Esthesioneuroblastoma: Good Local Control of Disease by Endoscopic and Endoscope Assisted Approach. Is it Possible?

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Received: 17 December 2012 / Accepted: 12 February 2013 / Published online: 26 February 2013
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Abstract To present a short report on nine patients of esthesioneuroblastoma, managed endoscopically or endoscope assisted. To describe the technique and discuss the results at an average of 36.7 months of follow up. A retrospective study in a tertiary care centre. The present communication describes a series of 9 cases harbouring esthesioneuroblastoma, 6 managed endoscopically and 3 endoscope assisted between January 2005 and December 2009. All the nine patients remained free of disease at the primary site by endoscopic and radiological evaluation on an average of 36.7 months of follow up. One of the patients developed cutaneous and systemic metastasis for which she received chemotherapy and another one died during post-operative period due to unrelated causes. None of the patients showed recurrence or residual disease locally. Endoscopic and endoscope assisted approach provides a cosmetically better and surgically comparable outcome for local control of disease in early stages of esthesioneuroblastoma in expert hands without significant complications.

Keywords Esthesioneuroblastoma ·
Olfactory neuroblastoma · Endoscopic approach

Introduction

Esthesioneuroblastoma (ENB) is an uncommon neoplasm of the nasal cavity constituting about 3 % of all endo-nasal tumours. This clinical entity remains a challenge to onco-surgeons, owing to its border-zone location and proximity to cerebral parenchyma. Complete resection of this tumour involves not only an anterior craniotomy but also an external facial incision to gain wide exposure. With the advancements in endoscopic surgery, various attempts have been made to combine the functional and aesthetic techniques for resection of nasal and sinus tumours using an endoscopic assisted traditional craniofacial approach and also a complete resection via an endoscopic approach. The objective of this report was to illustrate the use of endoscopic technique as an evolving surgical modality for removal of cribriform plate and anterior cranial fossa tumours.

The present report describes 9 cases, managed endoscopically (6 patients) or endoscope assisted (3 patients), extent of surgical excision and their functional outcomes.

Materials and Methods

From January 2005 till December 2009, nine patients with histologically proven ENB were treated at our department. Six of these patients underwent pure trans-nasal endoscopic resection of tumors, along with reconstruction of skull base. Rest of the 3 patients underwent an open approach, craniofacial resection and immediate reconstruction, with endoscopic assistance for sino-nasal clearance. There were 7 males and 2 female, with a mean age of 42 years (range 18–52 years). One patient had cervical metastasis at the time of presentation and another developed cutaneous metastasis

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at back of thoraco-lumbar region, pre-auricular lymph nodes and peri-splenic, para-renal, peri-cardiac and peritoneal metastasis. Mean follow-up time was 36.7 months.

Preoperative planning was performed with the aid of computer tomography (CT) and magnetic resonance imaging (MRI). The tumors were staged according to the Kadish staging system [1]. Endoscopic resection was considered, when the tumor was small, without significant intracranial extension (Kadish stage A or B). In all cases, neurosurgical standby was available. Lesions with extensive intracranial spread were still approached through an external craniofacial approach with endoscopic assistance thereby avoiding an incision over the face. Patients were evaluated for any associated intra-operative or post-operative complications. Serial head and neck examination including regular endoscopic evaluations were done. In addition, annual MRI brain and skull base and chest radiographs were done for close follow up.

Endoscopic Surgical Technique

Draping was adjusted so as to leave both the eyes uncovered. This helps in detecting any trauma to optic apparatus during surgery. Third-generation cephalosporin was administered intra-operatively as prophylactic antibiotic. After preparatory setup was complete, an endoscopic resection was undertaken. Using nasal endoscopes for visualization, representative sections of the tumor were initially removed with surgical punch forceps for pathological evaluation. Subsequently, additional tumor tissue was removed by powered suction debrider. Removal was started from the centre of the tumor, so that the surrounding pseudo-capsule was not breached. Once some space was created in the centre the surrounding capsule was easily dissected from the sinuses and the nasal vault. This could then be completely removed and the attachment could be cauterized with bipolar cautery.

Anterior Craniotomy Technique

This was required in three patients. The neurosurgical team took over once the intranasal portion of the tumour had been removed and the nasal cavity was packed. The anterior bifrontal craniotomy was performed through a typical bi-coronal skin flap, preserving the pedicled pericranium's vascularity. This was later utilized for the repair of skull base. The intracranial extension of the tumor could be identified after extending the head, fixed in 4-pin head rest.

The lateral margins of the tumor at the ethmoidal roof and the medial margin of the orbit could be identified by the neurosurgeon with assistance from the light shone transnasally by the endoscope. Bone chisels were used to enter from above into the ethmoid area, giving a good

margin around the tumor base. The cribriform plate and any anterior cranial fossa extension were removed en block. The caudal defect was inspected endoscopically by the otolaryngologist to ensure complete tumor removal. Margins were close or sometimes difficult to obtain in cases in which the tumor reached the optic nerve or important orbital structures. All tumor tissue visible through the magnification made possible by endoscopic telescopes was removed completely.

Results

All the 9 patients received post operative radiotherapy (Table 1). One patient developed systemic metastasis in the pericardiac, perisplenic, perirenal and peritoneal region and multiple subcutaneous metastasis in the thorax and abdomen (Fig. 1a, b). This patient was started on chemotherapy for palliation and is presently alive 33 months post surgery and free of disease at local site (Fig. 1c, d). The second patient had a recurrence of disease in the nasal cavity, ethmoids and cribriform area, after undergoing a bifrontal craniotomy and external ethmoidectomy 8 years previously. The revision surgery was done by an endoscopic assisted approach followed by chemotherapy (Fig. 2). The third patient, who underwent total maxillectomy with orbital exenteration and neck dissection for lymph node metastasis, died 6 months post surgery due to unrelated causes. (Fig. 3). He was however disease free during that time. All the rest of the patients remain free of disease at the primary site by endoscopic and radiological evaluation on an average of 36.7 months of follow up.

The most common complication encountered secondary to surgery was excessive crusting in the nasal cavity. Two patients had significantly prolonged crusting for 6 months post surgery.

Two patients in our study did not do very well. One of them died due to unrelated causes. The other one developed cutaneous and systemic metastasis, though she is still alive on chemotherapy. Both these patients had involvement of the facial skin which rarely occurs in these tumours and is probably associated with increased incidence of metastasis in the cervical lymph nodes and hence a poorer prognosis. Such an observation has not been reported earlier in the literature. Local control however remained good at the local site and there was no recurrence.

Discussion

Olfactory neuroblastoma is an uncommon neuro-epithelial tumor that typically arises in the superior nasal cavity from olfactory epithelium. This neoplasm accounts for 1–5 % of

Table 1 Details of the nine patients included in the study

Age/ sex	Tumor location	Intracranial extension	Kadish stage	Human grade	Systemic spread	Presence of neck ds	Approach open/ endoscopic	Radiotherapy	Chemotherapy	Post op complication	Local recurrence	Current status	Follow up (months)
30/F	Maxillary sinus	Nil	D	IV	+	–	Endoscopic	60 Gy	Cisplatin based	Nasal Crusting	Involvement of facial skin	Alive	33
18/ M	B/L ethmoids, nasal cavity, cribriform plate	Present	C	III	–	–	Open approach. Pt. developed recurrence after 8 yrs. Endoscopic revision surgery.	60 Gy	Cisplatin based	CSF leak	Local recurrence at primary site, 8 years after the first surgery.	Alive	47
38/ M	B/L ethmoids, nasal cavity, cribriform	Nil	C	III	–	+	Combined approach. maxillectomy with orbital exenteration with neck dissection	60 Gy	Nil	Excessive nasal crusting	Involvement of facial skin.	Died after 6 months of follow up- unrelated causes.	21
42/F	B/L ethmoids, nasal cavity	Nil	B	II	–	–	Combined approach	60 Gy	Nil	None	Nil	Alive	37
44/ M	Nasal cavity	Nil	A	II	–	–	Endoscopic	60 Gy	Nil	None	Nil	Alive	44
32/ M	Nasal cavity	Nil	A	I	–	–	Endoscopic	60 Gy	Nil	None	Nil	Alive	57
48/ M	B/L ethmoids nasal cavity	Nil	B	II	–	–	Endoscopic	60 Gy	Nil	None	Nil	Alive	35
52/ M	Nasal cavity	Nil	A	I	–	–	Endoscopic	60 Gy	Nil	None	Nil	Alive	31
58/ M	B/L ethmoids, maxillary sinus	Nil	B	II	–	–	Endoscopic	60 Gy	Nil	None	Nil	Alive	26

Fig. 1 **a** coronal section (computed tomography) showing enhancing mass right inferior nasal cavity and maxillary sinus which was operated outside. **b** Ct scan nose and paranasal sinuses, coronal sections, 18 months after surgery showing no recurrence or residual disease. Mild mucosal hypertrophy is seen. **c** clinical photograph showing fine needle aspiration mark at the skin of the back where patient reported metastasis. **d** Ct scan abdomen, axial section showing multiple hypodense shadows in perisplenic region suggestive of metastasis

Fig. 2 **a** Ct scan nose and paranasal sinuses, coronal sections, showing enhancing mass bilateral nasal cavities, bilateral ethmoids and intracranial extension on right side. **b** Ct scan nose and paranasal sinuses, coronal sections, 32 months after surgery showing no recurrence or residual disease. Mild mucosal hypertrophy is seen. **c** Ct scan nose and paranasal sinuses, axial sections, showing enhancing mass bilateral nasal cavities displacing both the orbits outwards. **d** Ct scan nose and paranasal sinuses, axial sections, 32 months after surgery showing no recurrence or residual disease

all intranasal tumors [2–5]. Although relative rarity of this tumor in the past was caused by the histo-pathologic underdiagnosis, immuno-histochemical analysis has increased

the diagnostic ability. Olfactory neuroblastoma is known to occur at all ages; two-thirds of cases present in the 10–30-year age group, with slight male preponderance [6].

Fig. 3 **a** Ct scan nose and paranasal sinuses, coronal sections, showing enhancing mass right nasal cavity, right maxillary sinus and orbit. **b** Ct scan nose and paranasal sinuses, coronal sections, showing disease free status at 6 months of follow up

Previously called ENB, olfactory placode tumour, esthesioneurocytoma, esthesioneuroepithelioma, these terms highlight the olfactory and primitive neuroectodermal origins, however the controversy remains. The most accepted theory of origin is from the rounded basal cells of the olfactory mucosa. These cells are embryologically derived from the neural crest cells. Therefore, it is natural for most of the ENB to arise in the nasal vault. There are few reports of this tumor arising at other sites, such as the sphenoid and petrous apex, maxillary sinus, and pituitary gland [7–9].

A high index of suspicion is necessary in patients presenting with symptoms of nasal obstruction, epistaxis, and anosmia as the extension of tumour may be considerable at the time of presentation. MRI can help in the initial diagnosis by differentiating neoplasm from obstructive sinus disease and in the identification of intracranial extension [10, 11], as well as for postoperative surveillance.

The Kadish staging system continues to be used widely as the main prognostic indicator [1]. According to this classification tumour is staged into (A, B, and C) depending on whether the tumor is limited to the nasal cavity, paranasal sinuses or outside the paranasal sinuses, respectively.

Today, the standard treatment is an external craniofacial resection followed by postoperative radiotherapy [12–16]. Chemotherapy when given for recurrent or advanced disease has shown dramatic improvement in the long-term survival for tumors previously considered to be “unresectable”. Even though cervical metastatic rates are as high as 27 %, the salvage rate for ENB still carries a better prognosis than other superior nasal vault malignancies [17]. The overall 5- and 10-year survival rate for ENB has been reported in literature as 80 and 50 %, respectively [12, 17, 18]. Local, regional and distant metastasis can be expected to occur for as long as 10 years after treatment. Surgeons who advocate craniofacial resection argue that this approach offers better exposure and allows en block resection of the tumour. However, to experienced endoscopic

Fig. 4 Clinical picture of the patient showing an alar crease incision of previous surgery with a bulge at the same place due to residual tumour

surgeons, external incisions may not be necessary to attain as good, if not better, exposure and visualization, with cure rates comparable with those achievable with external surgery. In our series of patients two of our patients had involvement of facial skin one after alar skin crease incision and the other due to extensive disease (Fig. 4). Both developed dissemination to the pre auricular and cervical lymph nodes respectively. The illumination and magnification afforded by rigid telescopes combined with the ability to extend visualization into anatomic recesses with the aid of angled scopes virtually has eliminated the need for external incisions and allows complete resection of these tumors. Additionally, endoscopic approaches generally result in less collateral damage and offer superior cosmetic results besides having less amount of blood loss, less morbidity and a shorter hospital stay. Furthermore, less mucosa of the nasal cavity is destroyed leading to better

functional preservation. This approach may be indicated for tumors limited to nose and paranasal sinuses without deep infiltration of the dura, orbit or involvement of the pterygopalatine fossa.

An advanced skull base surgeon experienced in both the open and endoscopic techniques should be able to convert an endoscopic approach to an open approach if necessary. There have been numerous complications reported by traditional craniofacial resections. In a recent series by Levine et al. [12] central nervous system complications (intracranial hypertension, pneumocephalus, cerebrovascular accident, and CSF leak) were noted in up to 25 % of their series. In addition, 23 % had orbital complications (epiphora, radiation-induced cataracts or keratopathy, transient diplopia, or cranial nerve dysfunction), 9 % had infectious complications (meningitis, epidural abscess, or infected bone flaps), and 14 % had cosmetic complications (saddle nose deformity, nasocutaneous fistula, resorbed frontal bone flaps, and enophthalmos). Systemic complications (hyponatremia, respiratory arrest, abdominal wound seroma from fat/fascia graft, pulmonary embolus, diabetes insipidus, amenorrhea and prolactinemia, and hypothyroidism) occurred in 20 % of the patients. Many of the patients in this series were Kadish stage C. Therefore, it is difficult to compare with the endoscopic group consisting of Kadish A and B tumors. With the exception of prolonged crusting and intraoperative csf leak, none of the patients in our series developed any other significant problems. The crusting occurs due to a secondary atrophic rhinitis from the degree of tissue removal combined with the radiotherapy and would have occurred regardless of the resection technique. However, in a selected group of patients short-term oncological results appear to be excellent for local control.

Patients with significant medical comorbidities or with primary or recurrent disease without intracranial extension (Kadish stage A or B) appear to be excellent candidates. Long-term follow-up in a larger series is necessary to determine whether oncological cure is equivalent to more traditional approaches for comparable stage neoplasms.

All patients in our series were subjected to post operative radiotherapy. As has been discussed in literature, surgery followed by post operative radiotherapy offers definitely better survival advantage than surgery or radiotherapy alone [2, 4, 16]. Although early reports on chemotherapy in ENB focused on patients with recurrent or metastatic disease, adjuvant chemotherapy is now commonly used for patients with advanced locoregional disease. Numerous protocols have been published in literature presenting favourable results with cisplatin based chemotherapy [12, 19–21]. Two of our patients received post operative chemotherapy after RT, one having systemic metastasis and the other with regional recurrence. Both are doing well at 33 and 47 months of follow up respectively.

We also wish to highlight that one of our patients had an unusual presentation and showed isolated maxillary sinus involvement, with cutaneous metastasis over dorsolumbar region and systemic metastasis to pericardiac, perisplenic and perirenal areas, which would be the first case of this kind to be reported in literature. A possible explanation for the origin of this isolated tumor in the maxillary sinus without nasal vault involvement may be the presence of ectopic olfactory cell rests. ENB has also been reported in a patient with Kallman's syndrome, in which the olfactory cells were supposed to be lacking [22]. The possible origin proposed in this patient is from the separate neuroendocrine cell population, and this could explain the origin of tumor in sites distant from the olfactory mucosa, as in our case. There are various existing reports in the literature regarding origin of ENB in ectopic locations [7–9].

Cutaneous metastasis from ENB has never been reported in the literature at present. Presence of the tumour at an early age, early involvement of the skin of the face (due to previous excision via alar crease incision and consequent seedling of the scar), partial removal of tumour and aggressive tumour handling could have been contributory to explain the highly metastatic potential of this tumour.

Endoscopic and endoscope assisted approach provides a cosmetically better and surgically comparable outcome for local control of disease in early stages of ENB in expert hands without significant complications. Aggressive and advanced tumours should be approached via bicoronal approach and radiotherapy should be a standard protocol for all cases post surgery. Chemotherapy needs to be preserved for recurrent or metastatic disease.

Conflict of interest None.

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