International Journal of Health Sciences
December 2014, Vol. 2, No. 4, pp. 73-80
ISSN: 2372-5060 (Print), 2372-5079 (Online)

Published by American Research Institute for Policy Development
DOI: 10.15640/ijhs.v2n4a6
URL: http://dx.doi.org/10.15640/ijhs.v2n4a6

Multidisciplinary Approach in Advanced Case of nasal Esthesioneuroblastoma: a Case Report and Review of Literature

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Introduction

Esthesioneuroblastoma (ENB) is a rare neuroectodermal tumor originating from the olfactory epithelium.

ENBs are often found in the upper nasal cavity and ethmoidal region. They typically spread through the cribriform plate to involve intracranial structures. They represent 3% of all intranasal neoplasms. ENBs are equally distributed between

both sexes, and relatively rare in children and young adults; in literature only 12 case reports document patients under 10 years of age[1] are reported. Usually first symptoms are nonspecific and include epistaxis, anosmia, nasal obstruction, and migraine, so most patients are diagnosed late. Exophthalmos and amaurosis are late and more specific symptoms.

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Etiology and pathogenesis are unknown. Current therapeutic options include surgery, radiotherapy (RT), adiuvant and neoadiuvant radiotherapy chemotherapy (CTX) and high-dose CTX followed by autologous bone marrow transplantation[2-3].

In literature there is not consensus about therapeutic strategies.

Case Report

A 45 years old women came to our Department referring cronic rhinorrea, and recent left orbital pain. No other patologies were referred in the anamnestic report. At the ENT examination the patient showed left esophtalmus and swelling at the left side of the nose. Ageusia and anosmia were also present. Head and neck CT scan demonstrated an infiltrating mass involving the left nostril and the omolateral maxillary sinus, the ethmoidal cells, the frontal sinus (figure 1); the mass was extended also to the left orbit and to the anterior cranial fossa inducing an edema of the frontal lobe and the compression of the olfactory bulb. No pathologic cervical nodes were found. MRI confirmed the same items (figure 2). An endoscopic biopsy was then performed with the hystological finding of ENB with high mithotic index. We decided to perform an endoscopic transnasal approach combinated with frontal craniotomy; the mass was completely removed.

One month later a MRI scan was performed showing a 3cm mass at the left ethmoidal region and a pathological left cervical node (Ib level, 1,2 cm). FDG-PET/CT scan revealed a SUV of 16.1 related with the nasal mass, and a SUV of 8.9 related to the node (figure 3 and 4). After multidisciplinary consulting we decided for a chemotherapy and radiochemotherapy sequential approach. Patient received 3 cycles of cisplatin (80 mg/m^2 day1), etoposide (100 mg/m^2 day1-3) every 21 days. During the chemotherapy, the patient's persistent dysosmia resolved and nodes in II level decreased from 2,5 cm to 0,5 cm.

After chemotherapy MRI demonstrated a partial response according to Recist criteria (total mass volume reduction up to 50%) (figure 5). Four weeks after induction chemotherapy, radiation therapy concomitant with weekly Cisplatin (40 mg/mq) was delivered. The planned dose to the tumor bed and involved cervical lymphatic region was 64 Gy in 32 fractions. Elective cervical lymph node irradiation (50 Gy, 25 fractions) was performed. Target volume for elective nodal irradiation was bilateral neck levels IB and II, and level III. Radiation delivery was Intensity Modulated Radiation Therapy (IMRT).

Six months after the ending of radiotherapy FDG-PET/CT scan total body showed complete rosponse (figure 6).

After 30 months the patient is disease-free.

Discussion

Nowdays in carefully selected cases, the recent introduction of endoscopic transnasal surgical thecniques in malignancies of nose and skull base (alone or in association with neurosurgical approaces) resulted in a less operative morbility (brain exposure or retraction) and mortality. Morover endoscopic approaches highly reduces facial cosmetic defects. [5]

The histologic similarity of ENB to other chemosensitive neoplasms such as neuroblastoma, small cell lung carcinoma, and primitive neuroectodermal tumors indicated a possible efficacy of chemotherapy in the treatment of ENB. Thereafter, chemotherapy was generally reserved to patients with relapses, metastatic or inoperable disease[6], Chemotherapy combined with radiation treatment may have a role, but there are few datas to support this hypothesis[7]. The additional use of chemotherapy seems to have a strong impact on the reduction of metastatic spread in comparison with the combined modality group (surgery plus RT) which has been considered the best treatment so far[8]. There were no serious complications from multimodality therapy.

Various chemotherapeutic combination regimens have been used involving alkylating agents and anthracylines in the adjuvant treatment of ENB in recent years with significant toxicities, especially platinum-based regimens and combination therapy using cyclophosphamide, vincristine, and occasionally doxorubicin. Some clinical responses have been reported to mechlorethamine, dacarbazine (DTIC), actinomycin, methotrexate, BCNU, procarbazine, and thiotepa.

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[5] Krischek B1, Godoy BL, Zadeh G, Gentili F From craniofacial resection to the endonasal endoscopic approach in skull base surgery World Neurosurg. 2013 Jul-Aug;80(1-2):56-8. doi: 10.1016/j.wneu.2013.01.106. Epub 2013 Feb 1.

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7 Zanation AM, Ferlito A, Rinaldo A, Gore MR, Lund VJ, McKinney KA, Suárez C, Takes RP, Devaiah AK.When, how and why to treat the neck in patients with esthesioneuroblastoma: a review. Eur Arch Otorhinolaryngol. 2010 November ; 267(11): 1667–1671.

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In a retrospective analysis of ten patients, McElroy et al. have demonstrated that cisplatinum-based chemotherapy is active in advanced, and especially high-grade ENB. Response to chemotherapy may be dependent upon the Hyam's grading of the original tumor and high-grade olfactory neuroblastoma was sensitive to cisplatin-based chemotherapy[9].

Neoadujvant chemotherapy for estesioneuroblastoma with Kadish stage B and C disease is the most widely used in varying protocols[10] . In this study patients received two cycles of cisplatin (33 mg/m^2/d) and etoposide (100 mg/m^2/d) and were re-assessed with repeat imaging. If less than a partial response was noted, surgical resection prior to radiotherapy was recommended. Alternatively, if the patient experienced a significant response to induction chemotherapy went directly to radiotherapy followed by 2 additional cycles of chemotherapy. For persistent disease after radiation in this group, salvage surgery was offered. With a median follow up of 45 months, 15 of the 19 patients were alive and free of disease. There were 2 local recurrences and the 5-year local control rate and overall survival were 88% and 74% respectively. however the significant response to initial chemotherapy was used to aid surgical management of what was previously unresectable tumor.

These survival rates are significantly higher than those cited for surgery followed by adjuvant radiation (65% at 5 years) cited by Dulguerov *et al.* in their meta-analysis[11]. In another study the neodjuvant chemotherapy is a combination with etoposide (75 mg/m^2), cisplatin (20 mg/m^2), and ifosfamide (1000 mg/m^2). In their study they reported objective responses in 9 of 11 patients (2 complete, 7 partial)[12]. There is a lot of study with preoperative radiation with or without chemotherapy (not given concurrently) that have demonstrated an increase of recurrence-free survival in those responders but there is only a case report with preoperative cisplatin (60 mg/m^2) with etoposide (120 mg/m^2) with concomitant radiotherapy of 50 Gy for the preoperative treatment of Kadish stage C and Hyams grade 3 and 4 tumors in 2 patients. Both patients enjoyed complete pathologic responses[13].

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10 Fitzek MM, Thrornton AF, Varvares M, et al. Neuroendocrine tumors of the sinonasal tract. Results of a prospective study incorporating chemotherapy, surgery, and combined proton-photon radiotherapy. Cancer. 2002;94:2623–34.

11 Dulguerov P, Allal AS, Calcaterra TC. Esthesioneuroblastoma: a meta analysis and review. Lancet Oncol. 2001;2:683–90.

12 Kim DW, Jo YH, Kim JH, et al. Neoadjuvant etoposide, ifosfamide, and cisplatin for the treatment of olfactory neuroblastoma. Cancer. 2004;101:2257–60

13 Sohrab Sohrabi, Joseph J. Drabick, Henry Crist, David Goldenberg, Jonas M. Sheehan and Heath B. Mackley, Neoadjuvant Concurrent Chemoradiation for Advanced Esthesioneuroblastoma: A Case Series and Review of the Literature. JCO May 1, 2011 vol. 29 no. 13 e358-e361

After surgery the role of chemotherapy is controversial, and usually chemotherapy was utilized in concomitant modality with radiotherapy. Little information is available regarding chemotherapy in the adjuvant setting. Prior reviews have found efficacy of chemotherapy for high grade tumors in the adjuvant setting[14]. In a small retrospective series Porter et al suggest that adjuvant therapy for patients with high grade, Stage C esthesioneuroblastoma is of benefit following complete resection and radiation therapy alone provides an improvement in time to relapse, which may be increased further with the addition of cisplatin and etoposide based chemotherapy[15]. In regional recurrence, radiotherapy or chemoradiation may be more effective as salvage therapy than chemotherapy is, and in cases of local recurrence, neck dissection should be considered for more successful salvage therapy[16]

A combined approach with postoperative RT is reported to result in better local control (0–40%), In a recent study was reported 86% local recurrences after surgery and 8% after surgery plus RT[17]. The authors recommend adjuvant RT particularly for high-grade tumors according to Hyam's system and high-stage tumors according to the Kadish system[18]. Regarding the timing of RT,

Eden et aldid not find a significant difference in survival between pre- and postoperative RT[19]. However, they were able to show improved local tumor control after preoperative RT but preoperative neoadjuvant RT with or without chemotherapy showed a significant reduction in tumor burden leading to a greater chance of gross total tumor resection and long-term disease-free progression.

In conclusion the multidisciplinary approach choosen to treat this case of advanced ENB is effective and safe, without long term consequences.

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Figure1

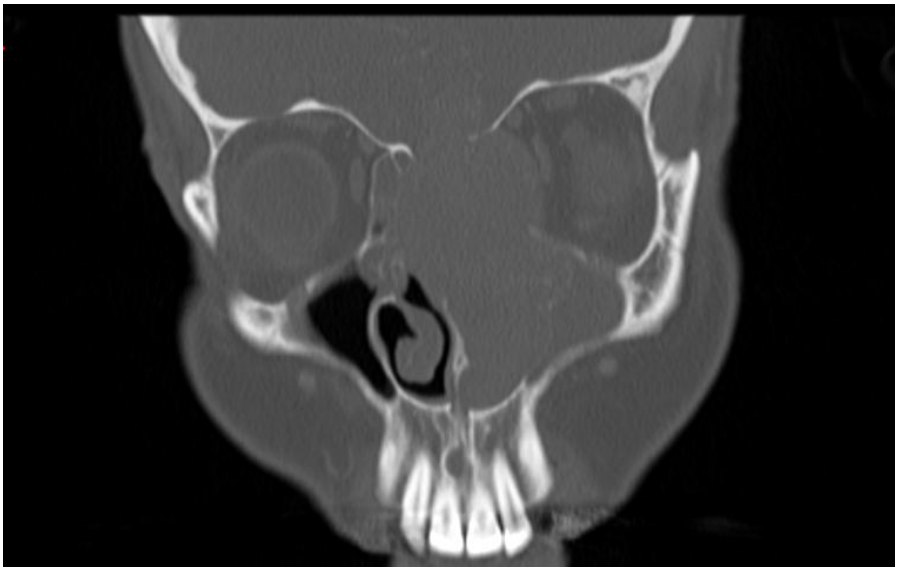

Figure 2

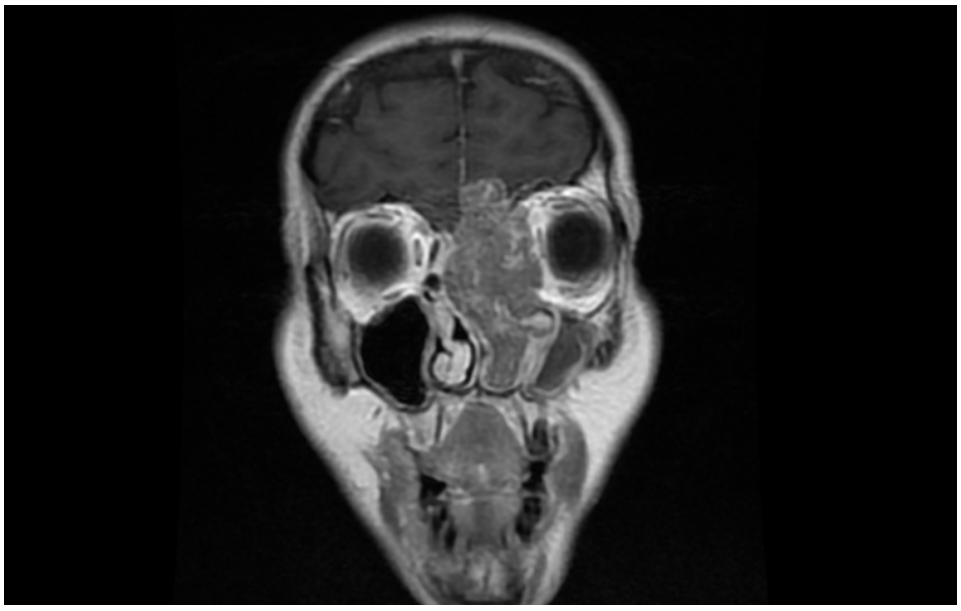

Figure 3

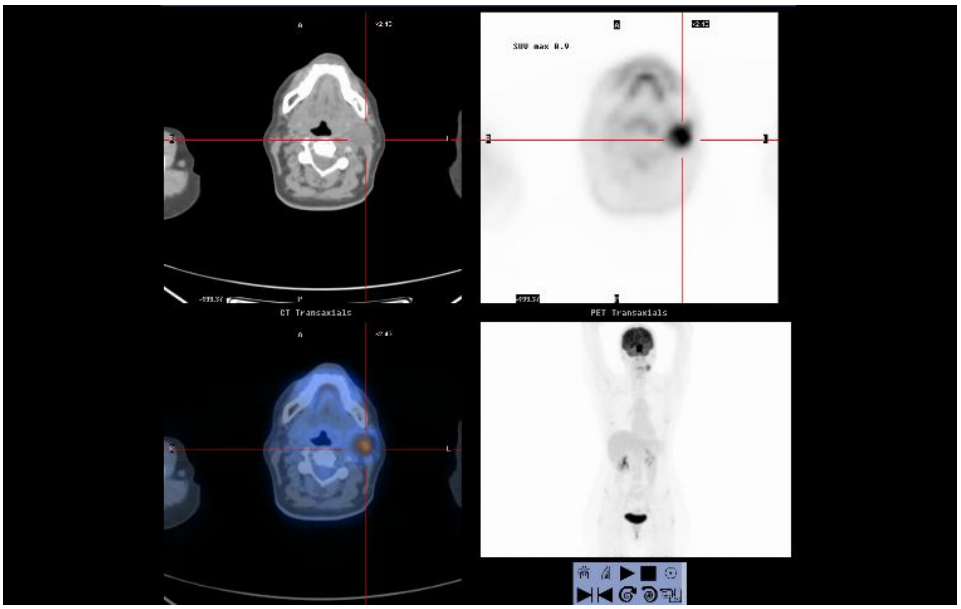

Figure 4

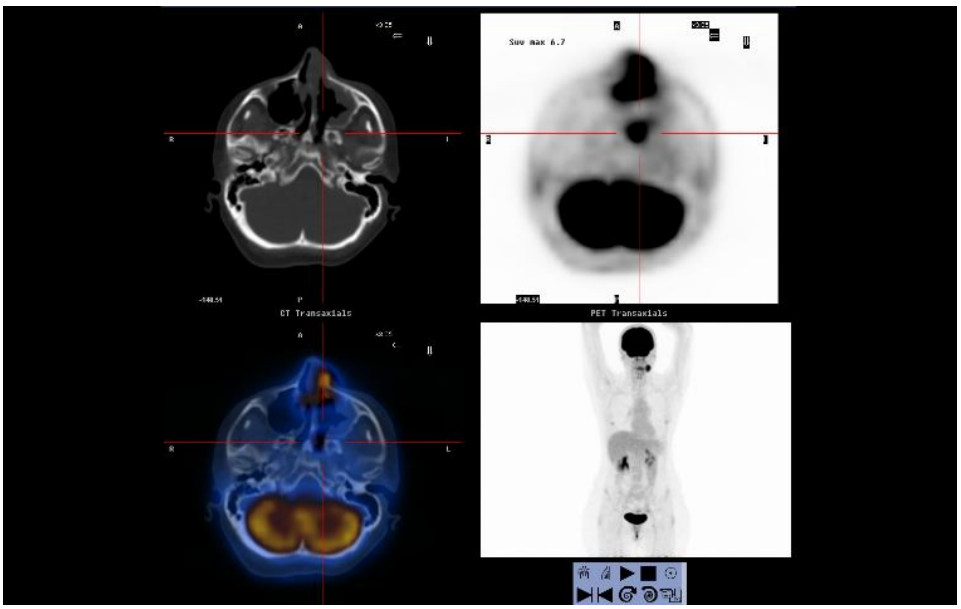

Figure 5

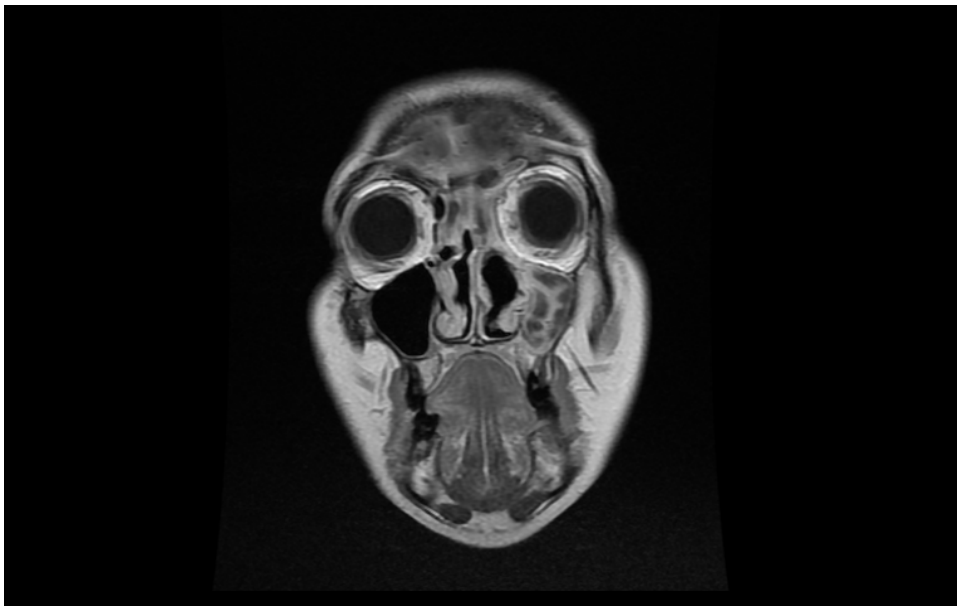

Figure 6