



ORIGINAL ARTICLE

# Importance of neoadjuvant chemotherapy in olfactory neuroblastoma treatment: Series report and literature review<sup>☆</sup>



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## KEYWORDS

Esthesioneuroblastoma;  
Olfactory neuroblastoma;  
Neoadjuvant chemotherapy;  
Endoscopic surgery;  
Adjuvant radiotherapy

## Abstract

**Introduction and objectives:** Olfactory neuroblastoma (ONB) is a rare entity that constitutes less than 5% of nasosinusal malignancies. Mainstream treatment consists in surgical resection +/- adjuvant radiotherapy. By exposing results observed with apparition of new therapeutic options as neoadjuvant chemotherapy, the objective is to evaluate a series and a review of the current literature.

**Methods:** A retrospective review was conducted including patients diagnosed and followed-up for ONB from 2008 to 2015 in our institution.

**Results:** 9 patients were included. Mean follow-up of 52.5 months (range 10–107). Kadish stage: A, 1 patient (11.1%) treated with endoscopic surgery; B, 2 patients (22.2%) treated with endoscopic surgery (one of them received adjuvant radiotherapy); C, 6 patients (66.7%), 4 patients presented intracranial extension and were treated with neoadjuvant chemotherapy followed by surgery and radiotherapy. The other 2 patients presented isolated orbital extension, treated with radical surgery (endoscopic or craniofacial resection) plus radiotherapy. The 5-year disease free and overall survival observed was 88.9%.

**Conclusion:** Neoadjuvant chemotherapy could be an effective treatment for tumor reduction, improving surgical resection and reducing its complications.

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**PALABRAS CLAVE**

Esthesioneuroblastoma;  
Neuroblastoma olfatorio;  
Quimioterapia neoadyuvante;  
Resección endoscópica;  
Radioterapia adyuvante

## Importancia de la quimioterapia neoadyuvante en el tratamiento del neuroblastoma olfatorio: serie de casos y revisión de la literatura

**Resumen**

**Introducción y objetivos:** El neuroblastoma olfatorio es una entidad rara que se corresponde con menos del 5% de las neoplasias nasosinuales. El tratamiento principal consiste en la resección quirúrgica ± radioterapia adyuvante. El objetivo es evaluar la sobrevida en una serie de casos y la literatura actual, mostrando resultados observados con la aparición de nuevas opciones terapéuticas como la quimioterapia neoadyuvante.

**Métodos:** Se realizó un estudio retrospectivo incluyendo pacientes tratados y seguidos en nuestro centro desde 2008 a 2015.

**Resultados:** Dentro del estudio fueron incluidos 9 pacientes. El seguimiento medio fue de 52,5 meses (rango 10-107). Estadío Kadish: A) un paciente (11,1%) fue tratado con resección endoscópica; B) 2 pacientes (22,2%) tratados con resección endoscópica (uno de ellos recibió radioterapia adyuvante); C) 6 pacientes (66,7%), de los cuales 4 presentaron extensión intracraneal y fueron tratados con quimioterapia neoadyuvante, cirugía y radioterapia adyuvante. Los otros 2 pacientes presentaron invasión intraorbitaria aislada, tratados con cirugía radical y radioterapia adyuvante. La sobrevida y periodo libre de enfermedad a 5 años fue del 88,9%.

**Conclusión:** La quimioterapia neoadyuvante puede ser un tratamiento efectivo para la reducción del tamaño tumoral, mejorando la resección quirúrgica y reduciendo sus complicaciones. © 2017 Elsevier España, S.L.U. y Sociedad Española de Otorrinolaringología y Cirugía de Cabeza y Cuello. Todos los derechos reservados.

**Introduction**

ONB, also known as Esthesioneuroblastoma is a rare entity of malignant neoplasm which is believed to be formed at the neuroepithelial cells of the olfactory tract. It constitutes less than 5% of all malignant tumors of the nasal fossa and paranasal sinuses.<sup>1</sup> Mean age of presentation oscillates between 40 and 70 years old and has no gender predisposition.<sup>2</sup> The most common clinical manifestation described is nasal obstruction secondary to the presence of a mass in the nasal cavity, but it can debut with episodes of epistaxis, rhinorrhea and/or facial pain or facial fullness. Clinical examination usually demonstrates a polypoid mass located in the cranial portion of the nasal cavity. Depending on the extension and location of the tumor, different symptomatology can be observed: anosmia if it affects the cribriform plate; if it has orbital extension, can produce ocular pain, diplopia or epiphora; otalgia or otitis media with effusion if it extends to the eustachian tube; cognitive/behavioral changes with headaches if it extends to the anterior cranial fossa.<sup>3-6</sup> Paraneoplastic syndromes are rarely described.<sup>7</sup>

The diagnostic procedure requires a positive biopsy and the most commonly used staging classification is the Kadish clinical system<sup>8</sup> (Table 1), TNM known as Dulguerov staging system has also been described (Table 2). Hyams histological grading system grades ONB in four groups, from I to IV depending on mitotic activity and necrosis, being I/II as low grade tumors and III/IV as high grade tumors.

ONB are slow-growing tumors with unspecific symptomatology leading to a delayed diagnosis. At the moment of diagnosis most of the cases correspond to Kadish B or C

stages.<sup>2</sup> Imaging with MRI and CT scan are essential for staging and extension. While CT gives better information about bone invasion, MRI defines more accurately margins and adjacent soft tissue extension, such as the anterior cranial fossa and orbital tissues.<sup>9-11</sup> PET/CT scan has importance in assessing extension in locally advanced Kadish C or Hyams III/IV cases, which have high risk of distant metastases.<sup>12,13</sup> Imaging studies do not differentiate ONB from other nasosinusal neoplasms.

Differential diagnosis must include neuroendocrines carcinomas, sinonasal undifferentiated carcinoma, rhabdomyosarcoma, melanomas and metastases.

To this day, due to the low frequency of this entity, treatment has not been established by randomized clinical trials and has been only assessed by retrospective observational studies.<sup>14</sup> Historically, management of the primary tumor has been surgery with or without adjuvant radiotherapy (ART) and in selective cases, also adjuvant chemotherapy (ACT).<sup>15</sup> It has been generally indicated in observational studies that overall survival (OS) and disease free survival

**Table 1** Kadish staging system.

Stage	Extension
A	Confined to the nasal cavity
B	Involvement of one or more paranasal sinuses
C	Extension beyond the nasal cavity and paranasal sinuses involving cribriform lamina, skull base, orbit or intracranial cavity
D	Regional lymph node or distant metastasis

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