CASE REPORT

Ectopic olfactory neuroblastoma: case study and literature review

Neuroblastoma olfatório ectópico: estudo de caso e revisão da literatura

Hugo Gonçalves Couto[1], Leonardo Andrade Ribeiro[1], Dionísio da Silva Vilaça[1], Núbia Bernardes Carvalho[2]

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ABSTRACT

Olfactory neuroblastoma, also known as esthesioneuroblastoma (ENB), is a slow-growing malignant tumor of that originates mainly in the neuroectodermal cells in the nasal cavity. The peak incidence of ENB is at age 53, with the majority of cases occurring between 40 and 70 years, and mostly among men. There are a few reports of ENB in the ethmoid, maxillary, and sphenoid sinuses, or in the pituitary and nasopharynx. This tumor usually presents as an invasive disease with a tendency for later recurrence. The most frequent dissemination of ENB is to the cervical lymph nodes, which represents a worse prognosis. Its symptoms are nonspecific and nasal obstruction is the most common complaint. Imaging tests are important for the diagnosis of ENB, along with histopathological and immunohistochemical tests to help in the differential diagnosis. Surgical treatment of craniofacial resection associated with radiotherapy can achieve the best results for survival. We present a discussion of an illustrative clinical case of the disease in a male patient aged eight months, an unusual age for ENB, brought to attention by an initial family complaint of nasal obstruction and bloodstained hyaline rhinorrhea.

Key words: Neuroblastoma; Esthesioneuroblastoma, Olfactory; Otolaryngology.

RESUMO

O neuroblastoma olfatório, também conhecido como estesioneuroblastoma (ENB), é tumor maligno de crescimento lento, com origem principalmente na neuroectoderme da cavidade nasal. O pico de incidência do ENB é aos 53 anos, com a maioria dos casos ocorrendo entre os 40 e 70 anos, principalmente em homens. Há poucos relatos de ENB nos seios etmoidal, maxilar e esfenoidal, hipófise e nasofaringe. Esse tumor geralmente apresenta-se como doença invasiva e tendência a recorrer tardiamente. A disseminação mais frequente do ENB é para os linfonodos cervicais e, se presente, significa pior prognóstico. Seus sintomas são inespecíficos, sendo a obstrução nasal o mais comum. Os exames de imagem são importantes no diagnóstico do ENB, juntamente com o histopatológico e o imuno-histoquímico, que também auxiliam no diagnóstico diferencial. O tratamento cirúrgico de ressecção craniofacial associado à radioterapia apresenta os melhores resultados na sobrevida. Descreve-se seguidamente um caso clínico ilustrativo dessa doença em paciente masculino de oito meses, faixa etária incomum da ENB, com queixa familiar inicial de obstrução nasal e coriza hialina com rajas de sangue.

Palavras-chave: *Neuroblastoma; Estesioneuroblastoma Olfatório; Otolaringologia.*

[1] Physicians at the Hospital São Sebastião. Três Corações, Minas Gerais – Brazil.
[2] Medical student, Universidade Federal de Ouro Preto, Ouro Preto, MG – Brazil.

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Institution:
Fundação Hospitalar São Sebastião
Três Corações, Minas Gerais – Brazil

Corresponding Author:
Nubia B Carvalho
E-mail: nubia_bc@hotmail.com

CLINICAL CASE

An eight-month old male patient was taken to the ENT service 30 days previously due to nasal obstruction and bloodstained hyaline rhinorrhea. Amoxicillin was prescribed, but there was no improvement. The condition progressed with facial swelling (sic) in the previous 15 days (Figure 1).

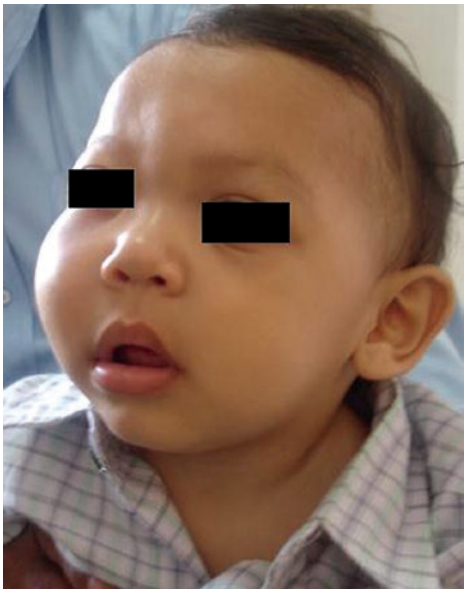

Figure 1 - Patient photograph two weeks after the first appointment.

Computed tomography (CT) showed an expansive mass in the right maxillary sinus with bone destruction in the medial wall of the maxillary sinus and the right jaw's lower wall (Figure 2 and 3).

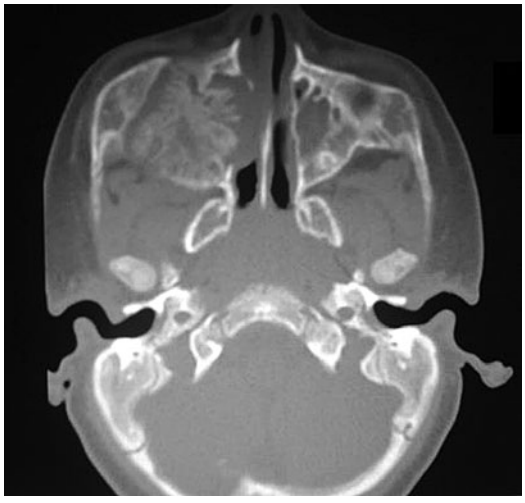

Figure 2 - Presence of expansive mass in the maxillary sinus evidenced by CT.

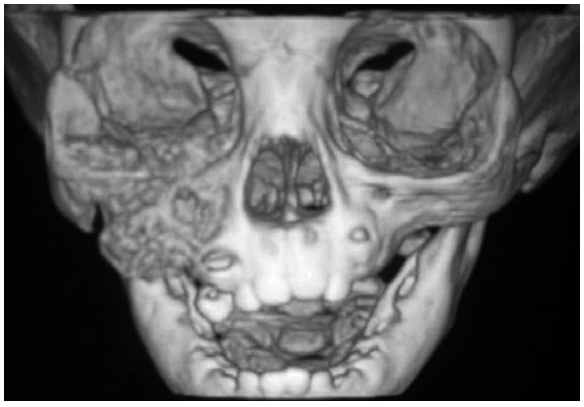

Figure 3 - Bone destruction of the medial wall in the maxillary sinus and the right jaw's lower wall, shown in three-dimensional tomographic reconstruction.

A biopsy of the mass was done and the anatomopathologic examination identified small, round, blue cells of lobular architecture. The immunocytochemical exam was positive for neuron-specific enolase (NSE), neural cell adhesion molecule (N-CAM), and negative for cytokeratins, CD45, CD99, and S-100 protein.

The diagonosis of ectopic olfactory neuroblastoma was made at the Kadish stage C.

DISCUSSION

Olfactory neuroblastoma, also known as esthesioneuroblastoma (ENB), is a rare malignant tumor that probably originates in the olfactory epithelium.[1,2] It generally originates in the upper portion of the nasal passages, but it is also described in other locations, such as the ethmoid, maxillary, and sphenoidal sinuses, pituitary gland, and nasopharynx, possibly as a result of ectopic cells that remain after the migration of neurons in the olfactory placode during the embryonic period.[3,3].

The largest casuistry of ENB reported so far comes from an analysis of 311 cases for a span of over 30 years.[4] It affects people predominantly ranging from 40 to 70 years; especially when they are 53[2,4]; with a man:woman ratio of 55:45.

Its growth is slow and the symptomatology nonspecific, which makes early diagnosis difficult.[4] Nasal obstruction is the most common complaint and is related to the presence of nasal mass. Physical examination usually reveals a red-brownish polyp located in the upper part of the nasal cavity. Other local manifestations include epistaxis, nasal discharge or pain. The invasion of adjacent structures can cause anos-

mia, proptosis, epiphora, otitis media and headache. It can cause paraneoplastic syndrome due to the production of ectopic hormones, including ectopic ACTH syndrome, hypercalcemia, and hyponatremia.[1]

Because there is no systematized staging for ENB, the Kadish system is mostly used based on the extent of the primary tumor. Kadish has been modified to encompass patients with lymph nodes affected by the tumor or with distant metastases, such as: A: confined to the nasal cavity, B: involving one or more paranasal sinuses, C: affecting beyond the nasal cavity and paranasal sinuses, D: affected regional lymph node or distant metastasis. The Dulguerov method is based on the TNM system and uses the computed tomography (CT) and magnetic resonance imaging (MRI) to determine the local range of the tumor.[1] After diagnosis, almost 61% of patients are in the Kadish stage C, which compromises the prognosis.[5]

ENB most frequently disseminates to the cervical lymph nodes (appearing in 5 to 20% of the cases) and, if present, results in a worse prognosis.[5,6] The tumor can spread to the paranasal sinuses, anterior cranial fossa, encephalon, spinal cord (via meninges), bones and lungs.[2] Late involvement (six months after the diagnosis) is also common.[6]

Radiography images can reveal the existence of intranasal masses. When the tumor is more extensive, bone destruction and opacification of the paranasal sinuses may appear. CT and MRI help differentiate the tumor from other causes of nasal obstruction and also help in define the stage[1]. These exams, however, cannot distinguish ENB from other tumors, so a definitive diagnosis requires histological analysis, immunohistochemistry or electron microscopy.[1]

Hyams *et al*.[7] created an histological grade system (grades I to IV) based mainly on the level of cellular differentiation. ENB is a typically a tumor with small round blue cells, with lobular architecture, and possible rosette formation. There is, however, a variety of small, round, blue cell tumors that appear in the sinuses and can be confused with ENB, among them sinonasal undifferentiated carcinomas, rhabdomyosarcomas and Ewing's sarcomas. The differential diagnosis requires use of additional techniques, such as immunohistochemistry.

In immunohistochemistry, ENB appears positive for neuron-specific enolase (NSE); 65% for synaptophysin and a lesser amount for chromogranin. In some cases, the tumor cells can be positive for neurofilament, cytokeratins, S-100 protein or glial fibrillary acidic protein (GFAP). The tumor cells are negative for various other markers, such as epithelial membrane antigen (EMA), common leukocyte antigens, kappa and lambda light chain, HMB45, desmin, myoglobin, vimentin, MIC2 (CD99) and the marker for Ewing's sarcoma.[1]

The difficulty in establishing standards for ENB treatment is due to the existence of only non-randomized, observational and clinical studies, with a limited number of participants, as well as its natural history, which requires prolonged observation to ensure adequate results. Both radiotherapy (RT) and chemotherapy, as well as surgical resection have been used in the initial treatment of EBN.[8] The surgical treatment followed by postoperative RT results in high survival rates when compared with just surgery or RT.[5] The use of combined treatments is important for patients with tumors that extend beyond the paranasal sinuses or for patients with surgical resection margins overtaken by the tumor.[1] The need for prophylactic irradiation of the cervical region is controversial. The frequency cervical metastasis formation upon diagnosis is of 5% and occurs in 14 to 33% of patients in the course of the disease, serving as an argument to justify irradiation.[9]

The role of chemotherapy is still unknown, and so is its effectiveness compared to surgical resection combined with RT. Molecular therapy is being studied for treatment of the systemic disease, but there is still no evidence with which to indicate routine use.[10,11]

There is no standard protocol for appropriately monitoring patients after ENB treatment. Multiple studies have documented that local or regional recurrences can occur after 10 to 15 years after the initial treatment, but most happen in the first few years. Based on this information, clinical and imaging long-term monitoring is indicated for these patients.[1,2]

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