<table>
<thead>
<tr>
<th>Title</th>
<th>Long-term results of endoscopic-assisted cranionasal resection for olfactory neuroblastoma - single centre experience of fourteen patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Tsang, RKY; Tsang, ACO; Lam, JW; Ho, WK; Leung, GKK</td>
</tr>
<tr>
<td>Citation</td>
<td>Clinical Otolaryngology, 2015, v. 40 n. 3, p. 274–277</td>
</tr>
<tr>
<td>Issued Date</td>
<td>2015</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/10722/209346">http://hdl.handle.net/10722/209346</a></td>
</tr>
<tr>
<td>Rights</td>
<td>The definitive version is available at <a href="http://www.blackwell-synergy.com">www.blackwell-synergy.com</a>; This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.</td>
</tr>
</tbody>
</table>
Long-term results of endoscopic assisted cranionasal resection for olfactory neuroblastoma – single centre experience of 14 patients

Raymond K. Tsang, FRCSEd(ORL) 1
Anderson C. Tsang, MBBS2
Jacky W. Lam, MBBS, MPhil1
Wai-Kuen Ho, FRCSEd 1
Gilberto K. Leung, MS, FRCSEd2

1Division of Otolaryngology, Department of Surgery, University of Hong Kong, Hong Kong
2Division of Neurosurgery, Department of Surgery, University of Hong Kong, Hong Kong

Short title: Long-term results of cranionasal resection

Correspondence:

Dr. Raymond K. Tsang
Department of Surgery, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong SAR, China.

Tel: (852) 2855 4394
Fax: (852) 2819 3780
Email: rkytsang@hku.hk

Conflict of Interests: None

Financial Disclosure: None

Keywords: olfactory neuroblastoma; esthesioneuroblastoma; craniofacial resection; cranionasal resection; endoscopic skull base surgery
Key Points

- Olfactory neuroblastoma is a rare tumour in the anterior skull base with frequent intracranial extension. Combined management between otolaryngologist and neurosurgeons are best to ensure complete tumour resection and to minimize the complications of treatment.

- Endoscopic resection of the nasal part of the tumour is not only for aesthetic consideration. The superior illumination and visualization offered by the endoscopy enables the surgeon to adequately resect the tumour especially in the posterior ethmoid and sphenoid sinuses.

- A frontal craniotomy approach allows the surgeon to better appreciate the intracranial extent of tumour and to ensure an adequate dura resection margin. In addition, a craniotomy approach allows a water-tight dura closure with stitches and reinforcement by a vascularized galeal-pericranial flap, minimizing post operative cerebrospinal fluid leakage.

- In our case series of 14 patients spanning 14 years, only one patient died of disease. The ten-year overall survival is 93%. Seven patients have local or regional recurrence; all except one was salvaged with additional surgery and/or radiotherapy. The survival results are comparable to open craniofacial resection.

- Our results showed that intracranial extension of disease (Kadish stage C) increased the risk for disease recurrence. Loco-regional regional recurrence can be salvaged with addition surgery and/or radiotherapy and can achieve long-term survival.

Keywords: olfactory neuroblastoma; esthesioneuroblastoma; craniofacial resection; cranionasal resection; endoscopic skull base surgery
Dear Editor,

Olfactory neuroblastoma is a rare malignancy in the anterior skull base, originates in the upper nasal vault with frequent extension to intracranial structures. The gold standard of management has been open craniofacial resection. A meta-analysis by Dulguerov et al. in 2001 analyzed the 390 cases reported in the literature from 1990 to 2001 and found a mean 5-year overall survival of 45%\(^1\). With the improvement of endoscopic instruments and maturation of the endoscopic surgical techniques, there are increasing reports of resection of olfactory neuroblastoma with an endoscopic approach, with or without craniotomy. Our center had reported the use of an endoscopic-assisted approach for resection of olfactory neuroblastoma in 1997 and 2005\(^2,3\). We would like to report the long-term results of our cohort of patients with olfactory neuroblastoma managed by an endoscopic-assisted technique.

**Patients and methods**

The present cohort is a retrospective review of a series of 14 consecutive patients with olfactory neuroblastoma treated with an endoscopic assisted plus frontal craniotomy approach from 1998 to 2012. The review has been approved by the institute review board. There are 10 male and 4 female patients with age ranged from 24 to 76 (median 49). All patients had contrast computer tomography (CT) scans and contrast magnetic resonance imaging (MRI) scans before the operation. The Kadish staging system is used\(^4\).

The surgical technique is similar to the technique described by Yuen et al. in 1997 and 2005\(^2,3\). The operation is a two-team approach by neurosurgeons working from the anterior cranial fossa and otolaryngologist working from the nasal cavity.
The two teams started the operation simultaneously. The otolaryngologist debulked the tumour, performed an ethmoidectomy and removed the area of the lamina papyracea in contact with tumour. The whole skull base and the cribriform plate would be exposed. The neurosurgeon started with a bifrontal craniotomy and opened the frontal lobe dura to expose the frontal lobes. Cerebrospinal fluid (CSF) was allowed to drain through the dura incision and the brain was allowed to fall posteriorly under gravity, exposing the olfactory nerves, crista galli and cribriform plate. There was no need for retraction of the frontal lobe. Depending on the extent of dural invasion, the anterior fossa dura was incised circumferential around the cribriform plate with a margin from the tumor. Both olfactory nerves would be divided as they emerged from the frontal lobe and if there were any area of frontal lobe invasion, these would be resected enbloc with the dura and cribriform plate. Figure 1 shows the view of the cribriform plate from above with the tumour in situ. The dura basal defect would be repaired with a free temporalis fascia and a galeal-pericranial flap would be harvested for future repair of the skull base defect. The skull base was then drilled on both sides, just medial to the lamina papyracea and lateral to the cribriform plate, usually from above by the neurosurgeon, with the otolaryngologist shining the light of the endoscope from below to guide the site for drilling. The whole cribriform plate was drilled out in four sides and removed enbloc with both middle turbinates and the nasal septum from the cranial side. Figure 2 showed the photo of the resected specimen. The dura was then repaired with a temporalis fascia graft and the skull base repaired with the galeal-pericranial flap. The nasal cavities would be packed with bismuth iodoform paraffin gauze. No external ventricular drainage, lumbar drain or tracheostomy was performed and the
patients were extubated and allowed to wake up in the neurosurgical intensive care unit.

All patients were followed up regularly in our hospital by both neurosurgeons and otolaryngologists. Depending on the final pathological reports, patients would be referred for post-operative radiotherapy. All patients with disease involving the dura or beyond (Kadish C) would be referred for radiotherapy.

The primary end-points assessed in the present cohort are overall survival and recurrence free survival. Survival curves were plotted with the Kaplan Meier plots and univariate analysis for survival was performed with log rank test. All statistics were calculated with the software Statistical Package for Social Sciences version 20.0 (International Business Machines, Armonk, NY, USA). A p-value <0.05 was considered as statistically significant.

Results

The majority of patients (9, 64.3%) had advanced Kadish C stage disease. Four (28.6%) patients Kadish B and one (7.1%) had Kadish A disease. One patient had ipsilateral neck lymph node metastasis on presentation. The median operating time is 360 minutes (210-527 minutes), with the longest operating time for the patient with neck dissection. All patients had clear frozen section margins intraoperatively but 3 patients had positive dural margins on formal histological analysis. The median hospital stay was 13 days (9-25 days). All patients were ambulatory upon discharge. Seven patients received post-operative radiotherapy. Two patients refused radiotherapy.
Survival

One patient died of disease at 17 months after surgery, all other patients survived. For all the survivors, the follow up period ranged from 25 to 188 months (median 110). The estimated mean overall survival of the cohort is 176 months (95% CI 153-199). The 5-year and 10-year overall survival rates are both 93%. Seven patients developed recurrence, three intracranially and three in the cervical lymph node. One patient had recurrence in the ipsilateral maxillary sinus. The time to first recurrence ranged from 3 months to 47 months. The 2-year recurrence free survival (RFS) is 71% and 5-year RFS is 49%. Figure 3 is the Kaplan-Meier plot of the overall and recurrence free survival. All patients with recurrence were further salvaged with surgery and/or radiotherapy. At the time of review, one patient died of disease and two patients are alive with disease. Univariate analysis showed that only intracranial disease (Kadish C) is marginally significant poor RFS (p=0.086, log-rank test). There were no factors predicting overall survival. Figure 4 is the Kaplan-Meier plot of RFS versus intracranial disease.

Complications

No patients had cerebrospinal leakage. One patient had convulsion at second day after operation and no patient developed late convulsion. Intranasal complications were rare. Only one patient developed a sphenoid mucocele 10 months after the operation and was treated with endoscopic drainage. Our surgical technique removed the whole cribriform plate and both olfactory nerves, so all patients developed anosmia after operation.
Discussion

The current cohort presented one of the long-term survival data on olfactory neuroblastoma. The median follow up is more than ten years (110 months) and the majority of the patients (11, 78.5%) have been followed up for more than ten years. Olfactory neuroblastoma can have late recurrence up to ten years and long follow up is required to critically analyze the oncological efficacy of a particular management protocol. Levine et al. reported the long-term results of one of the largest cohort of patients with olfactory neuroblastoma treated with open craniofacial resection, with excellent 15 years disease free survival of 82.6%\(^5\). The other large cohort of patients treated with open craniofacial resection for olfactory neuroblastoma report by Lund et al. reported a less favorable picture of 5-year overall survival of 61% and 10-year overall survival of 42%\(^6\). Our present cohort achieved 10-year overall survival of 93%, which is comparable to the figures achieved in open craniofacial resection.

There have been concerns regarding the endoscopic technique of resecting olfactory neuroblastomas\(^7,\)\(^8\). The main concern was the piece meal removal of tumour and the uncertainly in achieving a clear resection margin. The inability of obtaining a clear resection margin is a genuine concern as shown in the present cohort. Although we had achieved clear frozen section margins for all patients in the cohort, three patients had positive resection margin in the anterior fossa dura on histological analysis of the resected specimen. Our practice is to offer post-operative radiotherapy to the anterior skull base and nasal cavities for all patients with intracranial involvement of the tumor, though we were not able to prove statistically that post-operative radiotherapy improved recurrence free survival. On the other hand, the use of the endoscope allows better illumination and visualization of the extent of the tumour in the nasal cavities. This is especially significant in dealing with the
posterior aspect of the tumour near the sphenoid sinus, where the visualization of the area around the sphenoid sinus was especially poor in open craniofacial resection. Better visualization of the extent of the tumor allowed a more complete resection and in turn, translated to better tumor control.

The current cohort has no cerebrospinal fluid leakage. We attributed this to the craniotomy approach, allowing a watertight closure if the dura reinforced with the vascularized galeal-pericranial flap.

The main deficit of the current cohort is the limited number. Olfactory neuroblastoma is a rare tumour and any single centre study would suffer from the same limitation. Further studies would need multicenter cohorts to pool the patients for analysis.

**Conclusion**

The current cohort demonstrated that the endoscopic-assisted technique of cranionasal resection of olfactory neuroblastomas allow enbloc resection of the anterior skull base and could achieve a high long-term survival rate comparable to the best results obtained by open craniofacial resections.
References


**Figure Legends**

Figure 1. Intraoperative photo showing the view of the cribiform plate from above. The blue arrow points to the intracranial portion of the tumour.

Figure 2. Clinical photo of the resected specimen. The arrow points to the nasal portion of the tumour between the left middle turbinate and the nasal septum.

Figure 3A. Kaplan Meier plot of the overall survival of the cohort. 3B. Kaplan Meier plot of the recurrence free survival of the cohort.

Figure 4. Kaplan Meier plot of the recurrence free survival between patients with no intracranial extension of tumour (Kadish A and B) and patients with intracranial extension (Kadish C). Patients with intracranial extension of disease are marginally significant for poor recurrence free survival (p=0.086, log rank test).