“How Much Is Enough?” Endonasal Surgery for Olfactory Neuroblastoma

The birth of modern cranial base surgery in the 1980s was associated with the development and refinement of surgical techniques for removal of the anterior cranial base. The anterior craniofacial resection combining transcranial and transfacial approaches quickly became the gold standard for the management of neoplasms involving the anterior cranial base. Further refinements allowed complete resection of the anterior cranial base without facial incisions using a midfacial degloving approach, a completely transcranial approach and endoscopic-assisted approaches. Prior studies have evaluated the outcomes after craniofacial surgery for malignant skull base tumors and paranasal sinus tumors.^{1–5} In an international collaborative study by Patel et al, the most common tumors in the adult population were squamous cell carcinoma (29%) and adenocarcinoma (16%).¹ The 5-year disease-specific survival rate for all tumor types was 60%.

Esthesioneuroblastoma is the poster child of cranial base surgery. Because it arises from the olfactory neuroepithelium, it frequently involves the bone of the cranial base and may spread intracranially by direct extension through bone or by perineural infiltration of olfactory filia. Early attempts to resect these tumors without a craniotomy were associated with high recurrence rates. Routine performance of a craniofacial resection (with resection of the bone and dura of the skull base along with the olfactory nerves) was recommended to achieve clear resection margins and prevent recurrence due to intracranial extension through the cribriform plate. Improved local tumor control resulted and modern series now demonstrate a 5-year survival rate of 78% when a craniofacial resection is performed, usually in conjunction with postoperative radiotherapy.¹ Interpretation of the medical literature on the therapy of esthesioneuroblastomas is made difficult by small series of patients treated over a long time span. The evolution of surgical and radiation therapy techniques and changing

histological criteria for differentiation of esthesioneuroblastoma from other skull base tumors (neuroendocrine carcinoma, sinonasal undifferentiated carcinoma, small cell cancer, melanoma) have an obvious impact on reported outcomes. In addition, prognostic factors other than stage and resection margins, such as Hyams grade and nodal status, are frequently omitted.

Over the last decade, completely endoscopic endonasal approaches to the ventral skull base have been developed that allow resection of the bone and dura of the anterior cranial base.⁶ As described, the “endoscopic craniofacial resection” achieves the same resection margins as a conventional craniofacial approach. Skull base meetings are now replete with presentations on completely endonasal endoscopic resection of sinonasal malignancy, and multiple centers are reporting their early experience with completely endoscopic excision of esthesioneuroblastomas.^{7–11} Although the follow-up is limited, early results are encouraging with few local recurrences. A recent meta-analysis by Devaiah et al¹² demonstrated that endoscopic surgery was associated with better survival rates ($p = 0.0019$) than open surgery, even when stratifying for publication year ($p = 0.0018$). Confounding factors were increased long-term follow-up and a higher proportion of advanced tumors in the open surgical group.

However, a review of individual published series demonstrates that there is inconsistency of surgical techniques with surgeons performing resection of sinonasal tissues only (extracranial resection), removal of bone with preservation of dura (extradural resection), limited dural resections (preservation of olfactory bulb and tract), and complete transdural resection including the olfactory bulb and tract. Although there may be a selection bias with endoscopic techniques, it is not obvious that endonasal approaches are being selectively used for smaller tumors. Unfortunately, frequent use of the Kadish staging system for reporting of results does not provide adequate detail regarding tumor extent.

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A valid criticism is that anything less than a complete craniofacial resection may violate oncological principles.¹³ Can the extent of surgery be tailored to the patient such that lesser surgery may be performed with preservation of dura and olfactory nerves? It is obvious that some olfactory neuroblastomas occur in sinonasal regions separate from the olfactory cleft, but these are not the norm. Extradural resection of a Kadish B tumor may miss microscopic tumor infiltration along olfactory filia. Parenthetically, we have observed intradural tumor extension to the olfactory bulb in patients without skull base erosion or radiographic evidence of intracranial extension. However, small tumors without bone erosion can be excised in continuity with ipsilateral dura with preservation of the contralateral olfactory region.

How do we interpret the encouraging results of endoscopic reports despite variable techniques? Either our concepts regarding oncological surgery for esthesioneuroblastomas are wrong or the good results are attributable to other factors. Possibilities include early stage tumors, inadequate follow-up, or more effective post-operative therapies (sterilization of microscopic residual disease with radiation therapy). Parallel to surgical advances in cranial base surgery, we have witnessed dramatic changes in radiation therapy techniques. Intensity-modulated radiotherapy has replaced conventional external beam therapy for treatment of the skull base postoperatively. Radiosurgery techniques also allow radiation boosts to areas of suspected residual disease.

At this juncture in time, it is prudent to err on the side of conservative thinking and “radical” surgery until major skull base centers have treated an adequate number of patients with extended follow-up. If too many treatment strategies are adopted, the role of endonasal surgery will become muddled by disparate results and progress will be stalled. Endonasal surgeons should strive to obtain the same resection margins that they would with an open craniofacial resection. For a patient with a Kadish B/C stage tumor, this would include a complete resection of the bone, dura, olfactory bulb, and tract on at least one side. If the tumor crosses the midline, the resection should extend from orbit to orbit and include the contralateral olfactory bulb and tract. These recommendations apply even if a “chemotherapy first” approach is adopted with surgery being reserved for nonresponders to chemotherapy or treatment of residual disease following radiation therapy.¹⁴ There is minimal biological cost or risk to the patient of extending the margins of resection to include the dura and olfactory bulb/tract. In addition, surgeons should also adopt uniform reporting with a clear description of histological criteria and inclusion of known prognostic factors.

The goals of endoscopic resection should be identical to that of open craniofacial approaches: complete removal of disease with minimal morbidity. Negative margins should be meticulously pursued and only

limited by a conscious decision to leave residual disease, based on a desire not to compromise critical neurovascular structures (optic nerves, internal carotid artery) that may result in unacceptable morbidity for the patient. The degree or margin of resection should not be compromised merely to provide a “minimally invasive approach.”

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