

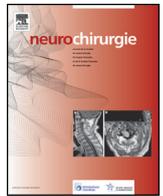


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Original article

Treatment of esthesioneuroblastomas

Traitement des esthésioneuroblastomes

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ABSTRACT

Objective. – To analyze the clinical features, treatment outcomes, pattern of failures, and course of the disease of a cohort of patients treated for esthesioneuroblastoma (ENB) with craniofacial resection (CFR) at a single institution during a 12-year period.

Material and methods. – Retrospective analysis of 11 patients with ENB treated with CFR in a tertiary care academic medical center from 1998 to 2009.

Results. – Median age at diagnosis was 51 years (range 41–67 years). The most common presenting symptom was nasal obstruction (91%). Four patients (36%) presented with Kadish stage B, six patients (55%) with Kadish stage C, and one patient (9%) with Kadish stage D. The initial treatment was craniofacial resection (CFR) alone for three patients (23%), CFR followed by postoperative radiation therapy (RT) in seven patients (64%), while one patient (9%) received both neoadjuvant and adjuvant RT in addition to surgery. The mean and median follow-up times were 66 and 58 months, respectively (range 23–158 months). Seven patients are currently alive with no evidence of disease (64%), while two patients are alive with disease (18%). Overall survival was 100% at one year postoperatively and 80% five years after the primary treatment. The progression free survival was calculated to 73% at one year and 64% at five years.

Conclusions. – ENB is an uncommon diagnosis with an incidence of 0.037/100,000 persons/year in the catchment area of our institution. Treatment can be challenging, especially with advanced disease. CFR with RT offers good oncologic disease control with minimal morbidity.

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R É S U M É

Objectif. – Analyser les causes de la maladie, ses caractéristiques cliniques, les résultats du traitement sur une cohorte de patients traités pour esthésioneuroblastome (ENB) par résection crâniofaciale (RCF) au sein d'une seule institution sur une période de 12 ans.

Patients et méthodes. – L'analyse rétrospective de 11 patients avec ENB traités par RCF dans un centre médical universitaire de soins tertiaires, de 1998 à 2009.

Résultats. – L'âge médian au moment du diagnostic était de 51 ans (extrêmes : 41–67 ans). Le symptôme de présentation le plus courant était l'obstruction nasale (91%). Quatre patients (36%) présentaient un stade B, six patients (55%) un stade C et un patient (9%) un stade D selon la classification de Kadish. Le traitement initial a été : RCF seule chez trois patients (23%), RCF+ radiothérapie postopératoire (RT) chez sept patients (64%), tandis qu'un patient (9%) recevait des RT adjuvante et néo-adjuvante en plus de la chirurgie. La moyenne et la médiane du temps de suivi était de 66 et 58 mois, respectivement (extrêmes : 23–158 mois). Sept patients sont en vie sans signes de maladie (64%), tandis que deux patients sont toujours porteurs de la maladie (18%). La survie globale est de 100% à un an postopératoire et de 80% à cinq ans après traitement primaire. La survie sans progression est calculée à 73% à un an et à 64% à cinq ans.

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Conclusions. – L'ENB est un diagnostic rare avec une incidence de 0,037/100 000 personnes/an dans le secteur de notre institution. Le traitement peut être difficile, surtout à un stade avancé de la maladie. La RCF avec RT offre un bon contrôle de la maladie oncologique avec une morbidité minimale.

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1. Introduction

Esthesioneuroblastoma (ENB) accounts for approximately 2–6% of nasal cavity and paranasal sinus cancer cases [1,2] and 0.3% of all upper aerodigestive tract malignancies [3]. ENB may occur at any age, although it occurs predominantly in young adults. There is a second peak of incidence in later adult life [2].

Patients with ENB commonly present with unilateral nasal obstruction and epistaxis [4,5]. These symptoms usually predate the diagnosis by 6 to 12 months as its special anatomical location and the initial, relatively innocuous symptoms often lead to delayed diagnosis and treatment [6].

The tumor is usually confined to the olfactory mucosa, involving the superior nasal cavity, sinuses and cribriform plate [2,7]. ENBs may cross the cribriform plate to infiltrate the dura and the brain. Diagnosis of ENB with no involvement of the cribriform plate should be a diagnosis of exclusion [8]. Metastases occur in 10–30% of the cases, either hematogenously or to locoregional lymph nodes [5,9].

ENBs are most commonly stratified by a system first described by Kadish et al. [10]. Since the original classification system did not incorporate regional or distant metastases, it was subsequently modified by Foote et al. [11] and Morita et al. [12]. The modified system categorizes patients into 4 stages based on radiological findings, including patients with distant metastases (Kadish stage D). It has been shown to be a good predictor of outcome by numerous studies published, but has been criticized for failing to stratify patients completely, since very few patients present at Kadish stage A, while Kadish stage C can reflect a wide spectrum of presentations [5,6,13,14].

The Hyams' grade is a histological grading scale (1–4) used in further classification of ENBs [15]. The impact of this grading system is not fully understood, however, it is suggested to predict patient survival as well as being a good tool for selecting patients for adjuvant radiotherapy [16,17].

A TNM (tumor/nodes/metastasis) style staging system was also proposed by Dulguerov [6,18] allowing the inclusion of nodal status, this system was later reported to correlate closely with survival and recurrence [5].

It is important to note, that radiologic staging and tumor grading are not directly related. In a report published by Kane et al., only 14% of all Kadish A tumors were low grade based on Hyams' grading (grades 1 and 2) [19].

Magnetic resonance imaging (MRI) and computed tomography (CT) play a central role in the investigation of these tumors, and provide important information supporting the staging and treatment. It is advocated to complete clinical staging with metastatic assessment in patients with advanced local disease or regional metastasis on presentation. Wu et al. showed that evaluation with positron emission tomography with CT (PET/CT) altered the clinical staging in 3 of their 9 patients. Seven of all nine patients with ENBs were PET positive [20]. Other studies have also suggested to use PET/CT in the evaluation of ENBs [21].

Different treatment modalities have been proposed including craniofacial resection (CFR), radiotherapy (RT) and chemotherapy [18,22–25]. There is no class I evidence to guide the appropriate management of ENB [26]. Historically, surgery resulted in a high morbidity and mortality, but with the advent of CFR both safety and overall survival (OS) rates improved [6,26]. Resection with negative

margins is a cornerstone of the treatment. Despite the extensive nature of the surgery necessary in these patients, serious complications are usually limited in modern series [5,27]. Anosmia, epistaxis, and visual symptoms may occur [5] and more serious complications include epidural hematoma [9] and tension pneumocephalus [5], but overall, the resultant functional and cosmetic deficits are minimal.

Evidence in the literature regarding the treatment of ENBs consists mainly of retrospective studies. The diagnostic workup and treatment modalities in form of different surgical techniques, RT and chemotherapy regimens have evolved significantly in recent years. Based on current evidence, surgery followed by postoperative RT is the main treatment for patients with localized ENB [6,9,26,28–31]. Chemotherapy has a role for more advanced cases, but the utility of chemotherapeutic agents is not well defined [5,26,32–34].

We report our series of patients with ENB who underwent craniofacial resection at the Oslo university hospital.

2. Material and methods

2.1. Patients

The patients for this study were retrieved from a prospectively collected database and the data were studied retrospectively. This database consists of patients with histologically verified ENB who underwent CFR at Oslo university hospital – Rikshospitalet from 1998 onwards. Patients were not considered suitable for CFR if they had to extensive unresectable intracranial extension, known metastatic disease, were older than 80 years, or in a general health condition prohibiting CFR.

The defined catchment area of our institution is the southeastern health region of Norway, with a population of 2.7 million inhabitants (56% of the Norwegian population), but referrals from outside this region are common due to the higher level of competence needed in cases of ENBs.

A multimodal evaluation and treatment was carried out in cooperation with different departments (departments of neurosurgery, head and neck surgery, ophthalmology, oncology and pathology).

The following data were recorded for all patients: sex, comorbidity, presenting symptoms, age at diagnosis, grading and staging (TNM, Kadish stage), metastases (yes/no, preoperative/postoperative), orbital affection (yes/no), dura affection (yes/no), cerebral affection (yes/no), age at surgery, type of surgical and non-surgical treatment (neoadjuvant and adjuvant, chemotherapy and radiation therapy), *en bloc* resection (yes/no), free histological margins (yes/no), postoperative sequelae or neurological deficits, complications (yes/no/type), and treatment of complications.

The histological diagnosis and resections – including surgical margins – were evaluated by pathologists using light microscopy and immunohistochemical staining for synaptophysin, chromogranin, and S100.

2.2. Ethics

The study was approved by the Data Protection Official at Oslo university hospital.

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