Esthesioneuroblastoma: Endonasal Endoscopic Treatment

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ABSTRACT

Objectives: To illustrate endoscopic techniques used in the treatment of esthesioneuroblastoma and to advocate this method of management followed by radiation therapy in selected cases. **Methods:** A retrospective case series of 10 patients with esthesioneuroblastomas treated between 1999 and 2004 at a tertiary referral center using endonasal techniques. **Results:** Mean age of patients at presentation was 56.2 years (median 57 years). Seven patients were female and 3 patients were male. Kadish staging at presentation was: A – 3 patients, B – 5 patients, C – 2 patients. Dulguerov stage at presentation was: T1 – 4 patients, T2 – 4 patients, T3 – 2 patients. The period of follow-up ranged from 11 months to 74 months (mean 38.1 months, median 39 months). To date no recurrence has developed in any patient. **Conclusions:** Our experience suggests that endoscopic surgery can be an effective method of management. Strict attention to selection criteria, careful surgical techniques, and regular follow-up are key elements for success.

KEYWORDS: Olfactory neuroblastoma, esthesioneuroblastoma, cranio-facial resection

Esthesioneuroblastoma (olfactory neuroblastoma) is a rare malignant tumor of the superior nasal vault that arises from the olfactory neuroepithelium and invades the paranasal sinuses, the orbit, and the brain.¹ It was first described by Berger and Luc in 1924 as “esthèsioneuroèpitheliome

olfactif.”² Fewer than 1000 cases have been described in the literature since 1924.

Esthesioneuroblastoma accounts for 6% of tumors arising in the nasal cavity and paranasal sinuses and less than 1% of all malignant tumors.³ It can develop at any time of life. Cases have been

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reported at the extremes of life, in children as young as 18 months and also in those in the ninth decade of life. In general, peaks of incidence are apparent in the second and sixth decades.¹ It affects both sexes equally and no racial influence has been reported.

Like other sinonasal tumors, esthesioneuroblastoma presents with unilateral progressive nasal obstruction, nasal discharge, epistaxis, and headache. Extension of disease into the orbit may result in proptosis, diplopia, and retrobulbar pain. Intracranial growth may cause raised intracranial pressure, cranial nerve deficits, and eventually coma leading to death. The tumor has been described sometimes as having neuroendocrine activity which regresses after therapy.⁴

Esthesioneuroblastoma usually grows slowly but with locally aggressive behavior. It spreads through submucosal planes to surrounding structures and invades the anterior cranial fossa, destroying the cribriform plate with propagation along the perineural spaces of the olfactory nerves. Orbital extension takes place through erosion of the lamina papyracea.

The cervical lymph nodes are the most frequent site of metastases and tend to develop late in the natural history of the disease.⁵ Metastases at the time of presentation are uncommon; reports appear in 6 to 20% of cases.⁶ Distant metastases also develop in 9 to 13% of patients and tend to involve the bones, lungs, or liver.^{7,8} Local recurrence is relatively frequent no matter what treatment has been employed previously and tends to develop 2 to 3 years after initial treatment, though later recurrences have been documented up to 10 years.

On clinical examination using an endoscope, esthesioneuroblastoma presents as a polypoid mass arising in the superior part of the nasal cavity. Careful imaging is pivotal in the initial evaluation. Axial and coronal CT images provide useful information about the extent of bone erosion while multiplanar gadolinium-enhanced MR gives better information about the soft tissue extension.

From a histopathological standpoint, esthesioneuroblastoma is composed of small, round cells, which are organized in "neural rosettes" and display

immunohistochemical positivity to markers of neural differentiation. This helps distinguish this tumor from melanoma, lymphoma, and sinonasal undifferentiated carcinoma. Recently, a series of chromosomal alterations have been discovered in esthesioneuroblastoma cells, which can be useful in the identification process.⁹

A clinical staging system was originally introduced by Kadish in 1976. According to this scheme, disease confined to the nasal cavity defined stage A, stage B occurred when the tumor extended into the paranasal sinuses, and stage C developed when the tumor had spread beyond the paranasal sinuses into the orbit or intracranial or infratemporal fossa.¹⁰ An alternative staging system was proposed by Dulguerov and Calcaterra in which T1 disease indicated tumors that were located in the nasal cavity and/or paranasal sinuses, T2 tumors extended to the cribriform plate, T3 tumors involved the orbit and/or the anterior cranial fossa, and T4 tumors invaded the brain.¹¹

A histological grading system was proposed by Hyams¹² that intended to correlate microscopic findings with clinical outcomes. It took into account the formation of pseudorosettes, degree of cellular differentiation, mitotic activity, and the presence of necrosis.¹³

Surgical resection through an anterior craniofacial approach is considered to be the treatment of choice.¹⁴ Radiotherapy and chemotherapy also play a significant role in the management of this tumor. Radiotherapy is employed mainly postoperatively when microscopic positive margins are present or when local recurrence develops that would be too dangerous to resect. Chemotherapy has been found to be useful, particularly for the control of metastatic tumors or those deemed to be unresectable.

PATIENTS AND METHODS

We conducted a retrospective chart review of 10 patients with esthesioneuroblastoma who were

Table 1 Classification of Our Series of Patients According to Different Staging Systems

Kadish	Dulguerov	Hyams
A – 3 patients	T1 – 4 patients	I – 2 patients
B – 5 patients	T2 – 4 patients	II – 4 patients
C – 2 patients	T3 – 2 patients	III – 4 patients
	T4 – 0 patients	IV – 0 patients

treated at the Department of Otorhinolaryngology of the University of Pavia and Insubria (Varese) from 1999 to 2004. Three patients were male and seven were female. Their age at the time of diagnosis ranged from 14 to 72 years (mean 56.2 years, median 57 years). Presenting symptoms and signs were nasal obstruction (9/10), epistaxis (3/10), nasal discharge (2/10), while in one case there were no symptoms at all. No patient had regional or distant metastases. One patient had previously undergone a craniofacial resection elsewhere. The tumors were staged according to Kadish-Dulguerov-Hyams systems (Table 1). All patients underwent endonasal microendoscopic surgical resection.

RESULTS

The endoscopic approach allowed an en bloc resection of small tumors only. Larger tumors were resected in piecemeal fashion but this had no influence on the prognostic outcome.¹⁵ In our experience it was crucial to maintain the dissection of the neoplasm in the subperiosteal plane and to use a centripetal technique, starting at the periphery and moving toward the center. In patients with dural involvement, the resection was extended to the olfactory bulb. Reconstruction of the anterior skull base using a “sandwich” technique is recommended. The graft should be composed of three layers. The two most internal layers are made of autologous connective tissue such as temporal fascia or fascia lata, while the superficial layer is made of nasal mucoperiosteum. A synthetic heterologous dural substitute was used to replace the connective tissue layers in a few cases.

Microscopically clear margins were obtained and tumor control was achieved in all patients. No patient had significant postoperative complications. Nine patients received adjuvant radiation therapy and one patient also received chemotherapy because of the advanced stage of disease. One patient refused radiotherapy. Every patient developed and complained of nasal crusting after treatment. All patients have been monitored after treatment by serial endoscopic examination and interval radiological assessment. MR scans were acquired every 4 months for the first year and then every 6 months. All patients continue to be free of disease. The length of follow-up ranged from 11 to 74 months (mean 38.1 months, median 39 months). All patients maintained contralateral olfactory function and, although some are hyposmic, none complained of anosmia. No patient has developed recurrent or metastatic disease. All the patients in this series continue to be regularly assessed (Fig. 1).

DISCUSSION

Esthesioneuroblastoma is usually managed by surgery followed by postoperative radiotherapy.⁵ The conventional surgical approach for malignant tumors of the anterior skull base is a combined craniofacial resection.¹³ Postoperative complications have been reported in 15 to 40% of cases. Major complications include cerebrospinal fluid leakage, frontal lobe abscess, intracranial hemorrhage, and infection. Some of these complications necessitate further surgical intervention. Postoperative irradiation has been shown to improve local control.¹⁶ The role of chemotherapy as part of the curative process has not been adequately evaluated. In some studies, this tumor and its metastases have been shown to be sensitive to platinum-based chemotherapy and further clinical trials are necessary.¹⁷

In our series, endonasal microendoscopic resection was performed instead of a conventional transfacial approach. All patients were very carefully studied preoperatively to assess the feasibility and

Figure 1 (A–C) Sagittal and coronal view of preoperative MRI showing tumor extension. (B–D) Sagittal and coronal view of postoperative MRI showing complete tumor excision.

suitability of the procedure. In our selected series, we achieved complete resection of the tumor with excellent local control. No skin incisions were required and the period of hospitalization was short. Furthermore, there were no postsurgical complications and no long-term cosmetic deformities. Our data suggest that the conventional craniofacial approach may be replaced by the endonasal microendoscopic surgical approach in selected cases, even when the tumor is classified as Kadish Stage C, as long as there is no gross brain invasion.

The endoscopic approach should only be performed in very select cases and only by trained

surgeons. The endonasal endoscopic skull base reconstruction with duraplasty requires specific skills and abilities. If adjacent areas are found to be involved that cannot be resected endoscopically, it is essential that the surgeon convert the surgical procedure to an external approach.

In our experience, the combination of endonasal microendoscopic surgery followed by radiotherapy provided excellent disease control. This is a minimally invasive approach with few complications in experienced hands. As a result of our experience, we recommend its use as an alternative to craniofacial resection, in selected cases.

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