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Case Report

Primary Neuroendocrine Carcinoma of Sinonasal Tract Infiltrating Maxilla

Kanwal Zahra, Shaista Khurshid, Ahmareen Khalid and Ashok Kumar Tanwani
Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad

Abstract

Objective: Report an unusual case of primary neuroendocrine carcinoma of sinonasal tract involving maxilla.

Background: Neuroendocrine tumors are rare in head and neck region and pose a challenge in regard of pathologic diagnosis. Neuroendocrine carcinoma of sinonasal tract is extremely uncommon tumor and despite aggressive management strategies it carries a poor prognosis with a high risk of local recurrence or distant metastases. Very few cases of sinonasal neuroendocrine carcinoma have been reported till date.

Case Presentation: A 35year female resident of Rawalpindi presented with slowly growing expansile swelling of left maxilla since two and a half years. Initial biopsy was labeled as fibrous dysplasia. We received a maxillectomy specimen. After reviewing the morphology on H&E slides and with help of immunohistochemistry she was diagnosed with sinonasal neuroendocrin carcinoma (moderately differentiated) infiltrating maxilla. Patient is now on palliative chemoradiotherapy.

Conclusion: Neuroendocrine carcinoma is a rare entity in head and neck region especially in sinonasal area. It is important to recognize their morphology and pattern of growth because they cannot be mistaken with more common tumors of this area e.g squamous cell carcinoma (poorly differentiated), sinonasal undifferentiated carcinoma (SNUC) and olfactory neuroblastoma.

Key words: Neuroendocrine carcinoma, Olfactory Neuroblastoma, Squamous cell carcinoma, Sinonasal Undifferentiated Carcinoma (SNUC).

Introduction

Squamous cell carcinoma is the most common tumor in sinonasal region followed by adenocarcinoma, sinonasal undifferentiated carcinoma, malignant melanoma, and olfactory neuroblastoma.[1] Primary neuroendocrine carcinomas are rare in this region and represent a histological spectrum of differentiation. According to 2005 WHO classification of head and neck tumors they are classified as typical carcinoid, atypical carcinoid, small cell carcinoma neuroendocrine type and combined small cell with non-small cell carcinoma type. Typical carcinoid has most favorable prognosis followed by other three.[2, 3] Due to disease rarity, lack of sharp histological distinction and close proximity to vital structures standardize treatment criteria's are yet to be evolved.[4] The purpose of this report is to analyze available information regarding this uncommon malignancy, to recognize their morphology and to avoid the confusion with more common tumors of this area.

Contribution of Authors: Dr. Kanwal Zahra conceived the idea, study designed, examined the slides, wrote the manuscript. Dr. Shaista Khurshid reviewed the slides, Dr. Ahmareen Khalid diagnosed the case, helped in writing the manuscript and Dr. Ashok Kumar helped as Head of the Department.

Correspondence: Dr. Kanwal Zahra
Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad

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Case Presentation

A 35 yrs female resident of Rawalpindi presented with slowly growing expansile swelling of left maxilla since two and a half years. On examination, she had a hard, painless 4.5x3 cm swelling in left maxillary area near left ala of nose extending downwards towards upper jaw. Computed tomography (CT) revealed soft-tissue mass occupying the entire left maxillary sinus extending into left nasal cavity (Figure. 1)

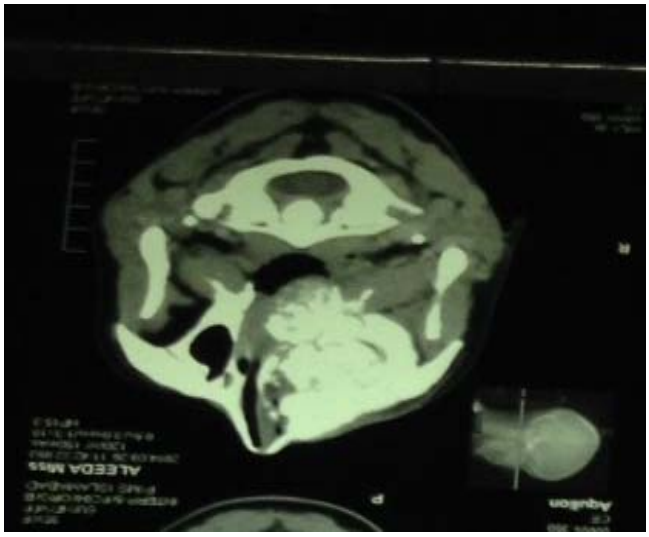

Figure 1: CT scan of head and neck showing a soft tissue mass of left maxillary sinus, extending to left nasal cavity and involving the left maxilla.

An incisional biopsy of the mass was labeled as fibrous dysplasia from some other institute. We received her maxillectomy specimen. Microscopic examination revealed a malignant neoplasm infiltrating the maxillary bone in the form of nests of small round blue cells. These cells had round to oval nuclei with salt and pepper chromatin and scant cytoplasm. Frequent mitotic figures are also seen with a mitotic count of 8-9 mitoses/10HPF. It was reported as poorly differentiated malignant neoplasm with differentials of neuroendocrine tumor, poorly differentiated squamous cell carcinoma, sinonasal undifferentiated carcinoma (SNUC) and olfactory neuroblastoma. (Figure. 2)

A immunohistochemical panel of pan CK, LCA, NSE, Synaptophysin, S-100, TTF1 was applied. A cytoplasmic (dot like positivity) was noted for Cytokeratin along with cytoplasmic positivity for Neuron specific enolase (NSE) and membranous positivity for Synaptophysin (Figure. 3). Negative staining was noted for S-100, TTF1 and LCA ruling out the possibility of neuroblastoma, metastatic neuroendocrine carcinoma from lung and lymphoma. Dot like cytoplasmic positivity of CK and positive staining for two neuroendocrine markers ruled out squamus cell carcinoma and sinonasal undifferentiated carcinoma (SNUC). Based on morphology and immunohistochemistry a diagnosis of primary sinonasal neuroendocrine carcinoma (moderately differentiated) was made.

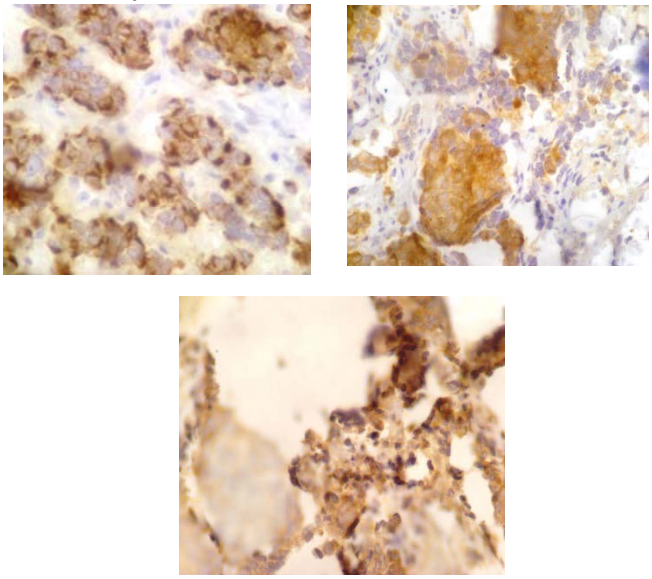

Figure. 3: Immunohistochemistry: Dot like positivity for CK along with cytoplasmic and membranous positivity for NSE and Synaptophysin respectively.

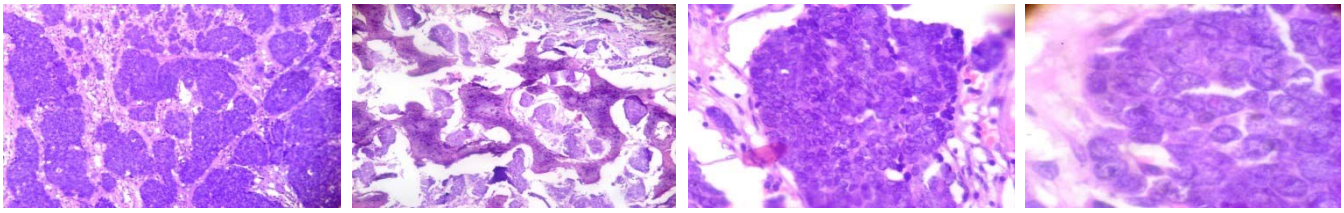

Figure. 2. Light microscopy: Nests of round blue cells with salt and pepper chromatin infiltrating maxilla

Discussion

Neuroendocrine tumors are broad spectrum neoplasms. Their cell of origin is not clearly known. Some think that they are derived from endocrine cells of the dispersed neuroendocrine system, according to others they arise from pluripotential stem cells that are capable of both epithelial and endocrine differentiation. So they can be classified in to neural or epithelial types. Paragangliomas belong to the neural group and neuroendocrine carcinomas belong to the epithelial category.[5, 6]

Sinonasal neuroendocrine carcinoma of nasal cavity was first identified as a separate entity by Silva et al. in 1982[7]. Limited number of cases has been reported till date. The reported mean age of patients is between 5th and 6th decades and it is slightly more common in males.[8, 9, 10] Unlike squamous cell carcinoma, which is seen most commonly in maxillary sinuses, neuroendocrine carcinoma is most common in ethmoid sinuses.[11]

The clinical features of sinonasal neuroendocrine carcinoma are nonspecific and similar to those of other sinonasal tumors. Common presentations include nasal obstruction, epistaxis, and facial mass along with pain. Majority have advanced disease at presentation with extensive involvement of skull, orbit, and brain. They may also be recurrent and locally destructive.[11]

Hisological they are classified in to well-differentiated (typical carcinoid), moderately differentiated (atypical carcinoids), and poorly differentiated (small and non-small cell types). Well differentiated type usually presents with a variety of histological patterns including organoid, trabecular, pseudoglandular, rosettes, cribriform, solid and single-filing with minimum cellular pleomorphosm, scanty mitotic figures and no necrosis. Moderately differentiated neuroendocrine carcinomas (atypical carcinoids) generally retain the organized cellular patterns in the form of nests or cords of tumor cells but with cellular pleomorphism, increased mitoses and focal areas of necrosis. Poorly differentiated carcinoma lacks any differentiation with brisk mitotic activity and multiple areas of necrosis. Lymph-vascular, perineural, and soft tissue invasion is usually seen.[10] Present case showed a nesting pattern of tumor cells infiltrating the maxillary bone. It was of intermediate grade with a mitotic count of <10/10HPF and focal areas of necrosis. No lymphovascular invasion was seen.

Sinonasal neuroendocrine carcinoma has to be differentiated from other neoplasms involving nasal cavity and paranasal sinuses such as squamous cell carcinoma, olfactory neuroblastoma, sinonasal undifferentiated carcinoma (SNUC), lymphoma and melanoma. Conventional microscopy is usually insufficient for definite diagnosis and immunohistochemistry studies are invariably needed. They are usually strongly positive for Synaptophysin, Neuron specific enolase (NSE) and CD 56, show a weak reaction for Chromogranins and CAM5.2 with a dot like positivity for AE1:AE3[12, 13]. The present case showed a positive staining for both Neuron specific enolase (NSE) and Synaptophysin along with dot like positivity for Cytokeratin favouring the diagnosis of neuroendocrine carcinoma.

Ideal treatment strategies for this entity have yet to be evolved. Unlike the neuroendocrine tumors of other sites which are treated with surgery with and without chemotherapy, problem in this area is related to rarity, lack of specific histological distinction and closeness to vital structures. Some recommendations have been developed from retrospective data suggesting surgery or radiotherapy may provide enduring control. Chemotherapy can be used for metastatic disease or to look for the outcome of the disease.[4]

Conclusion

Sinonasal Neuroendocrine carcinoma of head and neck is a rare malignancy, the clinical behavior of which is not well known. It is important to recognize their morphology due to difference in management and prognosis with other common tumors of this area.

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