Esthesioneuroblastoma (Olfactory Neuroblastoma) with Hemorrhage: An Unusual Presentation

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ABSTRACT

Esthesioneuroblastoma (olfactory neuroblastoma) is an uncommon neuroectodermal tumor. Its biological activity ranges from indolent growth to local recurrence and rapid widespread metastasis. Treatment options consist of surgical resection followed by radiation therapy for primary lesions and the addition of chemotherapy for advanced, recurrent, or metastatic lesions. Patients often present with nasal obstruction, rhinorrhea, recurrent epistaxis, hyposmia, or anosmia. However, we report the highly unusual case of a patient with an esthesioneuroblastoma who presented with atypical symptoms of headaches, sinus congestion, and fatigue before acutely losing consciousness. Imaging showed a large frontal skull-based tumor associated with intratumoral hemorrhage. The findings prompted an emergent combined anterior craniofacial resection with gross total resection of the tumor. Except for anosmia, the patient recovered almost completely. Postoperatively, she received adjuvant intensity-modulated radiation therapy and chemotherapy. This is the first reported case of an esthesioneuroblastoma presenting with hemorrhage and rapidly declining mental status, an acute neurological manifestation of which clinicians should be aware.

KEYWORDS: Esthesioneuroblastoma, hemorrhage, neurological deterioration, olfactory neuroblastoma

Olfactory esthesioneuroblastoma is an uncommon neuroectodermal tumor that originates

from the olfactory sensory epithelium in the upper nasal fossa at the level of the cribriform plate.¹⁻⁵ It

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Skull Base 2006;16:169-174. Copyright © 2006 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

Received: March 11, 2005. Accepted after revision: November 17, 2005. Published online: May 3, 2006.

DOI 10.1055/s-2006-939677. ISSN 1531-5010.

represents up to 5% of malignant tumors of the nasal cavity.^{6,7} First described by Berger et al in 1924,⁸ almost 1000 cases have been published.⁷ The probable origins reported for this tumor include the sphenopalatine ganglion, the vomeronasal organ of Jacobson, the neuroepithelial cells of the olfactory membrane, the ectopic olfactory epithelium in the nasal mucosa, and the amine precursor uptake and decarboxylation cells.^{6,7,9,10}

Computed tomography (CT) and magnetic resonance imaging (MRI) usually show a homogeneous soft tissue mass in the nasal cavity, producing some erosion of the lamina papyracea, cribriform plate, and fovea ethmoidalis.¹¹ On T1-weighted MRI, the tumor is hypointense to the gray matter, and it is isointense or hyperintense on T2-weighted MRI.⁵ Histochemical analysis is necessary to differentiate the variable appearance of the tumor from other lesions such as lymphoma, melanoma, undifferentiated carcinoma, extramedullary plasmacytoma, or embryonal rhabdomyosarcoma.¹²

The incidence peaks between 11 and 20 years old and again between 51 and 60 years old.¹³ The most common presenting symptoms are nasal obstruction, epistaxis, and persistent nasal discharge; less common presenting symptoms include sinus pain, visual changes, headache, proptosis, diplopia, hyposmia, anosmia, facial pain, facial swelling, and syncope.^{2,5,11,14-19} Symptoms may be present for years before the patient seeks medical advice. An esthesioneuroblastoma very rarely manifests with acute neurological deterioration. Therefore, we report a patient with a previously unreported clinical presentation of esthesioneuroblastoma: intratumoral hemorrhage and acute neurological decline. This presentation required emergent intervention which was associated with a very favorable outcome.

CASE REPORT

A 37-year-old woman newly diagnosed with depression was brought to the emergency room unresponsive. She had a 4-week history of headaches,

sinus congestion, and progressive fatigue. An urgent CT scan of the head showed a large frontal lesion. MRI showed a large, heterogeneous mass measuring 5.5 cm anteroposteriorly and 5.5 cm transversely. Its volume was 5 cc (Fig. 1). It was centered at the cribriform plate and extended inferiorly into the right nasal cavity abutting the superior turbinates. The largest volume of the mass extended superiorly, displacing the right frontal lobe superiorly, laterally, and medially. A 1 × 1.5-cm area of increased signal on T1-weighted MRIs superiorly was consistent with intratumoral hemorrhage. Extensive edema involved the white matter of the right frontal lobe and the medial left temporal lobe. There was also mass effect on the medial right frontal lobes, under the falx, and on the frontal horn of the right lateral ventricle, along with pneumocephalus. The left lateral ventricle was displaced laterally. The mass was very heterogeneous, but its signal intensity was predominantly high on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images. With contrast, there was marked heterogeneous enhancement.

The patient underwent an emergent combined anterior craniofacial resection with gross total resection of the tumor. The intracranial portion of the tumor was removed through an anterior cranial resection via a bicranial incision with a frontal sinus osteotomy. Then a transfacial approach using a modified Weber-Ferguson incision with a complete ethmoidectomy was performed to resect the remainder of the tumor arising from the right nasal cavity. Tumor medial to the middle turbinate and within the ethmoid cavity was also removed. A pericranial flap was developed through the frontal craniotomy approach and a split thickness bone graft from the craniotomy was used to close the anterior cranial fossa and cribriform plate.

Follow-up MRI (Fig. 2) confirmed a gross total resection of the tumor and remarkable relaxation of the brain. A small area of enhancing residual tumor was present along the posterosuperior margin of the resection cavity. Acute

Figure 1 (A) Axial flash, (B) T2-weighted, and (C) gradient echo MRI sequences of the brain show a heterogeneous mass with a focal area of intratumoral hemorrhage and extensive edema involving the white matter. Postgadolinium images, (D) axial, (E) coronal, and (F) sagittal MRIs, show a heterogeneously enhancing lesion. Arrows indicate the pneumocephalus. MRIs, magnetic resonance images.

hemorrhagic infarction of the right occipital lobe, likely from uncal herniation at presentation, was reported.

Microscopically, the tumor in the anterior fossa consisted of large islands of small cells with scant cytoplasm (Fig. 3). The nuclei showed a

Figure 2 Postoperative axial (left), axial (middle), and sagittal (right) MRIs of the brain with gadolinium confirm gross total resection and a remarkable relaxation of the brain. A small residual enhancing tumor along the posterosuperior margin of the resection cavity is visualized. MRIs, magnetic resonance images.

Figure 3 Esthesioneuroblastoma. The tumor consists of large islands of small cells with hyperchromatic nuclei showing a vesicular pattern and scant cytoplasm. Mitotic activity is brisk and areas of necrosis can be seen. Hematoxylin and eosin stain, magnification $\times 200$.

vesicular pattern with occasional prominent small nucleoli. Mitotic activity was brisk. There were areas of necrosis and of individual cell necrosis. Occasional nuclear molding was seen. Hemorrhage within the tumor was evident. Immunohistochemical studies showed the tumor cells to be immunoreactive with antibodies to cytokeratin and synaptophysin and focally with epithelial membrane antigen. The proliferation index was high; approximately 75% of the tumor cells were found to be immunostained with MIB-1 (proliferation marker). These findings were consistent with hemorrhagic esthesioneuroblastoma.

Postoperatively, the patient's condition steadily improved. During her hospital stay, she recovered completely, except for her olfactory loss. Eventually, she was discharged in stable condition. She was referred for postoperative radiotherapy and chemotherapy. Intensity-modulated radiation therapy (IMRT) was delivered to the tumor targets in 23 fractions. The larger residual tumor target received 46 Gy, and the smaller target received 60 Gy. The patient tolerated the radiotherapy well, except for developing the common side effects of skin erythema and nasal mucositis. The patient remains disease-free and neurologically stable 3 years after the surgery.

DISCUSSION

The incidence of esthesioneuroblastoma, an uncommon malignant neoplasm of the upper nasal cavity, is low. A relatively small number of cases have been reported in a variety of heterogeneous series that span long periods. Consequently, no one physician or institution has accumulated broad experience in the treatment of this tumor.^{2,18} The natural history of the disease, which ranges from slow progression to aggressive local recurrence and distant metastasis, has yielded various treatment protocols and recommendations.^{2,5,7,11,13-19} No standardized treatment protocol is available for the treatment of esthesioneuroblastoma. However, consensus supports the current recommendation for treatment: craniofacial resection followed by radiotherapy for primary low- to moderate-grade lesions with the addition of chemotherapy for patients with advanced, recurrent, or metastatic disease.^{5,11}

When treated with aggressive surgical therapy such as craniofacial en bloc tumor resection, in conjunction with adjuvant therapy of radiation with or without chemotherapy, esthesioneuroblastoma can be a curative disease with local control of the disease.^{2,5,7,11,13-19} Dulguerov and colleagues reported a 5-year survival rate of 45%. Others have reported a survival rate as high as 70% with a local recurrence rate of 30%.⁵ Prognosis depends on the stage and grade of the disease. Negative prognostic factors are age (more than 50 years at presentation), female gender, tumor recurrence, and metastasis.¹⁴

We present a hitherto unreported case of acute neurological deterioration caused by an esthesioneuroblastoma associated with intratumoral hemorrhage and pneumocephalus. This tumor had eroded through the anterior skull base and the dura to involve a significant portion of the frontal lobes, and it had penetrated the ventricular cavity. This manifestation is highly unusual. Despite the moribund condition of the patient at presentation, an excellent outcome can be achieved with an aggressive approach. Although no standard treatment protocol has been established, we strongly believe

a multidisciplinary approach with judicious use of craniofacial resection and IMRT is an excellent treatment paradigm for these tumors. We believe that chemotherapy is best used to treat advanced or recurrent disease.

SUMMARY

We offer a case report of esthesioneuroblastoma presenting with acute hemorrhage and rapid neurological deterioration, prompting an emergent combined craniofacial resection and administration of adjuvant treatment with radiation and chemotherapy postoperatively.

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