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### Clinico- histopathological study of sinonasal malignant tumours- A 5 years experience at a tertiary cancer institute

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#### Abstract

Sinonasal malignancies (SNM) are rare (0.2 -0.8 %) but aggressive tumours. These tumors are usually diagnosed at an advance stage, as symptoms are nonspecific and mimic common ailments. The complex and difficult-to-access anatomy of the paranasal sinuses, its intimate relation with the orbit and brain, and the presence of multiple natural pathways promoting early tumour-spread add up to the practical challenges faced by oncologist. This retrospective study was done to study the spectrum of different sinonasal malignancies, their clinical presentation and histo-pathological characteristics in patients presenting in our institute in last 5 years.

**Result:** In our study of 81 patients (median age of 51+/-12 years, M:F = 1.6: 1) the commonest presenting symptoms were blood stained nasal discharge (85%) and unilateral nose block (71%). Commonest primary site was Maxillary sinus (52%). Squamous cell carcinoma was the commonest malignancy (40%). Small round cell tumors (SRCT) comprised a significant 34% of outpatients (n=28). Immunohistochemical evaluation of these SRCTs derived the final diagnosis as SNUC (n=8), Lymphoma (n=6), PDSCC (n=4) and Melanoma (n=3) among others.

**Conclusion:** Sinonasal malignant tumours are aggressive in nature. Immunohistochemistry plays an important role in proper histopathological diagnosis and further treatment planning. However, further prospective studies are required to understand the spectrum and clinical behaviour of these tumours. **Keywords**: Sinonasal tumour, undifferentiated carcinoma, Lymphoma, Small round cell tumours, Immunohistochemistry.

#### Introduction

Sinonasal malignancies (SNM) are rare but aggressive tumours. They account for 0.2 - 0.8 % overall and nearly 3% of all head & neck cancers.<sup>(1)</sup> These are a heterogenous group of tumours originating from both epithelial and

mesodermal cell lines. Symptoms of early Sinonasal malignancies are usually nonspecific and mimics common benign diseases e.g. sinusitis, thus are frequently neglected by the patients. Because of the rarity, clinicians are less suspicious about their possibility. The complex

and difficult-to-access anatomy of the paranasal sinuses (PNS), its intimate relation with the orbit and brain, and the presence of multiple natural pathways promoting early tumour spread add up to the practical challenges faced by oncologist. As a result these tumours are usually diagnosed at an advanced stage further worsening their prognosis. Refocusing of attention on sinonasal malignancies is required because of two reasons:- 1)The lack of evidence based internationally accepted an treatment protocol different sinonasal for 2) malignacies. Prognosis/outcome of SN malignancies has remained unchanged despite of recent developments e.g. Image guided endonasal & skull base surgeries, robot assisted procedures and Image modulated/Image guided radiotherapy. These prompt the need to expand our understanding about the tumour-behavior of these rare malignancies by focusing more studies on their clinical and histopathological characteristics. This retrospective study was done to reveal the spectrum of different sinonasal malignancies, their clinical presentation and histopathological characteristics in patients presenting in our institute in the last 5 years.

### **Materials and Methods**

The hospital records was retrospectively reviewed to shortlist all patients who were treated for sinonasal malignancy in the department of Head & Neck oncology; Dr B Borooah Cancer Institute for the period from 2013 to 2017. After routine clinical and haematological evaluation, a Computed tomography (CT scan) of the nose and PNS was done in all patients. Magnetic Resonance Imaging (MRI) scan was used wherever indicated. Immunohistochemical (IHC) evaluation using relevant antibody panel was done wherever warranted by Histopathological examination (HPE) findings.

#### **Exclusion criteria**

- 1. Patients diagnosed with a nasopharyngeal carcinoma with extension to PNS.
- 2. Patients having synchronous or 2<sup>nd</sup> primary other than nose and PNS
- 3. Previously treated
- 4. Patients who have defaulted from the advised treatment.
  - 81 patients were included in the study.

#### Results

In our study of 81 patients, 50 were males and remaining were females (M:F = 1.6: 1). Age of the patients ranged from 3 to 90 years (median = 51+/-12 years). The highest incidence was seen in  $5^{th}$  and  $6^{th}$  decade (53%). 83% of patients presented with blood stained nasal discharge followed by unilateral nose block (73%), headache (59%), facial swelling/ deformity (47%) and facial numbness (44%). Clinical symptoms and their association with different histological subtypes are presented in Table 1 and 2.

Symptoms	Frequency (n)	Percentage (%)
Epistaxis	67	83
Unilateral nose block	59	73
Headache	48	59
Facial swelling	38	47
Facial numbness	36	44
Hyposmia/ Anosmia	23	28
Visual disturbance	15	19

Table1: Clinical	symptoms a	at presentation.
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Table 2: Symptoms	based on	different	histological	subtypes of	of SNM
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SYMPTOMS	SCC	ACC	SNUC	LYMPHOMA	EWINGS/PNET	MISC	TOTAL
Epistaxis	30	9	6	4	3	15	67
Unilateral nose block	26	8	6	3	2	14	59
Headache	23	7	5	3	2	8	48
Facial swelling	19	5	2	3	2	8	38
Facial numbness	23	3	2	2	2	7	36
Hyposmia/ Anosmia	9	2	4	1	1	6	23
Visual distrubance	7	2	2	-	1	3	15
SCC- Squamous call acrainame. ACC- Adapaid quatic acrainame. DNET- Drimitiva Nauroacta darmal Tumor							

SCC= Squamous cell carcinoma, ACC= Adenoid cystic carcinoma, PNET= Primitive Neuroectodermal Tumor SNUC= Sinonasal Undifferentiated Carcinoma

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Maxillary sinus was the site most frequently involved by the primary tumour (52%), followed by ethmoid sinus and nasal cavity. 23 patients (28%) had tumour involving multiple sites. Extension of the primary tumour into the orbit and brain was found in 18 patients.

Squamous cell carcinoma (SCC) was the most common histological variant found in 34 patients (40%). Adenoid cystic carcinoma (n=11) and Sinonasal undifferentiated carcinoma (SNUC) (n=8) were the other histological variant. SN Small round cell tumours (SRCT) comprises a diverse group of entities characterized by a monotonous population of undifferentiated tumor cells. In our study, IHC with relevant antibody panels were used to derive at a definitive diagnosis. Among the 28 cases of SRCTs, SNUC (n=8), Lymphoma (n=6) and PDSCC (n=4) were the most common histological variant (Fig 1).



Fig 1: Histological Spectrum of Sinonasal Malignancies.

All tumours were restaged using the 8<sup>th</sup> edition American Joint Cancer Committee (AJCC) classification system. Approximately 2/3rd of our patients presented in a fairly advance stage (stage III & IV), with significant destruction of adjacent anatomical structures (Fig 2, 3a & 3b).





**Fig: 3(a)** 

**Fig: 2** Photograph showing clinical presentation with advanced sinonasal malignancy



**Fig: 3(b)** 

**Fig: 3(a) & 3(b):** Photograph showing the axial and coronal sections of MRI showing a locally advance tumor with intracranial extension.

Clinically regional node metastasis was found in 13 patients. Five patients had distant metastasis at presentation. Lungs were the most common site of distant metastasis (n=4).

Multimodality treatment comprises of surgery followed by radiotherapy in 51 patients. Concurrent Chemo-radiation was used for treating 12 patients, and surgery followed by chemotherapy was given to 7 patients. Six patients underwent surgery alone as the sole treatment. Radiotherapy as single modality was used in 5 patients for inoperable cases with a palliative intent.

### Discussion

SN malignancies are a group of heterogeneous tumours arising from different epithelial lining of the sinonasal tract. Though grouped together because of their common site of origin, they exhibit different and unique tumour-behavior leading to varied prognosis and outcome.

In our study majority of the patients were male (M:F = 1.6:1), in their fifth and sixth decade of life, which is similar to the findings in the previous studies.<sup>(2,3)</sup> Common presenting symptoms were blood stained nasal discharge/ frank epistaxis, unilateral nose block, facial swelling and headache. Epistaxis, reported to be the most specific symptom for SN malignancy,

which was seen in 85% of our patients.<sup>(4-6)</sup> Fasunla et al in their study reported the presence of epistaxis in all the patients.<sup>(7)</sup> Seved et al reported nasal obstruction and diplopia as the most common presenting complaints. Epistaxis was reported in a minority of their patients, as also reported by Kazi M et al.<sup>(2,8)</sup> Such discrepancy between results of different studies is expected because of difference in the geographical location, education, health awareness and socio-economical background of different population. The interval from symptom onset to referral to a cancer care facility also differs according to existing health set-up. Majority of our patients had late presentation in advance disease stage thus epistaxis and facial swelling/ were common symptoms.

Similar to other published studies, SCC was the commonest histological variant in SN malignancy (40%).<sup>(2-7)</sup> Among those diagnosed with SCC, majority showed moderate differentiation (19/34). Poorly differentiated SCC (PDSCC) was confirmed using IHC reactivity for cytokeratin. Three patients with PDSCC were found to have focal Neuroendocrinal differentiation.

Adenoid cystic carcinoma (ACC) (n=11) was the second most common histological variant in our study. ACC is characterized by an intermediate growth rate and low chance of lymphatic spread. But sinonasal ACC had the propensity for early lung metastasis and perineural spread. It has a poor prognosis due to a high local recurrence rate of nearly 40%.<sup>(9)</sup> Of the 11 patients with ACC in our study, 3 had distant metastasis in lungs at the time of presentation. All the patients underwent surgery; postoperative HPE report showed perineural (PNI) spread in 5 patients. Dura and orbit were involved in 3 patients each.

The 'small round cell tumours' (SRCT) of nose and paranasal sinus include a heterogeneous group of malignant tumours with epithelial, haematolymphoid, neuroectodermal and mesenchymal origin. They are characterized by a monotonous population of undifferentiated tumor cells in conventional HPE. IHC using relevant panel of antibodies is an indispensable ancillary technique for arriving at a definitive diagnosis.

In our study, the majority of SRCTs were SNUC (n=8) and poorly differentiated non keratinizing SCC (PDNKSCC) (n=4). These were identified by their cytokeratin immunoreactivity and their reactivity absence of to synaptophysin, chromogranin, CD56, CD45 and HMB45. SNUCs were diffentiated from PDNKSCC by their expression of simple epithelial cytokeratins eg. CK8, CK7 and CK19, and absence of reactivity to EMA. Similar to previous studies, these tumours showed locally aggressive behavior with extensive destruction of adjacent bones and a short history of around 7 to 10 days compared to nearly a month in other SN malignacies. (10) In the study, SRCTs of haematolymphoid origins consisted of 6 cases of lymphoma and a case of 'Extra medullary Plasmacytoma'. Extranodal NK/T cell lymphoma characterised by expression of CD56,CD2 and CD43, was the commonest type (n=3). Ewing's sarcoma / Primitive Neuroectodermal Tumor (PNET) (n=4) was the commonest among Neuroectodermal SRCTs in our study. CD99 immunoreactivity is used to differentiate PNET from other sinonasal SRCTs. As reported in previous studies, they tend to occur in younger patients with an mean age of 22 years (range 8 to 32 years).<sup>(10)</sup> Three cases of amelonotic Mucosal malignant melanoma and 1 case of olfactory neuroblastoma. were other tumours of neuroectodermal origin.

Our study also consisted of 4 cases of rare 'sinonasal neuroendocrinal carcinoma', 3 of whom were poorly differentiated and very aggressive in nature. These were immunoreactive for CK and one of the neuroendocrine markers e.g. Chromogranin, as mentioned in literature.<sup>(11,12)</sup>Three patients with **Biphasic** malignant tumour exhibiting features and both immune-reactivity of epithelial and mesenchymal cell lines were also included in our study. We also had 3 patients of adenocarcinoma, 2 patients of mucoepidermoid carcinoma and 1 case of rhabdomyosarcoma in the study.

### Conclusion

Sinonasal malignancies are rare heterogenous group of cancers with squamous cell carcinoma as the most common histological variant. The majority of SNM are diagnosed at an advanced stage resulting in local recurrence as the main treatment failure. cause of An accurate histopathological classification is challenging because of overlapping features mostly in case of small round cell tumours. A precise diagnosis is important for determining the aggressiveness of the tumor and selecting the optimum treatment modality. However, further prospective studies are required to understand the spectrum and clinical behaviour of these tumours.

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