Case Report
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NEUROENDOCRINE CARCINOMA AS SINONASAL MALIGNANCY:

A Clinicopathological challenge and its varied treatment modalities

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Abstract:

Neuroendocrine neoplasms are defined as epithelial neoplasms with predominant neuroendocrine differentiation. Extremely rare site for neuroendocrine carcinoma are nasal cavity and paranasal sinuses and are aggressive neoplasm with a high recurrence rate and a tendency to metastasize.

A 19-year malepresented to the department of Otorhinolaryngology with left nasal obstruction, persistent headache for nine months and on and off bleeding from left nasal cavity for 2 months. Onexamination of the nasal cavity, a gross deviation of nasal septum with a red, friable, gelatinous, polypoidal mass with a tendency to bleed was seen in the left nasal cavity.The patient underwent endoscopic excision of mass under GA.Specimen was sent for histopathological examination which exhibited the properties of Neuro-endocrine carcinoma.

Sinonasal NEC is an extremely rare malignancy. CT scan with intravenous contrast is the most effectual early imaging study, additionally MRI will further make a fine description of the tumour extension. Furthermore,Immunohistochemistry is an important tool that can be valuable in reaching a diagnosis. There is no clear recommendation regarding the treatment of the sinonasal neuroendocrine carcinoma, but the multimodal approach with proper counselling of patient is favoured and generally accepted.

Key Words: Neuroendocrine, Paranasal sinus, Epistaxis, Carcinoma

Introduction:

In spite of the fact that the sinonasal compartment is highly vulnerable to carcinogenic substances, malignancies springing up in this region are unusual, putting together less than 5% of all head and neck cancers(1a). Neuroendocrine neoplasms are defined as epithelial neoplasms with predominant neuroendocrine differentiation. They can become apparent in almost every organ of the body even though they are most commonly found in the gastrointestinal tract and respiratory system. Extremely rare site for neuroendocrine carcinoma are nasal cavity and paranasal sinuses and are aggressive neoplasm with a high recurrence rate and a tendency to metastasize to other sites via the lymphatic system and blood stream (1,2). Head and neck sinonasal endocrine carcinoma have been described only since 1965(3).In addition, Neuroendocrine neoplasms are classified into well-differentiated (typical), moderately differentiated (atypical carcinoids), and poorly differentiated (small and non-small cell

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types).Well and, to a lesser extent, moderately differentiated neuroendocrine carcinomas sustain better prognosis with low metastatic rates and better survival [4-7], while poorly differentiated neuroendocrine carcinomas are characterized by rapid and fatal outcome prognosis. Very few cases of paranasal sinus neuroendocrine carcinoma have been reported till date. Treatment recommendations for this entity vary considerably largely due to a deficit of consensus and variable pathological classification hence, management of patients with these tumours remain unaddressed (8). Concomitant chemotherapy and radiotherapy appears to aid in definitive reduction in tumour burden. Further research is required to compare the efficacy of concurrent chemoradiation, primary chemotherapy or surgery as the initial approach for treatment of sinonasal Neuroendocrine tumors (NETs).

Case Presentation:

A 19-year male initially presented to the department of Otorhinolaryngology with left nasal obstruction, persistent headache for nine months and on and off bleeding from left nasal cavity for 2 months. Patient had a history of recurrent URTIs, mostly in winters and complained of alteration in smelling from bilateral nasal cavity by then. Patient also had a history of past surgery i.e. reconstruction of socket left eye under GA on 05/09/2006 in department of ophthalmology, King George Medical University, Lucknow. There was no history of nasal discharge, post nasal discharge, facial pain, facial swelling, diplopia, change in vision, aural fullness, fever, trauma, diabetes mellitus, hypertension, tuberculosis. After thorough clinical examination, in right eye his visual acuity was preserved. Upon examination of the nasal cavity using rigid endoscopy, the patient was found to have a gross deviation of nasal septum with a red, friable, gelatinous, polypoidal mass with a tendency to bleed was seen in the left nasal cavity. On physical examination, there were no palpable cervical lymph nodes .A computed tomography (CT) paranasal sinus (PNS) revealed gross deviation of nasal septum with turbinate hypertrophy in nasal cavity on right side. Mild mucosal thickening noted in left maxillary antrum and ethmoidal air cells on left side. Polypoidal mildly enhancing soft tissue lesion is noted in posterior part of left half of nasal cavity extending posteriorly and blocking left posterior choana and extending inferiorly upto hard palate. No obvious bony destruction or infiltration seen, suggestive of inflammatory polyp. (figure 1)

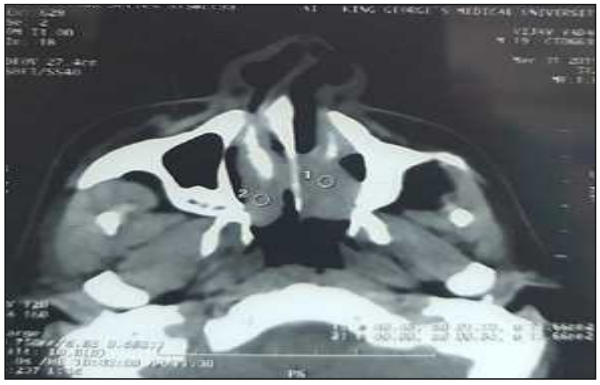

Figure 1: CT scan on presentation.

Patient underwent endoscopic excision of mass under general anaesthesia on 19/04/2019. Multiple tissue specimens were sent for histological examination. The specimens were fixed in formalin. Patient was lost to follow up for two months, when he reported with histopathological reports and symptoms recurrence.The final histologic evaluation of the excised biopsy specimens yielded a diagnosis of Neuroendocrinecarcinoma. On microscopy section shows multiple fragmented pieces of fibrocollagenous tissue infiltrated by a tumour disposed in sheets and nests. The tumour cells have high nucleo-cytoplasmic ratio, with stippled chromatin, inconspicuous nucleoli and moderate amounts of cytoplasm. Frequent mitosis seen.Foci of necrosis and haemorrhage are evident. On Immunohistochemistry: Pan-CK: positive, synaptophysin: positive, CD-56: weak positive, Ki-67 proliferation index: 70%, with the differential diagnosis lying at a point somewhere between poorly differentiated large-cell NEC and high-grade olfactory neuroblastoma.

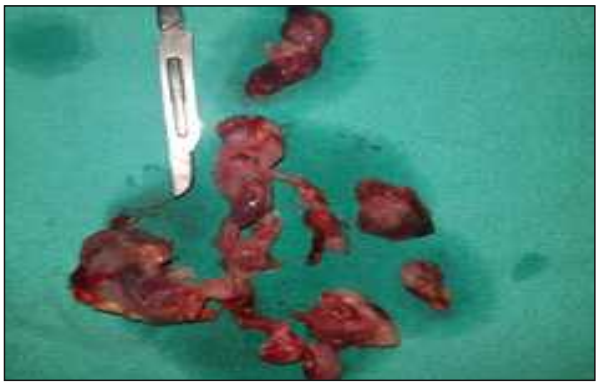

Figure 2: angiomatous fragile polypoidal reddish mass (intra-op)

Patient lost to follow up and presented with signs of recurrence after two months duration.Patient developed bilateral nasal obstruction with multiple episodes of epistaxis (2-3 drops/episodes) with dull headaches. Computed tomography (CT) of PNS revealed enhancing soft tissue in nasal cavity and ethmoidal air cells on both sides with cortical thinning and erosion of adjacent bones, erosion of cribriform plate with extension of soft tissue in basifrontal region probably of Neoplastic etiology. Following this patient was referred to department of radiotherapy for the further management.

Discussion:

Sinonasal NEC is an extremely rare malignancy, the clinical behaviour of which is not well known with no gender, geographical or racial predilection and no known association with smoking or radiation. The age range is from 26 to 77 years with a mean of 49 years(8a). Starting symptoms are absolute, in particular nasal obstruction, rhinorrhoea, persistent headache, hyposmia, epistaxis, , facial pressure and patients are often initially treated for benign conditions, slowing up diagnosis. Other significant clinical signs relate to an extensive lesion that takes in multiple sites of the sinonasal compartment and may include epiphora, diplopia, proptosis, facial pain, facial asymmetry, altered visual acuity. In our case , he presented with persistent headache , hyposmia , epistaxis and nasal obstruction. No signs of Ophthalmic manifestations.

The paucity of published literature on this subject had been compounded by the fact that previous studies of sinonasal NEC have included a subset of broad spectrum of neuroectodermal tumours, including olfactory neuroblastoma, small cell neuroendocrine carcinoma and sinonasal undifferentiated carcinoma. Unlike other types of carcinoma, such as squamous cell carcinoma, which are seen most commonly in maxillary sinuses, paranasal sinus neuroendocrine carcinoma is most common in ethmoid sinuses (9-12).Radiological findings reveal an aggressive tissue mass that erodes and invades the adjacent bone rather than remodelling it, and can extend to nearby structures, as the orbit and cranium (13). CT scan with intravenous contrast is the most effectual early imaging study that aids characterizing the lesion, detailing tumour vascularity, relevant skull base anatomy, bony destruction and the degree of invasiveness. MRI will further make a fine description of the tumour extension into the skull base, cavernous sinus and orbit, more accurately (14). Even more, Clinical presentation is similar to other malignancies arising in the sinonasal tract, thus diagnosis is based on histopathological analysis (15). Immunohistochemistry is an important tool that can be valuable in reaching a diagnosis. Although the case presented above lacked expression of S-100. Other neuroendocrine carcinomas should also be excluded, such as: paragangliomas, which are S-100 positive.

A staging system for olfactory neuroblastomas proposed by Kadish et al(16) is the most frequent staging system applied to NETs. In addition, the American Joint Committee on Cancer Staging system of nasal cavity and paranasal sinus tumours (listed below) is also used for classification. (17)

- Group A: tumour limited to nasal cavity.
- Group B: tumour limited to nasal cavity and

paranasal sinuses.

- Group C: tumour extends beyond nasal cavity and paranasal sinuses.
- Group D (proposed by Chao et al in 2001): cervical nodal metastases.

According to AJCC, this patient possessed a group B tumour initially, which progressed to group C due to loss of follow up and hence delayed onset of treatment.

Owing to their rarity, there is limited data regarding the management of sinonasal NETs. Some recommendations have been developed from retrospective archival data. Surgery, radiotherapy, and chemotherapy alone or in combination have been used in the past for the patients with NEC of the paranasal sinuses and nasal cavity with 5-year survival rate of 64% (18) ; it has been associated with a high local recurrence rate. Fitzeket al.(19) reported good results on patients treated with two initial cycles of cisplatin and etoposide. Responders underwent photon/proton radiotherapy followed by two cycles of etoposide and cisplatin. Nonresponders underwent surgical resection followed by postoperative photon/proton radiation. The reported 5-year survival rate was of 74%.

Conclusions:

Sinonasal neuroendocrine carcinoma is a quarrelsome tumour with a high propensity for local invasion, as well as regional and distant metastases. Because most patients present in advanced stages, the prognosis is poor. Due to the infrequency of this pathology, overlapping features with other entities and histological heterogenicity, a delineation of this particular histological type within the group of neuroendocrine neoplasms remains to be determined. There is no recommendation regarding the treatment of the sinonasal neuroendocrine carcinoma, but the multimodal approach is favoured and generally accepted. The patient in the current study also received a multimodal treatment in the form of surgery followed by adjuvant radiotherapy.

Conflict Of Interests:

The authors declare that they have no conflict of interests.

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Consent:

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Authors' Contributions:

All authors were involved in the design, interpretation and review of the study. All authors read and approved the final manuscript.

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