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ORIGINAL ARTICLE

Nasal and paranasal esthesioneuroblastomas: Clinical outcomes

J. Michel[a,*], N. Fakhry[a], L. Santini[a], J. Mancini[b], A. Giovanni[a], P. Dessi[a]

[a] *Service d'ORL et chirurgie cervico-faciale, Assistance publique—Hôpitaux de Marseille, CHU La Timone, Aix Marseille université, 264, rue Saint-Pierre, 13385 Marseille cedex, France*
[b] *Service de gestion de l'information médicale, Assistance publique—Hôpitaux de Marseille, CHU La Timone, Aix Marseille université, 264, rue Saint-Pierre, 13385 Marseille cedex, France*

KEYWORDS
Sinus cancer;
Paranasal sinus;
Overall Survival;
Disease-free survival

Summary Esthesioneuroblastomas (ENB) are rare tumours derived from the olfactory epithelium. Based on their experience and a review of the literature, the authors tried to identify the epidemiological, clinical, histological and therapeutic factors that influence overall and disease-free survival in their series of ENB.
Methods: This retrospective study concerned eleven patients treated in a single institution for ENB of the nasal cavity and sinuses between 1978 and 2006. The data collected were submitted to statistical analysis using R 2.0® software. Overall survival and disease-free survival were estimated by the Kaplan-Meier method and prognostic factors were identified by Log-Rank test.
Results: This series comprised three women (27.2%) and eight men (72.8%) (sex ratio: 2.6). The mean age at diagnosis was 56 years (range: 37—69 years). No risk factors were identified in this cohort. The mean follow-up was 110.2 months (range: 7—348 months). This series included three T1 (27.3%), one T2 (9.1%), four T3 (36.3%) and three T4 (27.3%) tumours. The 1-year, 5-year and 10-year disease-free survival rates were 81.8%, 54.5% and 18.2%, and the corresponding overall survival rates were 100%, 90% and 60%, respectively. The main prognostic factors reported in the literature are tumour stage at diagnosis, adjuvant radiotherapy and radiation dose.
Conclusion: ENB are characterized by a high recurrence rate and recurrences can occur a very long time after the diagnosis, indicating the need for prolonged follow-up of these patients. The 5-year and 10-year overall survival rates are about 90% and 60%, respectively.

Introduction

Esthesioneuroblastoma (ENB) was first described in 1924. These rare tumours are derived from olfactory epithelium and usually arise in the olfactory cleft [1,2]. Most published series concern retrospective studies based on small sample sizes. However, several international multicentre studies have been published, based on a greater number of cases, allowing identification of prognostic factors [3]. In a meta-analysis of all published cases from 1924 until 1997, Broich et al. reported a total of 945 cases [2].

* Corresponding author. Tel.: +33 4 91 38 60 71.
E-mail address: justin.michel@ap-hm.fr (J. Michel).

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Table 1 Dulguerov's TNM classification.

Dulguerov's classification [1992]
T1: tumour involving the nasal cavity excluding the sphenoid sinus
T2: tumour involving the nasal cavity including the sphenoid sinus
T3: tumour extending to the orbit or anterior cranial fossa
T4: tumour involving the brain
N0: no cervical lymph node metastases
N1: cervical lymph node metastases
M0: no metastases
M1: distant metastases

Based on our experience and a review of the literature, we tried to identify epidemiological, clinical, histological and therapeutic factors influencing overall survival and disease-free survival in our series of ENB.

Patients and methods

This retrospective study was based on 11 patients managed in our institution for ENB of the nasal cavity and sinuses between 1978 and 2006.

Epidemiological data, clinical and imaging findings, histology, treatment modalities and outcome of patients were studied. To ensure a homogeneous series, Dulguerov's TNM classification, presented in Table 1, was applied to all patients either retrospectively (patients managed before 1992) or prospectively (patients managed after 1992) [4].

The database was created with FileMaker Pro® software (version 5; Microsoft Corp. Ltd, Redmond, USA). Statistical analysis of overall survival and disease-free survival was performed according to the Kaplan-Meier method. The prognostic value of the following elements on overall survival and disease-free survival was investigated by univariate analysis (Log-Rank test): age, gender, T status, tumour extension (involvement of key structures such as the sphenoid sinus, frontal sinus, orbit, eyeball, anterior cranial fossa, cavernous sinus, brain), histological grade, surgical management and adjuvant radiotherapy. For all tests, a P value less than 0.05 was considered statistically significant. All statistical analyses were performed with R 2.0® software.

Results

Epidemiological data

This series comprised three women (27.2%) and eight men (72.8%), i.e. a sex ratio of 2.6. The mean age at diagnosis was 56 years (range: 37—69 years). The tumour was located on the right side in four cases (36.4%), the left side in three cases (27.2%) and the lesion was bilateral in four cases (36.4%). No occupational exposure risk factor (leather tannin, wood dust, exposure to nickel) was identified. The median follow-up was 102 months (range: 7—348 months).

Clinical features

Initial symptoms were unilateral in 90.9% of cases. The most common symptoms were nasal obstruction (70%) and epistaxis (30%). Other presenting complaints were pain (20%), diplopia or exophthalmos (20%), neurological signs (20%) and skin signs (10%).

Site, extension and TNM classification

The initial assessment in all patients managed after 1991 ($n = 10$) comprised contrast-enhanced CT scan of the facial bones for local staging and contrast-enhanced CT of the neck and chest for regional and distant staging. This assessment was completed by MRI of the facial bones in eight patients (80%). Review of imaging allowed assessment of tumour sites, modes of extension and staging. The initial assessment for the patient diagnosed in 1976 was not available for review.

In every case, the tumours arose from the olfactory cleft. The lesion was strictly confined to one nasal cavity in two cases (18.2%), and extended to the sphenoid sinus in one case (9.1%), the frontal sinus in one case (9.1%), the orbit in two cases (18.2%), the eyeball in one case (9.1%), the anterior cranial fossa in three cases (27.3%), the cavernous sinus in one case (9.1%) and the brain in three cases (27.3%).

This series comprised three stage T1 (27.3%), one stage T2 (9.1%), four stage T3 (36.3%) and three stage T4 (27.3%) tumours. One patient (9.1%) had positive lymph nodes at diagnosis and was staged as T4N2c (retropharyngeal, spinal and bilateral jugulo-carotid lymphadenopathy). No patients had metastatic disease at diagnosis.

The patient with a high-grade malignant tumour with lymph node invasion at the initial diagnosis was alive with disease at the time of data collection, i.e. 68 months after the diagnosis.

Histological data

The histological grade was determined for only eight (63.6%) of the 11 cases of histologically documented ENB: grade I in one case (12.5%), grade II in two cases (25%), grade III in three cases (37.5%) and grade IV in two cases (25%). The immunohistochemical profile of the tumour was determined in six6 cases. At least one neuroendocrine marker was present in all cases (Neuron-Specific Enolase [NSE], Chromogranin or synaptophysin). PS 100 was positive in four cases and negative in two cases. Epithelial markers were negative in five cases and positive in one case.

Treatment modalities

The initial treatment consisted of four different modalities: surgery alone: 27.3% ($n = 3$); surgery followed by adjuvant radiotherapy: 36.3% ($n = 4$); concurrent chemoradiotherapy (cisplatin/5-fluorouracil): 18.2% ($n = 2$); neoadjuvant chemotherapy (cisplatin/etoposide and cisplatin/5-fluorouracil) (18.2%) followed by chemoradiotherapy in one case and surgery in one case, both staged as T4N0M0.