ESTHESIONEUROBLASTOMA

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Esthesioneuroblastoma (ENB) is a rare tumor that usually occurs in young men, with a second peak at the age of 50-60 years[1]. Characteristic imaging features include origin from olfactory epithelium high in the nasal cavity and contrast enhancement either by computed tomography (CT) or magnetic resonance imaging (MRI)[2,3].

We report a patient with persistent nasal obstruction and epistaxis, submitted to biopsy and endoscopic resection of an esthesioneuroblastoma with extension to ethmoidal air cells.

CASE

This 40-year-old male, a former smoker, complained of bilateral nasal obstruction worse on the right side for about two years. This was accompanied by a clear, but sometimes bloody discharge, decreased sense of smell, pain and a feeling of pressure in the right eye with lachrymation. A polypoid mass was found which occupied the right nasal vestibule, shifted the nasal septum contralaterally and was covered with reddish mucoid exudate.

Computerized tomography (CT) and magnetic resonance imaging (MRI) disclosed a solid mass filling the right maxillary sinus and right nasal cavity, with areas suggestive of bone erosion and proptosis of the right eye. On MRI, the tumor measured 9.5 × 4.5 × 5.4 cm was isointense on T1 and T2 weighted images and enhanced diffusely and heterogeneously after contrast; a superior extension of the mass occupied part of the ethmoidal air cells (Fig 1). Other paranasal sinuses contained hydrated, contrast enhancing material interpreted as of inflammatory nature.

A biopsy taken from the lesion yielded the diagnosis of esthesioneuroblastoma by conventional hematoxylin-eosin (HE) stained sections, immunohistochemistry and electron microscopy (Fig 2).

The tumor was completely excised by transnasal approach and the patient referred to radiotherapy.

DISCUSSION

Olfactory neuroblastoma (also known as esthesioneuroblastoma), first described by Berger and Luc in 1924[4], is rare, accounting for 3% of all intranasal tumors[1]. It is usually found in young men, with a secondary peak at the age of 50–60 years[5]. Our patient was 40 years old.

ENB should be suspected in patients with persistent unilateral nasal obstruction and recurrent epistaxis. The latter reflects the marked vascularity of olfactory neuroblastomas. Penetration into the cribriform plate can cause anosmia. Orbital extension may induce pain, proptosis and excessive lachrymation. Almost all of these symptoms, which are non-specific, were found in our case. Ear pain and otitis media can result from the tumor obstructing the eustachian tube. Frontal headache suggests involvement of the frontal sinus. Other cranial nerves may also be affected. Patients tend to present with advanced stage disease because of the nonspecificity of symptoms and signs[2].

ENB arise in the upper nasal cavity, possibly from basal olfactory epithelial stem cells. This hypothesis is supported by their characteristic histology which includes Homer Wright pseudorosettes, and immunohistochemistry positive for cells of neuronal lineage. The most useful of these is synaptophysin, a protein found in synaptic vesicles, which is considered more specific, although less sensitive than other markers such as neuron specific enolase (NSE) and CD56. Neurofilament protein, though highly specific, often fails to react, as it is usually found only in well differentiated neurons. The panel should include antibodies to cytokeratin (AE1AE3, CK7, 34βE12, 35βH11) to help in the differential diagnosis with nasopharyngeal carcinoma, another small round blue cell malignancy common at this location. S-100 protein is helpful as it identifies sustentacular cells in better differentiated tumors with paragangliomatous features. The Hyams grading system is based on preservation of lobular architecture, mitotic index, nuclear polymorphism, fibrillary matrix, rosettes and necrosis[6]. Almost all these features were found in our specimen.

The first clinical staging system was proposed by Kadish et al. in 1976[7], and still is an important prognosis predictor[8]. Survival for stage A and B tumors is usually excellent. Tumor extension to orbits or through the cribri-

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Received 10 November 2008, received in final form 28 April 2009. Accepted 4 June 2009.

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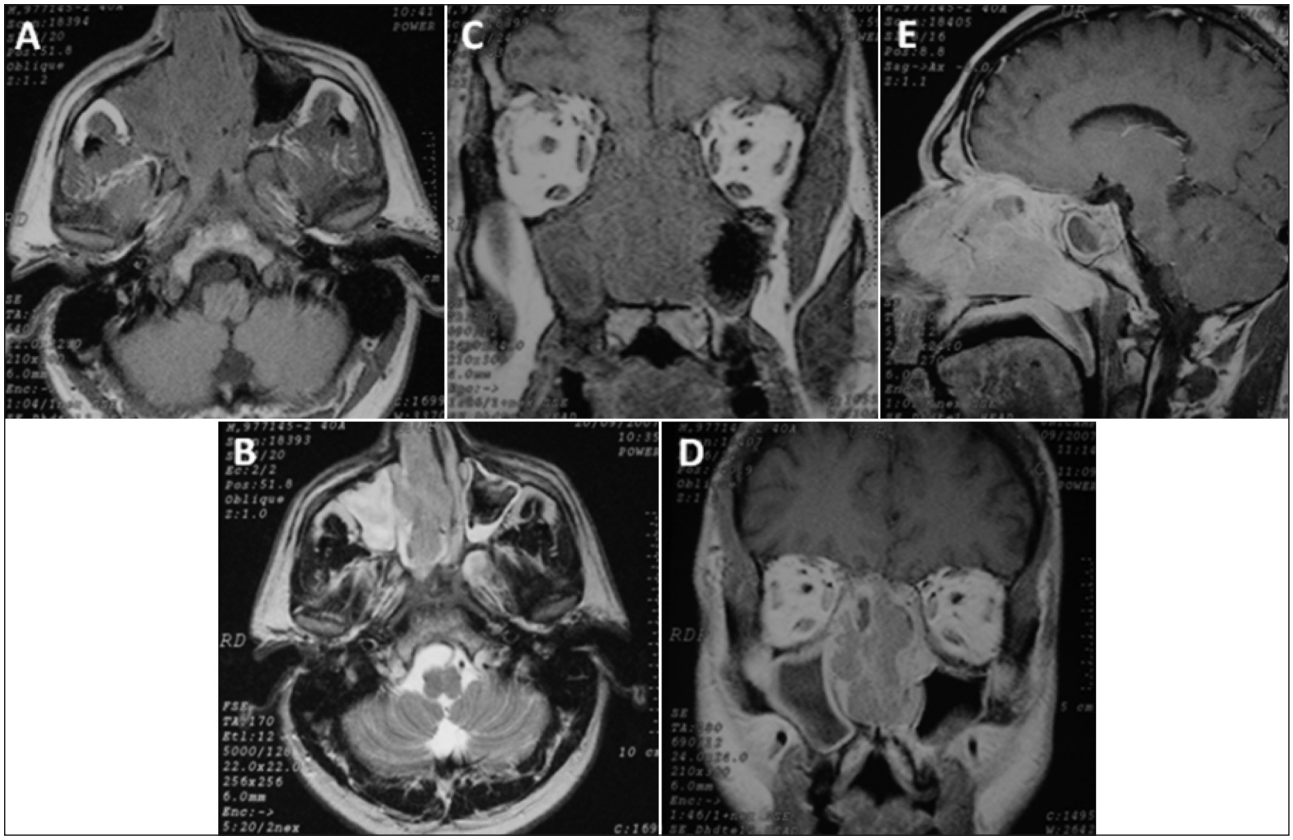

Fig 1. [A] (T1 - Weighted MRI, Axial) and [B] (T2-WI) - Expransive solid lesion filling the nasal cavity and right maxillary sinus, isointense in T1 WI and T2WI. The left maxillary sinus is lined by T2 hipermintense material suggestive of inflammatory sinusopathy. [C] (T1 - Weighted MRI, Coronal) e [D] (after Contrast) - Lesion shows irregular contrast enhancement and extends superiorly into the ethmoidal cells. [E] (T1 - Weighted MRI, Sagittal with contrast) - Lesion occupies nasal cavity but appears to have little if any intracranial extension. Frontal and sphenoidal sinuses display mucosal thickening and exudate.

form plate has significant prognostic implications[2]. Morita[9] proposed a revised Kadish staging, with stage C consisting of local disease extending beyond the paranasal sinuses and stage D consisting of cervical or distant metastases. Both Biller[10] and Dulguerov[11] have proposed systems based on TNM staging, but neither has been widely accepted, as there is no evidence that they provide better prognostic differentiation than the Kadish system[6]. Our case fits into the Kadish B stage, with extension to ethmoidal air cells, therefore carrying a good prognosis.

The radiologic appearance of ENB has been well described. CT and MRI are complementary examinations used for initial diagnosis, staging and follow-up. The MRI appearance is often that of a large, soft tissue, dumbbell-shaped mass centered within the superior nasal cavity and extending intracranially. The tumor is generally hypointense on T1-weighted images and iso- to hyperintense on proton density and T2-weighted images. Contrast enhancement is usually mild to marked and can be uniform or mildly heterogenous. These MR findings are however relatively non-specific. The present case showed a slightly different situation, with the mass being isointense on T1 despite the more usual finding of a hypointense tumor. Som et al. showed that cystic components at the intracranial margins of the tumor may be highly suggestive of ENB[3]. MRI is also important for staging, as it exhibits the extent of soft tissue invasion with involvement of local structures, such as orbits and sinuses. On CT, the tumor is iso- to slightly hyperdense to muscle and enhances homogenously. CT is most useful in demonstrating bone destruction. In addition, calcifications within the mass are reported to be a relatively specific diagnostic indicator of esthesioneuroblastoma. However, with erosion of the surrounding bone structures by the mass, it is difficult to distinguish true tumoral calcification from residual bone[1]. The use of both modalities is critical for discriminating between postobstructive secretion and tumor tissue[5]. In the case here reported, postobstructive secretions showed a markedly hyperintense signal on T2WI, thus differentiating them from the isointense tumor in the same images.

Thus, olfactory neuroblastomas can be detected, delineated and its characteristics suspected by CT and MRI, but definite diagnosis however is still based on histopathology[2].

Multi-modality treatment involving surgery, chemo-

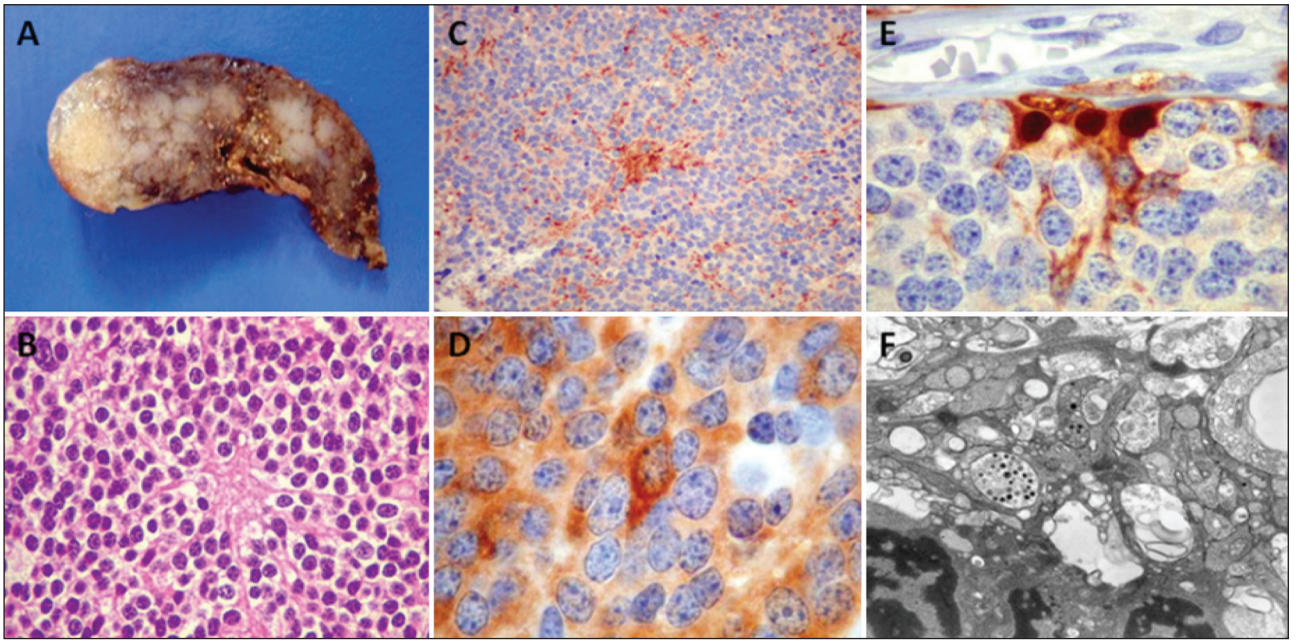

Fig 2. [A] (Surgical specimen) Elongated mass with smooth extemal surface, showing on section heterogeneous whitish nodules in a brownish background. Yellow calcified sports are visible near center. [B] (Hematoxylin and Eosin stained paraffin section): sheets of monotonous-looking cells, featuring rounded nuclei with little atypia and scant cytoplasm. Pink fibrillary areas known as Homer Wrigth rosettes punctuated the tumor. [C, D, E] (Immunohisto-chemistry): rosettes were characteristically positive for Synaptophysin [C], indicating neuronal lineage of neoplastic cells. Some cells were labeled for neuron specific enolase [D]. Several cells at the adge of lobules showed nuclear and cytoplasmic positivity for S-100 protein [E], an appearance similar to sustentacular cells in paragangliomas. [F] (Electron microscopy) disclosed tightly knit cell processes reminicent of neuropil, some profiles containing dense core vesicles of secretory type.

therapy and radiotherapy appears highly effective in preventing relapse in advanced ENB. The preferred surgical approach is cranio-facial resection, which was chosen in the patient we report, followed by radiotherapy. Large tumors are considered for pre-operative chemotherapy and post-operative radiotherapy[8].

In summary, olfactory neuroblastoma is an uncommon tumor of the superior nasal cavity that should be considered as a diagnostic possibility of a mass in this location demonstrating both expansible and destructive growth proprieties. Both CT and MRI are useful, each with its own characteristics, to stage tumor extent accurately and indentify extranasal tumor invasion, which is fundamental to operative planning.

REFERENCES

1. Schiro BJ, Escott EJ, McHugh JB, Carrau RL. Bone invasion by an esthesioneuroblastoma mimicking fibrous dysplasia. Eur J Radiol 2008; 65:69-72.
2. Pickuth D, Heywang-Kobrunner SH, Spielmann RP. Computed tomography and magnetic resonance imaging features of olfactory neuroblastoma: an analysis of 22 cases. Clin Otolaryngol 1999;24:346-350.
3. Som PM, Lidov M, Brandwein M, Catalano P, Biller HF. Sinonasal esthesioneuroblastoma with intracranial extension: marginal tumor cysts as a diagnostic MR finding. Am J Neuroradiol 1994;15:1259-1262.
4. Chirico G, Pergolizzi S, Mazziotti S, Santacaterina A, Ascenti G. Primary sphenoid esthesioneuroblastoma studied with MR. Clin Imaging 2003; 27:38-40.
5. Valenci M, Castill M. Congenital and acquired lesions of the nasal septum: a practical guide for differential diagnosis. Radiographics 2008;28:205-223.
6. Capelle L, Krawitz H. Esthesioneuroblastoma: a case report of diffuse subdural recurrence and review of recently published studies. J Med Imaging Radiat Oncol 2008;52:85-90.
7. Kadish S, GoodmanM, Wang CC. Olfatory neuroblastoma: a clinical analysis of 17 cases. Cancer 1976;37:1571-1576.
8. Sudip D, Kirsch CFE. Imaging of lumps and bumps in the nose: a review of sinonasal tumours. Cancer Imaging 2005;5:167-177.
9. Morita A,Ebersold MJ, Olsen KD, Foote RL, Lewis JE, Quast LM. Esthesioneuroblastoma prognosis and management. Neurosurgery 1993;32:706-714.
10. Biller HF, Lawson W, Sachdev VPO, Som P. Esthesioneuroblastoma: surgical treatment without radiation. Laryngoscope 1990;100:1199-1201.
11. Dulguerov P, Calcaterra T. Esthesioneuroblastoma: the UCLA experience 1970-1990. Laryngoscope 1992;102:843-851.