www.ijramr.com

ISSN : 2350-0743

International Journal of Recent Advances in Multidisciplinary Research

Vol. 07, Issue 08, pp. 6153-6156, August, 2020

RESEARCH ARTICLE

A RARE OCCURRENCE OF NEUROENDOCRINE CARCINOMA: CASE REPORT AND REVIEW OF THE LITERATURE

***Camelia NEFTAH, Othman AYOUCHE, Asaad EL BAKKARI, Youssef OMOR and Rachida LATIB**

Radiology Department, National Institute of Oncology, Mohamed V University, Rabat, Morocco

ARTICLE INFO

Article History:

Received 20th May, 2020
Received in revised form
26th June, 2020
Accepted 07th July, 2020
Published online 30th August, 2020

Keywords:

Neuroendocrine;
Carcinoma;
Sino Nasal, CT, MRI.

ABSTRACT

Introduction: Neuroendocrine carcinoma is an aggressive neoplasm with a high recurrence potential. Its location in the Sino nasal tract is considered a rare disease. CT and MR imaging features of these tumors are nonspecific. Paranasal sinus neuroendocrine carcinomas showed expansion and destruction of the sinus. Endoscopic examination is complementary to imaging and mandatory in order to reveal early stage tumour and its extension. Treatment recommendations for this entity vary considerably due largely to a lack of consensus and variable pathological classification. Given the high incidence of distant failure and the chemosensitivity of NEC, neoadjuvant chemotherapy followed by either chemoradiation or surgery and postoperative radiation therapy is a promising strategy. **Case report**: We report the case of a 17-years-old patient, with a history of a non-resolving rhinological burning pain evolving since 1 year. She didn't consult until a blistering lesion filled half of the oral cavity. Oral examination found an proliferative process of the posterior aspect of the oral cavity She received a CT scan and MRI that showed a destruction of the periodontium, with an extensive geographical osteolytic homogeneous mass destroying the left nasal cavity, as well as an infiltration of the ipsilateral orbit. The diagnosis of Sino nasal neuroendocrine carcinoma was suggested histologically after biopsy. After a regimen of etoposide and carboplatine supplemented by palliative radiotherapy no regression was noted. The evolution was characterized by the death of the patient. **Conclusion**: In conclusion, our case suggests that Sino nasal NEC is an exceedingly rare tumor that commonly presents as late-stage disease. Proper histopathologic diagnosis is paramount to dictate appropriate therapy. Poor prognostic factors affecting survival include TNM staging, tumor site, and bony or orbital invasion. Response to systemic therapy may play a greater role in defining the individualized treatment strategy for the management for these patients.

INTRODUCTION

Neuroendocrine carcinoma of the sinonasal tract is an uncommon neoplasm with aggressive clinical behavior with no, racial, or geographic predilection and no known association with smoking or radiation (van der Laan, 2016; Moran, 2007). It has a distinct male predominance with a median age of 53 year ranged between 12-89years (van der Laan, 2016). Poorly differentiated neuroendocrine carcinomas are characterized by rapid and fatal outcome prognosis (Moran, 2007). It's an aggressive lesion with a poor prognosis, frequent local recurrence, and distant metastasis despite multimodality therapy (Moran, 2007). We report a case of a 24years-old female patient with maxillary sinonasal poorly differentiated neuroendocrine carcinoma, Who underwent an etoposide and carboplatine chemotherapy regimen supplemented by palliative radiotherapy no regression was noted. The evolution was characterized by the death of the patient.

***Corresponding author:* Camelia NEFTAH.**
Radiology Department, National institute of oncology, Mohamed V University, Rabat, Morocco.

CASE REPORT

It's a 17 years old patient who presented with rhinological burning pain evolving since 1 year. Physical examination demonstrated the presence of a left jaw mass protruding into the oral cavity as well as homolateral exophthalmia. No palpable lymph nodes were identified. Contrast enhanced - CT showed a heterogeneous left jaw mass destructing the left maxillary bone with an extension to the homolateral oral cavity and temporal fossa. MR showed a heterogeneous hyper intense left jaw mass infiltrating the masseter and medial pterygoid muscles, invading the body of the tongue and the contralateral hemi mandible. Tumor biopsy was in favor of a round cell tumor process. Immuno-histochemical analysis showed a poorly differentiated neuroendocrine carcinoma, (Pancytokeratine+ , Ki67 at 30% , Chromogranine+ , Synaptophysine -). Patient was put on chemotherapy courses of carboplatin etoposide associated with palliative radiotherapy. Follow up CT evaluated for tumor response, which demonstrated a tumor progression. The decision was for to stop the treatment and an orientation for supportive care.
The evolution was characterized by the death of the patient 1 month after.

DISCUSSION

Extra pulmonary neuroendocrine carcinoma represents 4% of all neuroendocrine carcinomas (Ibrahim, 1984). Less than 250 cases of head and neck NEC have been published so far, including 48 cases of NEC in the nasal and paranasal cavities. Primary neuroendocrine carcinomas of the sinonasal tract are rare and represent a histological spectrum of differentiation (Rosenthal, 2004). The tumors most commonly arise in the superior or posterior nasal cavity often extending into the maxillary or ethmoid sinuses. Primary tumors of the maxillary or ethmoid sinuses without nasal involvement account for 45% of cases. Advanced tumors may invade the skull base, orbit or brain. No particular risk factor for this tumor appears to have been identified (van der Laan, 2016).

The most frequent symptoms are the rhinological syndrome (nasal obstruction, rhinorrhea and epistaxis) (Silva *et al*., 1982; Soussi, 1990). and ophthalmic signs (exophthalmos, visual acuity trouble and limitation of eye mobility) (Silva *et al*., 1982; Soussi, 1990). Less frequently, other signs suggesting loco-regional invasion have been reported such as local pain or anosmia. Metastatic cervical nodes have also been described (Silva, 1982).

Computerized tomography (CT) scan and magnetic resonance imaging (MRI) are essential to describe the masse , assess its size and extension, evidence of bone destruction, and infiltration to the orbit or brain(8). Moreover, CT combined MRI can provide more comprehensive information in the diagnosis and therapy. The masse is iso-dense or mild hyper-dense on CT scan, and isointense on T1WI and or mild hyper-intense on T2WI with mild or moderate homogeneous enhancement after the administration of a contrast agent (Campbell, 2009). SNEC in paranasal sinuses shows rare necrosis or hemorrhage on pathology, which is coincidence with the homogeneous signal on T2WI or enhanced T1WI (Hojreh, 2005).

In addition, the signals of this tumor is homogeneous iso dense or mild hyper-dense on CT, which could not be interpreted as hemorrhaging (Unal *et al*., 2006). This shows that the tumor contained neuroendocrine grana and that the neuroendocrine cells may have grown along the ethmoidal cells, which may have resulted in the existence of this mucus in the SNEC. The differential diagnosis of SNEC in paranasal sinuses includes inverted papilloma (IP), squamous cell carcinoma (SCC), adenocarcinoma, adenoid cystic carcinoma (ACC), lymphoma, and olfactory neuroblastoma (ONB). Those tumors have similar radiologic findings such as soft tissue mass, bony destruction, and different patterns of enhancement.

Three therapeutic methods are currently used: surgery, radiotherapy and chemotherapy, usually with cisplatin and etoposide. The treatment of NECs has varied considerably over time. Thus, in the 1980s, surgery followed by radiotherapy was favoured by the authors of the largest study20 and has also been recommended more recently (Smith, 2000). In the late 1990s, the association of chemotherapy and radiotherapy, with or without surgery, produced encouraging results at 14 months and 45 months for neuroblastoma and NECs of the nasal and paranasal cavities (Bhattacharyya, 1997).

Recent series have shown that a combination of surgery radiotherapy and chemotherapy can improve survival over dual or single modality therapy (Fitzek, 2002). Furthermore, it has been suggested that elective treatment of the neck will improve regional control (Lin, 2010). Surgery supplemented with postoperative radiotherapy or concomitant chemo radiotherapyis accepted as the primary treatment for localized disease. For patients with systemic disease, palliative chemotherapy or best supportive care remain appropriate options (Bell *et al*., 2016). Lymph node treatment with dissection and/or radiotherapy does not seem justified in the absence of a palpable node. Cerebral radiotherapy has been reported in only one case of a nasal cavity tumor extending to the maxillary sinus and orbit (Koss, 1972).

There is considerable controversy over the role of radiation in the treatment of patients with NEC. A convincing argument, based on a retrospective 40-year review, for the addition of radiotherapy was made in a report of 49 patients from the Mayo Clinic (Foote, 1993). The mainstay of treatment was surgery, and 25 patients also received radiotherapy. Of 22 patients who underwent macroscopic total resection alone, 13 patients developed local recurrence (59%). Of 16 patients who underwent macroscopic total resection plus postoperative radiotherapy, only 2 patients developed local recurrence. Radiotherapy appeared to have had a beneficial effect, because not only was the resulting local control rate much higher, but the patients who received postoperative radiotherapy were selected for higher grade tumors ((Foote, 1993). Doses of conventional radiation to the primary site have ranged from 50 Gy to 67 Gy (17, 18). The individual treatment doses reported in these studies differed by 10–15 Gy from patient to patient.

Fitzek and al treated patients with ENB and NEC with 2 courses of cisplatin and etoposide followed by high-dose proton-photon radiotherapy to 69.2 cobalt–Gray equivalents (CGE) using 1.6 –1.8 CGE per fraction twice daily in a concomitant boost schedule. Two further courses of chemotherapy were given to responders (Fitzek, 2002). The 5-year survival rate was 74%. The 5-year local control rate of initial treatment was 88% (Fitzek, 2002). Non-pulmonary NECs are reported to be associated with a survival rate of up to 13 per cent at five years. However, the prognosis in cases of head and neck NEC is very poor because of the high rate of metastases observed (Galanis, 1997) .Follow-up data have shown a survival rate of 13months,a local recurrence rate of 45% and a distant metastasis rate of 35%. Common sites of metastasis include cervical lymph nodes, lung, liver, and bone and bone marrow, particularly the vertebrae.

In a publication from MD Anderson on a series of sinonasal small cell neuroendocrine carcinoma spanning from 1990 to 2004, approximately 50% of the cohort received surgery as the primary treatment modality, whereas approximately one-third received chemo radiotherapy. The 5-year overall survival (OS), disease specific survival, and disease-free survival (DFS) rates were 66.9%, 78.5%, and 43.8%, respectively. The incidence of local, regional, and distant failure was 21%, 25%, and 18%, respectively, better than generally reported. Predictors of poor outcome were patients with foveal or orbital involvement and tumors originating outside of the nasal cavity. A complete response to neoadjuvant chemotherapy correlated with improved survival at 3 years. Given the high incidence of distant failure and the chemosensitivity of small cell neuroendocrine carcinoma, neoadjuvant chemotherapy

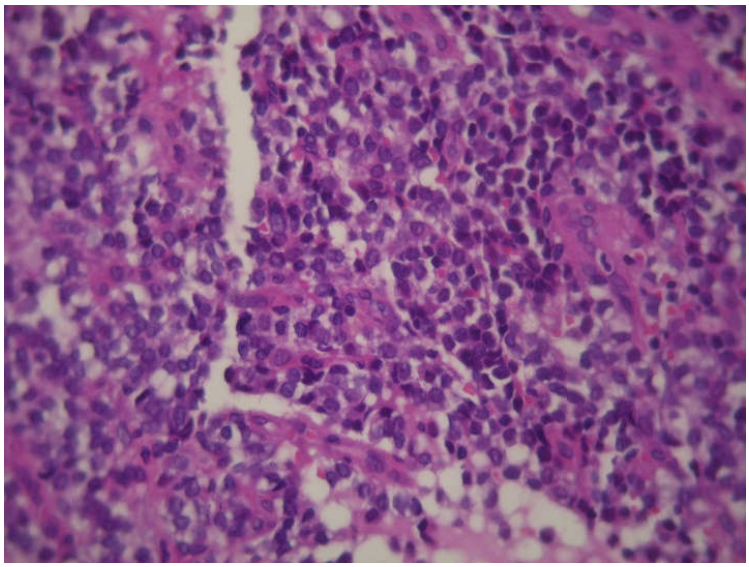

Figure 1. Microphotograph (x 100) showing acellular proliferation made of layers of small granular chromatin cells with nuclear molding.

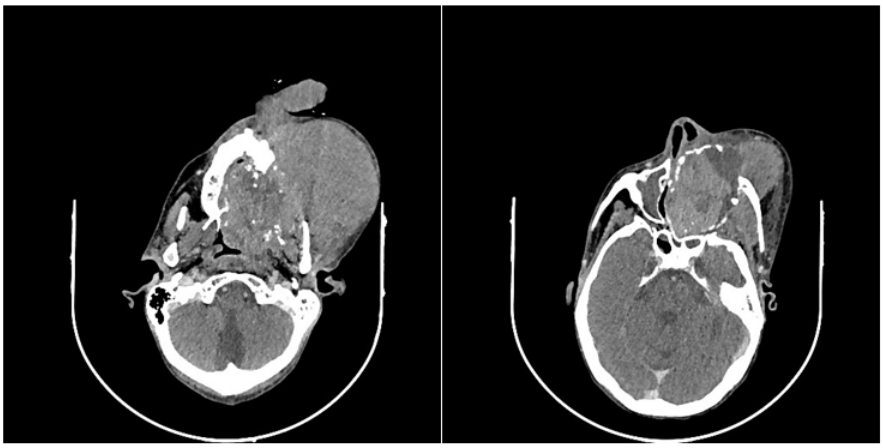

Figure 2. Axial viewCT angiography: Heterogeneous left jaw mass destructing the left maxillary bone with an extension to the homolateral oral cavity and temporal fossa

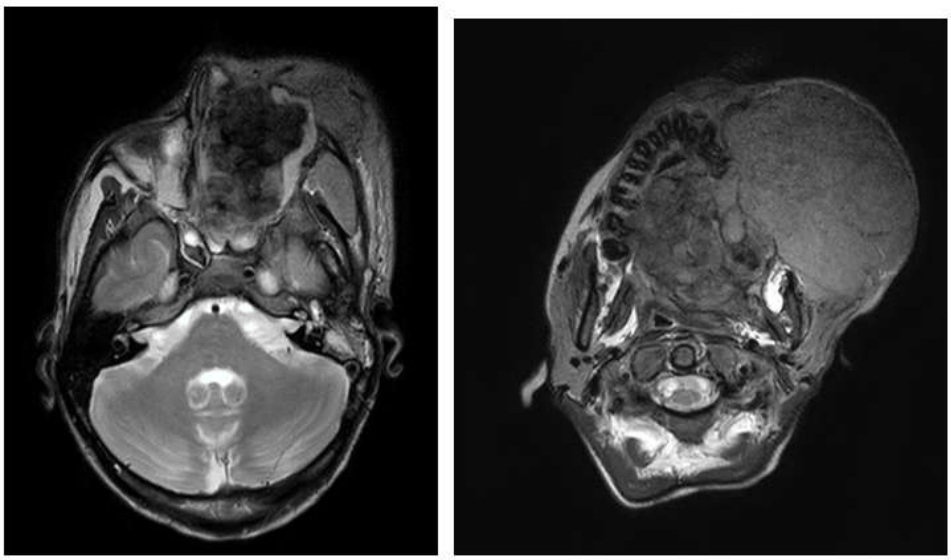

Figure 3. Axial MRI T2 sequence: heterogeneous hyper intense left jaw mass infiltrating the masseter and medial pterygoid muscles, invading the body of the tongue and the contra lateral hemi mandible

followed by either chemo radiation or surgery and postoperative radiotherapy shows promise for ideal management (Bell, 2016).

Only a few cases of large cell neuroendocrine carcinoma have been reported in the sinonasal region and nasopharynx (Kao, 2012). Outcome data are limited but it is considered that they have the same poor prognosis as small cell neuroendocrine carcinoma. Aggressive trimodality therapy seems to be the most effective approach, although survival remains poor (Bell, 2016).

Conclusion

In summary, sinonasal (NEC) is an exceedingly rare tumor that commonly presents as late-stage dis ease. Proper histopathologic diagnosis is paramount to dictate appropriate therapy. Poor prognostic factors affecting survival include TNM staging, tumor site, and bony or orbital invasion. Response to systemic therapy may play a greater role in defining the individualized treatment strategy for the management for these patients. In our case, a carboplatine-etoposide chemotherapy regimen with radiotherapywas prompted for the palliative care of the patient.

REFERENCES

van der Laan TP, Iepsma R, Witjes MJ, van der Laan BF, Plaat BE, Halmos GB. Meta-analysis of 701 published cases of sinonasal neuroendocrine carcinoma: The importance of differentiation grade in determining treatment strategy. Oral oncology. 2016;63:1-9.

Moran CA, Suster S. Neuroendocrine carcinomas (carcinoid, atypical carcinoid, small cell carcinoma, and large cell neuroendocrine carcinoma): current concepts. Hematology/oncology clinics of North America. 2007;21(3):395-407.

Eschelman DJ, Gardiner Jr GA, Deely DM. Osteochondroma: an unusual cause of vascular disease in young adults. Journal of Vascular and Interventional Radiology. 1995;6(4):605-13.

Ibrahim NB, Briggs JC, Corbishley CM. Extrapulmonary oat cell carcinoma. Cancer. 1984;54(8):1645-61.

Rosenthal DI, Barker Jr JL, El-Naggar AK, Glisson BS, Kies MS, Diaz Jr EM, *et al*. Sinonasal malignancies with neuroendocrine differentiation: patterns of failure according to histologic phenotype. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2004;101(11):2567-73.

Silva EG, Butler JJ, MacKay B, Goepfert H. Neuroblastomas and neuroendocrine carcinomas of the nasal cavity. A proposed new classification. Cancer. 1982;50(11):2388-405.

Soussi A, Benghiat A, Holgate C, Majumdar B. Neuro-endocrine tumours of the head and neck. The Journal of Laryngology & Otology. 1990;104(6):504-7.

Campbell PD, Zinreich SJ, Aygun N. Imaging of the paranasal sinuses and in-office CT. Otolaryngologic Clinics of North America. 2009;42(5):753-64.

Hojreh A, Czerny C, Kainberger F. Dose classification scheme for computed tomography of the paranasal sinuses. European journal of radiology. 2005;56(1):31-7.

Unal B, Bademci G, Bilgili YK, Batay F, Avci E. Risky anatomic variations of sphenoid sinus for surgery. Surgical and Radiologic Anatomy. 2006;28(2):195-201.

Smith SR, Som P, Fahmy A, Lawson W, Sacks S, Brandwein M. A clinicopathological study of sinonasal neuroendocrine carcinoma and sinonasal undifferentiated carcinoma. The Laryngoscope. 2000;110(10):1617-22.

Bhattacharyya N, Thornton AF, Joseph MP, Goodman ML, Amrein PC. Successful treatment of esthesioneuroblastoma and neuroendocrine carcinoma with combined chemotherapy and proton radiation: results in 9 cases. Archives of Otolaryngology–Head & Neck Surgery. 1997;123(1):34-40.

Fitzek MM, Thornton AF, Varvares M, Ancukiewicz M, Mcintyre J, Adams J, *et al*. Neuroendocrine tumors of the sinonasal tract: Results of a prospective study incorporating chemotherapy, surgery, and combined proton-photon radiotherapy. Cancer. 2002;94(10):2623-34.

Lin EM, Sparano A, Spalding A, Eisbruch A, Worden FP, Heth J, *et al*. Sinonasal undifferentiated carcinoma: a 13-year experience at a single institution. Skull Base. 2010;20(02):061-7.

Bell D, Hanna EY, Weber RS, DeMonte F, Triantafyllou A, Lewis Jr JS, *et al*. Neuroendocrine neoplasms of the sinonasal region. Head & neck. 2016;38(S1):E2259-E66.

Koss LG, Spiro RH, Hajdu S. Small cell (oat cell) carcinoma of minor salivary gland origin. Cancer. 1972;30(3):737-41.

Foote RL, Morita A, Ebersold MJ, Olsen KD, Lewis JE, Quast LM, *et al.* Esthesioneuroblastoma: the role of adjuvant radiation therapy. International Journal of Radiation Oncology* Biology* Physics. 1993;27(4):835-42.

Guedea F, Van Limbergen E, Van den Bogaert W. High dose level radiation therapy for local tumour control in esthesioneuroblastoma. European Journal of Cancer. 1994;30(12):1757-60.

Galanis E, Frytak S, Lloyd RV. Extrapulmonary small cell carcinoma. Cancer: Interdisciplinary International Journal of the American Cancer Society. 1997;79(9):1729-36.

Kao H-L, Chang W-C, Li W-Y, Li AC-H, Li AF-Y. Head and neck large cell neuroendocrine carcinoma should be separated from atypical carcinoid on the basis of different clinical features, overall survival, and pathogenesis. The American journal of surgical pathology. 2012;36(2):185-92.

****