients and big (square equals 32-70cm2) - in 8 patients).

Results: ASBD defects were closed mostly with pedicled flaps: frontal periosteum (71 case) and temporal muscle (8 cases). Concomitant dural defect was present in 55 patients (closed with fascia lata graft - 41 cases, periosteum graft - 11cases, artificial dura graft - 3 cases). MFD required closure in 10 cases (mostly closed with the temporal muscle - 8 cases). Liquorhea took place in 6 cases (in 5 of them the ASBD was 16cm2 and more) Meningitis took place in 4 cases not relating to the size of the defect. Postoperative brain herniation into the defect took place in 2 patients with the median-lateral defect (48 cm2 and 54 cm2)

Conclusions: Risks of complications (liquorhea) increase with the size of the defects, risk of brain herniation into lumen of the defect is high as the latter reaches 48-54cm2 (median-lateral defects). Closure enhancement (prolene mesh, titanium) is needed when planning the surgery with the expected median-lateral defects, ASBD closure with the periosteal flap is efficient and sufficient material in view of hermetic closure, MFD defects would require closure in rare cases, relating to big defects.
LONG-TERM RESULT OF ENDOSCOPIC-ASSISTED CRANIONASAL RESECTION OF OLFATORY NEUROBLASTOMA

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Craniofacial resection has been the gold standard operation for management of olfactory neuroblastoma. Recently endoscopic-assisted or total endoscopic resection have been utilized as the surgical approach for management of olfactory neuroblastoma with out orbital involvement with comparable short term oncological results. Most case series of endoscopic approaches are of short follow duration. As olfactory neuroblastoma can have late recurrences 8 to 10 years after operation, Claims of comparable results from endoscopic approaches with open approaches has been critizised as the follow up periods were shorter in endoscopic approaches. We here report our long-term result of endoscopic-assisted cranionasal resection of olfactory neuroblastoma.

Our cohort is a retrospective review of a single center experience on endoscopic-assisted cranionasal resection for olfactory neuroblastoma from 1998-2012. All patients underwent a endoscopic assited cranionasal resection where the nasal part of the operation was performed endoscopically while the intracranial resection and dural repair were done with a frontal craniotomy.

There were 14 patients, the Kadish stages were 1A, 4B and 9C. Median follow up was 85 months (12-186 months). There was no CSF leak. One patient had convulsion after operation. 7 patients received post operative radiotherapy to the skull base and paranasal sinuses. 3 patients developed nodal recurrence and 2 patients developed intracranial recurrence and 1 patient developed recurrence in the nasal cavity. One patient in died of disease. 5-year overall survival (OS) and recurrence free survival (RFS) were 92.8% and 48%, and the 10-year OS and RFS were also 92.8% and 48%. Due to the small sample size, survival analysis failed to identify and risk factors affecting survival or recurrence.

Endoscopic-assisted cranionasal resection for olfactory neuroblastoma can achieve excellent long-term oncological results comparable to open craniofacial surgery.
Evolving Role of Endoscopic Surgery in Management of Esthesioneuroblastoma: A 42 Year Experience at the University of California San Francisco.

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Title: Evolving Role of Endoscopic Surgery in Management of Esthesioneuroblastoma: a 42 year experience at the University of California San Francisco.

Introduction: Endoscopic resection of Esthesioneuroblastoma (ENB) is gaining acceptance, however some concerns still remain over the nature of piecemeal resection, ability to obtain clean margins, and equivalent long term control. Objective: To analyze the clinical features, treatment modalities, and outcomes of ENB at a single institution over time as endoscopic methods have been introduced.

Methods: A retrospective review of 51 patients treated surgically at the University of California San Francisco during the time period of 1971-2013. Patient medical records, images, and pathologic slides were reviewed by respective attendings (surgeon, radiologist, or pathologist).

Results: The median age at diagnosis was 52 years (range 13-92) and 67% were female. At presentation to our institution 6 (12%) were Kadish A, 14 (27%) were Kadish B, and 31 (61%) were Kadish C, including 3 Kadish D patients. Forty four patients had post operative and 4 had preoperative radiation while two had no radiation (data unavailable for one patient). Overall survival (OSS) at 5 and 10 year survival were 88% and 78%, and disease free survival (DFS) were 80% and 66% respectively. Thirty patients (59%) were treated with an open approach, 6 (12%) with an endoscopic-assisted approach, and 15 (29%) with a purely endoscopic approach. Prior to 2004 all the cases were performed open, while from 2004 to 2013, 84% were done either purely endoscopic or endoscopic-assisted, 8 of which were Kadish C. Another 7 Kadish C patient underwent an open bifrontal approach during this same time period after 2004. Median follow up was 48.7 months (range 13-307.9). Twelve patients (23.%) recurred, nine (17%) with local regional and 3 (5%) distant metastatic spread. No significant difference could be found between endoscopic vs open resection overall or when stratified by stage. Only the Dulguerov and Calcaterra staging system was associated with survival (p= .02). Median time to local recurrence was 72.8mo (N=7, sd=77.6 mo), to regional metastases was 43mo (SD=19.3), and to distant metastases was 46mo (N=3, SD 43mo). All seven of the local recurrences occurred in the open surgical group (p=.065).

Conclusion: Management of ENB has evolved to include purely endoscopic resection of Kadish A, B and select C tumors without reduction in OSS or DFS. Outcomes are favorable when a strategy of surgery and radiation is used, however median time to local recurrences at 72mo requires longer follow up to establish adequate local control for the endoscopic group. This study adds to the growing literature in the endoscopic management of ENB.
S176  TEN YEAR EXPERIENCE OF ENDOSCOPIC ENDONASAL SURGERY FOR SKULL BASE CHORDOMAS
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Introduction: The treatment of skull base chordomas represents a surgical challenge because of the location, invasiveness and tumor extension. In the last decade, endoscopic endonasal surgery (EES) has been employed in our department with notable outcomes.

Methods: From April 2003 to March 2013, 90 patients underwent EES for skull base chordomas at the University of Pittsburgh Medical Center. We evaluated the degree of resection, complications and recurrence rates following EES.

Results: Ninety patients (61% male) with a mean age of 45 years (range 4-88) underwent EES for primary (n=62) or recurrent (n=28) skull base chordomas. The overall rate of gross total resection (GTR) was 69% (81% in primary and 43% in recurrent cases). Near total resection (>95% of tumor) was achieved in 15%, subtotal (>85%) in 7% and partial in 9% of the patients. The most frequent complication was cerebrospinal fluid leak in 18 cases (20%) resulting in meningitis in 3.3%. Neurological complications included new cranial neuropathies in 4 cases (4.4%) and pontine hemorrhage in one patient. Carotid injuries occurred in 3 cases without any resulting deficit. There was no operative mortality in our series. Following EES, 48 patients (53%) received radiation therapy (proton beam in 39 cases). During a mean follow-up of 25 months (range 1-91), the tumor recurrence rate was 34% (26% after GTR and 54% after non-GTR) and most of these cases (74%) underwent repeat EES. The recurrence free period varied from 1 to 57 months (mean 15 months). In the most recent follow-up, 54 patients (60%) remain free of tumor and 11 (12%) have died due to disease progression.

Conclusions: EES represents a competitive alternative to craniotomies for the treatment of skull base chordomas with minimal morbidity and high rates of GTR when performed by an experienced skull base surgical team.
SINONASAL MUCOSAL MELANOMA: AN 11-YEAR EXPERIENCE ON 58 CASES

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Background: Primary sinonasal mucosal melanomas (SNMM) are rare and aggressive melanocytic neoplasms characterized by a high tendency to recur and metastasize to various distant sites. Non-surgical treatments have failed to demonstrate an impact on survival.

Patients and methods: The clinical records of all patients with SNMM who received surgery with curative intent by different approaches (endoscopic resection with [ERTC] or without [ER] transnasal craniectomy, cranio-endoscopic resection [CER], external approaches [Ext]) at the Universities of Brescia and Varese from January 2003 to December 2013 were retrospectively reviewed. The overall survival and the event-free survival (EFS) (recurrence or death) were estimated according to Kaplan-Meier method and compared according to the log-rank test. Statistically significant variables at univariate analysis were entered in a multivariate Cox regression model.

Results: Fifty-eight patients (21 males and 37 females) were considered eligible for the study. Age of patients varied between 19 and 87 years (median 71; mean: 69.9). The lesion originated from the naso-ethmoidal complex in 51 (87.9%) cases, from the maxillary sinus in 6 (10.3%), and from the frontal sinus and 1 (1.7%). ER, ERTC, CER, Ext were performed in 37 (63.8%), 10 (17.2%), 4 (6.9%), 7 (12.1%) cases, respectively. Definitive pT staging was as follows: pT3 in 30 (51.7%) patients, pT4a in 17 (29.3%), and pT4b in 11 (19%). Nodal metastases at presentation were observed and treated in only 3 (5.2%) cases. Surgical margins were clear in 42 (72.4%) patients, and 17 (29.3%) had positive margins. Adjuvant treatment was added in 16 (27.6%) patients: 13 received radiotherapy alone, 2 chemo-radiation, and 1 chemotherapy alone. Recurrence occurred in 39 (67.2%) patients; local recurrence, regional, and distant metastases developed in 26 (44.8%), 6 (10.3%), and 33 (56.9%) cases, respectively. Follow-up status was as follows: 32 (55.2%) patients died of disease, 20 (34.5%) were alive without disease, 5 (8.6%) were alive with disease, and 1 (1.7%) died of other causes. Overall survival at 3 and 5 years was 43.5% (±7.5%) and 29% (±7.8%), respectively. Upon univariate analysis, overall survival was affected by the development of recurrence (p<0.001). On multivariate analysis, overall survival was independently determined by male gender (HR=2.24 ± 0.86, p=0.035) and involved surgical margins (HR=2.32 ± 0.91, p=0.031). Age (p=0.265), dural involvement (p=0.085), pT category (pT4b vs pT3-T4a) (p=0.427), and surgical procedure (ERTC vs ER; CER-Ext vs ER) did not affect survival (p=0.102 and p=0.136, respectively). EFS was not significantly affected by any variable.

Conclusions: Prognosis of SNMM remains dismal, with a high recurrence rate despite radical surgery on the primary lesion. Male gender and positive surgical margins independently affected overall survival. Survival after ER is at least comparable to that achieved with more extensive surgical approaches.