Transcranial Resection of Olfactory Neuroblastoma

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ABSTRACT

From February 1995 to August 2004 at Chang Gung Memorial Hospital and Chang Gung University, eight patients with an olfactory neuroblastoma underwent transcranial resection alone. The transcranial surgical technique consisted of a bicoronal incision, followed by a standard frontal craniotomy with or without a separated orbital bar osteotomy. The tumor could be removed en bloc transcranially after the cranial base osteotomy according to the tumor extent delineated by preoperative magnetic resonance imaging and intraoperative findings. The defect in the floor of the anterior cranial fossa was reconstructed with a galeopericranial flap. Sinoscopy should compensate rather than compete with the transcranial approach. With thorough knowledge of the basic topographic anatomy of the anterior cranial base, transcranial resection can provide adequate surgical exposure to facilitate oncologically sound resection and to execute reliable skull base reconstruction in selected patients with an olfactory neuroblastoma. A transcranial approach alone may further decrease the rate of surgical morbidity by omitting the facial incision and osteotomy.

KEYWORDS: Olfactory neuroblastoma, transcranial resection, anterior skull base

Olfactory neuroblastomas (esthesioneuroblastomas) are rare malignant cranial base tumors, consistent with undifferentiated neuroectodermal tissue. These tumors were first recognized by Berger and Luc in 1924.¹ They originate from the olfactory neuroepithelium lining the roof of the nasal vault,

close to the cribriform plate. They account for 3% of all intranasal neoplasms and can invade the anterior cranial base by growing through the cribriform plate.²

Craniofacial resection has long been the standard surgical treatment for anterior cranial

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base tumors, including olfactory neuroblastomas.³ It can provide a wide surgical exposure and multidirectional approaches to the anterior skull base through transcranial and transfacial routes and thus facilitates oncologically sound surgical resections. However, the disadvantages of a facial incision or osteotomy include facial scars, possible facial bone defects, and even necrosis of translocated facial bone.^{4,5} Facial scars also have a psychiatric effect on patients.

We report our experience with the transcranial resection alone for selected patients with an olfactory neuroblastoma. The goal of the surgical approach is to remove tumors transcranially and to avoid facial incisions or osteotomies, thus preventing complications associated with transfacial approaches.

METHODS

The surgical outcomes of eight patients (six men, two women) with an olfactory neuroblastoma who underwent the transcranial resection alone with or without transnasal endoscopic assistance between February 1995 and August 2004 at Chang Gung Memorial Hospital and Chang Gung University were evaluated prospectively. At diagnosis, patients' ages ranged from 15 to 62 years old (median age, 48.9 years). The exclusion criteria included patients with extensive involvement of the orbit, maxillary antrum, nasal floor, or oropharynx. The patients were candidates for conventional craniofacial resection. Two patients had undergone previous surgery; the other patients had not yet been treated. All eight patients underwent postoperative radiotherapy. Six patients were treated only at the primary tumor site. One patient with simultaneous neck metastasis was treated at the primary tumor bed plus the entire neck after its dissection. One patient with a subsequent neck metastasis accepted elective neck radiotherapy 1 month after surgery.

Primary tumor dose of radiation therapy ranged from 5500 to 6500 cGy. All patients were

regularly followed in the clinics. Pathologic reports were reviewed by the Department of Pathology. Immunohistochemical stain was performed in all eight patients. The diagnosis of olfactory neuroblastoma was based on histopathologic features, including microscopic findings of uniform small round blue cells with scanty cytoplasm and hyperchromatic round nuclei and inconspicuous nuclei. Other features included neurofibril rosettes, pseudorosettes, and neurosecretory granules. Patients were retrospectively staged based on the Kadish staging system.⁶

Operative Technique

Surgery started with a bicoronal incision. The scalp, including the pericranium, was raised to the supra-orbital ridges on both sides.⁷ After the initial bifrontal or frontolateral craniotomy, the orbital bar was skeletonized and an orbitofrontoethmoidal osteotomy (Fig. 1) was performed (extended subfrontal approach).⁸ This piece of bone was removed separately. An extradural dissection to the floor of the anterior fossa was performed. The basal dura was removed along with the underlying cribriform plate. The torn dura was repaired with a patch of pericranium graft. If the frontal lobe was invaded, the involved dura was resected and the intradural tumor was removed by the neurosurgeon.

The frontal lobe was gently retracted backward to expose the planum sphenoidale, orbital roof, cribriform plate, and ethmoid roof. The osteotomy performed over the skull base was based on the area of involvement of the underlying nasoparanasal tumor. We attempted to remove the tumor en bloc transcranially based on the extent of tumor delineated on preoperative magnetic resonance imaging (MRI) and intraoperative findings. After the tumor was removed, specimens from suspicious margins were sent for frozen-section analysis. Every effort was made to obtain a negative margin.

During the reconstructive phase, a galeopericranial flap based on the supraorbital arteries was raised from the scalp flap and transposed to sit

Figure 1 (A) Standard bifrontal craniotomy with orbital bar osteotomy (extended subfrontal approach) for anterior skull base tumors. (B) The orbital bar, including the supraorbital ridge, orbital roof, and superior part of the lateral orbital wall.

between the basal dura and the underlying nasoparanasal cavity. The cranial compartment was thereby isolated from the extracranium to limit local contamination. This maneuver along with a watertight dural repair helped to minimize leakage of cerebrospinal fluid and ascending infection. The frontal sinus was cranialized by removing the posterior wall and then denuded of mucosal remnants that might act as seeds for bacterial infection and mucocoele formation.⁹ The craniotomy was repositioned with a Snyder hemovac[®] (Zimmer, Ohio, USA) left in the epidural space. A Foley catheter inserted through the anterior nostril was inflated to support the galeopericranial flap. The Foley catheter was removed 2 days after the operation.

Postoperatively, broad-spectrum coverage with intravenous antibiotics was administered with a combination of penicillin and gentamicin. Antibiotic therapy was discontinued after the drain was removed. All patients were monitored in the intensive care unit for a minimum of 24 hours. At discharge (usually within 7 to 10 days), patients were instructed to irrigate the nasal cavity daily with normal saline to remove crusting and secretions.

Postoperative radiotherapy was administered with an external megavoltage beam and three-field technique: an anterior part combined with wedged lateral fields delivering a dose of 550 to 650 cGy. Efforts were made to protect the orbit and brain during radiation therapy. Scanning was not repeated routinely during the early postoperative

period unless clinical deterioration was suspected. Patients underwent MRI at 6-month intervals for the first 2 years and then were followed annually.

RESULTS

Patients were followed in the clinics from 1.3 to 100.8 months (mean follow-up, 22 months). The most common presenting symptoms were epistaxis (75%) and nasal obstruction (63%). Visual symptoms and frontal headache occurred in 25% of patients (Table 1). One patient was initially treated by a neurosurgeon, but tumor of the anterior skull base and nasal cavity persisted. Two patients had previously undergone endoscopic excision of the nasal cavity tumor at another hospital. The other five patients had not previously been treated. One patient was Kadish stage A and seven were Kadish stage C.

Patient 2 had simultaneous neck metastasis and underwent transcranial resection with an ipsilateral modified neck dissection followed by postoperative radiotherapy; he has remained disease free (Table 1). Patient 3, who had undergone previous endoscopic excision, later underwent transcranial resection but subsequently developed metastasis to the left side of the neck and received elective neck radiotherapy 1 month after surgery. Three months after surgery, he developed bone and pancreas

Table 1 Clinical Summary of Eight Patients with Olfactory Neuroblastoma

Patient No.	Age/Gender	Kadish Stage	Presentation	Previous Treatment		Recurrence	Salvage Therapy	Postop	Final Status	Complications	F/U (mo)
				Nil/Surgery	Initial Treatment						
1	60/F	A	Nasal obstruction, epistaxis		OP & RT	None		RT	NER	No	100.8
2	52/M	C	Epistaxis, left neck mass		OP & RT & left RND			RT	NER	No	4.9
3	15/M	C	Nasal obstruction, visual acuity decrease	OP (persistent)	OP & RT	Regional (1 mo), distant (3 mo)	Neck CCRT	CCRT	Distant metastasis	No	5.2
4	54/M	C	Epistaxis		OP & RT	None		RT	NER	No	2.1
5	54/M	C	Frontal headache	OP (persistent)	*OP & RT	None		RT	Dead without disease	No	16.5
6	43/F	C	Nasal obstruction, epistaxis, right proptosis		*OP & RT	None		RT	NER	Frontal bone ORN, Epidural abscess	24.4
7	62/M	C	Nasal obstruction, epistaxis		OP & RT	None		RT	NER	Epidural abscess	20.4
8	51/M	C	Nasal obstruction, epistaxis		OP & RT	None		RT	NER	No	1.3

OP, transcranial excision alone; NER, no evidence of recurrence; *, sinuscope assistance; ORN, osteoradionecrosis; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; CT, chemotherapy; RND, radical neck dissection.

metastases. Patient 5 had undergone previous surgical excision by a neurosurgeon. However, he subsequently underwent transcranial resection to treat persistent tumor over the anterior skull base and nasal cavity. He died of hydrocephalus and encephalitis without evidence of recurrence 21 months after surgery. To date, the remaining five patients have remained free of disease during regular follow-up with clinical and radiographic monitoring.

There were no surgical deaths. Two patients had surgical complications. One patient had an epidural abscess and one patient had frontal bone osteoradionecrosis and an epidural abscess. None of the complications resulted in permanent sequelae. The complication rate was 25%.

DISCUSSION

Olfactory neuroblastomas are solid nasal cavity masses that can erode into nearby osseous structures such as the orbital plate of the ethmoid bone, cribriform plate, and fovea ethmoidalis. The most common finding on physical examination is a unilateral, broad-based, polypoid, friable, and gray-to-red nasal mass. The tumor usually is located high in the nasal vault. The two most common symptoms presented were unilateral nasal obstruction and epistaxis as it is a highly vascularized tumor.

The disease has a bimodal age distribution; it peaks first between 10 and 20 years and then between 50 and 60 years.¹⁰ The distribution between the sexes is about equal. The tumor can spread submucosally in all directions, thereby involving the paranasal sinuses, nasal cavity, and surrounding structures. These lesions can break through the cribriform plate and invade the brain or seed the cerebrospinal fluid. This uncommon neoplasm is locally aggressive and can metastasize by lymphatic or hematogenic routes.

The staging system of Kadish et al continues to serve as the main predictor of disease-related mortality.¹¹ The system classifies patients with

tumors limited to the nasal cavity as stage A. Patients with tumors involving the nasal cavity with an extension into the paranasal sinuses are stage B. In stage C, tumor has spread beyond the nasal cavity and paranasal sinuses. Despite criticism of this system and proposed modified staging systems such as Hyam's histopathological grading system¹² or the modified TNM (primary tumor, regional lymph nodes, distant metastasis) staging system¹³ for olfactory neuroblastoma, the Kadish staging system is most commonly used in the literature.

Computed tomography allows detailed assessment of associated bony erosion or destruction, particularly of the cribriform plate. Contemporary MRI can delineate the precise margins of skull base tumors because of its multiplanar display and superb tissue contrast.¹⁴ Tumors appear hypointense to gray matter on T1-weighted images and iso- or hyperintense to gray matter on T2-weighted images. Thus MRI defines invasion of the dura, optic chiasm, internal carotid artery, or brain more accurately than computed tomography; can identify skull base extensions; and can differentiate neoplasm from obstructive sinusitis (Fig. 2). It is also useful for postoperative surveillance.

Definitive diagnosis of an olfactory neuroblastoma is based on histopathology and immunohistochemical stains. Histologically, high-power microscopic examination shows small, round neuroepithelial cells arranged in rosette or pseudorosette patterns, separated by fibrous elements. Immunohistochemical methods for the detection of neuron-specific enolase, S-100 protein, and neurofilament are required to ensure the diagnosis of olfactory neuroblastoma.¹⁵

The overall survival rate in patients with olfactory neuroblastoma has changed dramatically since the disease was first described by Berger and Luc in 1924. Recent disease-free actuarial survival and overall survival rates have been 77% and 61% at 5 years and 53% and 42% at 10 years, respectively.^{16,17} Long-term endoscopic and MRI surveillance is mandatory because local, regional, and distant metastasis can be expected to occur for as

Figure 2 (A) The tumor appears hypointense to gray matter on T1-weighted images. (B) The tumor appears iso- or hyperintense to gray matter on T2-weighted images. MRI can help in the initial diagnosis by differentiating neoplasm from obstructive sinusitis and in the identification of an intracranial extension.

long as 10 years after treatment. Elective treatment of the neck is controversial.

Kadish and later Elkon^{17a} reported that fewer than 15% of patients developed cervical lymph node metastasis; therefore, elective treatment such as irradiation of the neck or dissection was not indicated. In contrast, a much higher rate of neck disease (20–44%) has been reported in patients with locally advanced disease.¹⁸ Thus, elective treatment of the upper neck should be considered in patients with more extensive disease, especially when tumor spreads beyond the nasal cavity or paranasal sinuses.

Patients with tumors arising from the superior vault of the nasal cavity and paranasal sinuses had a poor prognosis before the development of craniofacial resection. One explanation is that most patients manifest nonspecific symptoms of long-standing duration that can mimic chronic sinusitis; consequently, patients may have been treated for the latter. Another explanation is that, before the development of skull base surgery, the cribriform plate, fovea ethmoidalis, and planum sphenoidale area were relatively inaccessible.⁷ Therefore, the combined “craniofacial” approach became the standard approach for the resection of tumors that erode through the floor of the anterior cranial fossa.

Thorough understanding of the basic topographic anatomy of the frontal lobe, anterior cranial base, and underlying orbit and paranasal sinuses is crucial for en bloc resection (Fig. 3). For example, the crista galli connects to the underlying nasal spectrum; the cribriform plate is the nasal roof and its lateral margin corresponds to the attachment to the underlying middle turbinate. The fovea ethmoidalis is the roof of the ethmoid, and its lateral margin corresponds to the attachment for the lamina papyracea, which is the curved medial bony wall of the orbit. The planum sphenoidale is the roof of the sphenoid sinus, and its anterior margin corresponds to the anterior wall of the sphenoid sinus. Its posterior margin, where the optic chiasm usually lies, corresponds to the posterior wall of the sphenoid sinus. In the transcranial approach alone, based on the MRI findings, certain cranial base osteotomies can be customized to encompass the entire tumor, and possibly to achieve en bloc resection.

In our series, one patient developed osteoradionecrosis of the nasofronto-orbital segment and an epidural abscess. She underwent radical sequestrectomy, surgical drainage of the epidural abscess, and repair of the skull base defect with a free flap.

Figure 3 (A) Axial and (B) coronal views of the basic topographic anatomy of the frontal lobe, anterior cranial base, and underlying orbit and paranasal sinuses. CG, crista galli; CP, cribriform plate; FS, frontal sinus; ES, ethmoid sinus; LP, lamina papyracea; MT, middle turbinate; NS, nasal septum.

The other patient with an epidural abscess also underwent its surgical drainage. These two patients, who had large and extensive olfactory neuroblastomas, may have developed their epidural abscess because reconstruction of the skull base was suboptimal. Nonetheless, some patients had prolonged crusting in the sinonasal cavity and frequent self-cleansing was necessary. Although most tumors in our study were large and extensive, the surgical complication rate was acceptable. Indeed, it was less than those associated with traditional craniofacial resections (42–49%).^{16,19}

Malignant tumors involving the optic chiasm, cavernous sinus, temporal lobe, and carotid artery and representing surgically incurable disease are absolute contraindications for craniofacial re-

section.^{16,20} Dural or transdural involvement of the frontal lobe is no longer a strong contraindication to surgery, but it is a particularly poor prognostic factor.²¹ In some situations the transcranial approach alone can still be considered adequate for exposure without transfacial exposure. However, significant tumoral involvement with the orbit, maxillary antrum, nasal floor, or oropharynx is a contraindication for the transcranial approach. Transnasal endoscopy can be used as a surgical adjunct to assist with mucosal incisions within the underlying nasoparanasal cavity and to help achieve en bloc resection.

The classic bidirectional craniofacial resection and en bloc resection of the anterior cranial base remain the procedures of choice, but such

methods have several disadvantages. The duration of the surgery is longer than that of the transcranial approach alone. The transfacial approaches may involve facial incisions such as the Weber-Ferguson incision with a Diffenbach or Lynch extension, lateral rhinotomy, facial osteotomy, temporary removal and reposition of the facial skeleton, or midface degloving. These incisions leave facial scars and facial bone defects and cause necrosis of translocated facial bones and other postoperative cosmetic deformities.^{4,22} Hao proposed a modified facial translocation that uses an anteriorly based lateral nasal wall mucoperiosteal flap to cover the nude surface of the transfacial bone graft to prevent avascular necrosis, especially in patients who have undergone radiation therapy.²³ Furthermore, avoiding facial skin incisions and scars can decrease the psychiatric effect of the procedure and offers a good cosmetic outcome.

The advent of the minimally invasive sinoscopic approach has permitted treatment of small olfactory neuroblastomas.^{23,24} In our opinion, the technique of sinoscopy should compensate for rather than compete with the transcranial approach. Sinocopy may be applied to delineate the lower extent of the skull base tumor and to assist with incisions of the nasal mucosa within the underlying nasoparanasal cavity during the transcranial approach. Thus, the transfacial approach for anterior and inferior exposure can be replaced by transcranial exposure with sinoscopic assistance. However, sinoscopy alone is limited for dealing with tumors with significant transcranial or transdural involvement, for managing intracranial complications, or for repairing a large dural defect. In the transcranial approach, only bicoronal incisions leave scars and the duration of surgery is expected to be shorter than that required for craniofacial resection.

CONCLUSIONS

Transcranial resection can provide adequate surgical exposure to facilitate oncologically sound resection

and to execute reliable skull base reconstruction with a galeopericranial flap in selected patients with olfactory neuroblastoma. With understanding of the topographic anatomy of the complex skull base, the transcranial approach alone may decrease the rate of surgical morbidity by avoiding the need for facial incisions and osteotomies. In this small series, the short-term oncological results appear to be acceptable. However, longer follow-up is needed to determine the oncological outcome of patients undergoing this procedure.

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Commentary

I have been reading about transcranial approach for a variety of anterior skull base tumors since 1993. It can be supplemented by endoscopic

inspection and resection through the resection cavity. Extensive invasion of the maxillary sinus, however, will necessitate a transfacial or degloving approach. If the patient has previously undergone irradiation or surgery, a radial forearm free flap, rather than just a pericranial flap, should be considered for reconstruction. This strategy may obviate the occurrence of postoperative infections.

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Commentary

The authors present their series of eight patients treated for olfactory neuroblastoma with isolated transcranial resections. The traditional approach to these tumors has involved a combined approach using transfacial and transcranial routes. The authors eliminated the facial approach in an attempt to improve postoperative cosmesis by avoiding potentially disfiguring facial incisions. For carefully selected patients, they demonstrated that this approach is feasible and provides an appropriate en bloc oncological resection. The small size of the study prevents significant conclusions about this approach, but it demonstrates that further study and patient accrual are warranted. The authors appropriately explain that this approach is limited to tumors that do not extensively involve the orbit, maxillary antrum, nasal floor, or oropharynx. However, in patients with tumors lacking these features, the transcranial approach alone may provide long-term results equivalent to those of the traditional combined transfacial and transcranial approaches, while eliminating potentially disfiguring facial incisions.

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