

## Clinicopathological Analysis of Malignant Tumours of the Sinonasal Tract

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### Abstract

*Background:* The nasal cavity and the paranasal sinuses form a single functional unit. Malignant sinonasal tumours are characterized by low incidence, non specific symptoms, and late presentation. The malignant sinonasal tumours encompass an entire range of both epithelial and non-epithelial tumours. *Aims & Objectives:* Our study aims to determine incidence, age, sex, site, mode of presentation and histological types of various malignant sinonasal tumours over a 5 year period. *Methods:* 107 malignant sinonasal tumors biopsied or surgically excised over a period of five years were studied. *Results:* We encountered 107 cases of malignant tumors with an incidence of 0.24%. Malignant tumors occurred with a mean age of 52.05 years and the male to female ratio was 2.3:1. Among malignant tumors, epithelial tumors (97 cases) constituting 90.65% predominated over non epithelial tumors (10 cases) constituting 9.35% with a ratio of 9.7:1. Out of the 107 cases 58 tumors involved the nasal cavity (54.21%) and 49 involved paranasal sinuses (45.79%). The most common malignant tumor encountered was squamous cell carcinoma-60 cases (56.07%). *Conclusion:* The clinical and radiological features of masses of nasal cavity and paranasal sinuses are overlapping and often only a provisional diagnosis is possible. Definite diagnosis requires histopathological examination.

**Keywords:** Sinonasal Tract; Malignancy; Squamous Cell Carcinoma; Epithelial; Nonepithelial.

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### Introduction

The nasal cavity and paranasal sinuses including the maxillary, ethmoid, sphenoid and frontal sinuses are collectively referred to as the sinonasal tract. Although the nasal cavity and paranasal sinuses occupy a relatively small anatomic space, they are the site of origin of some of the more complex histologically diverse group of tumors of the entire human body [1,2].

These include neoplasms derived from mucosal epithelium, seromucinous glands, soft tissues, bone, cartilage, neural/neuroectodermal tissues, hematolymphoid cells and the odontogenic apparatus. Many of the tumours are similar to those found elsewhere in the body but a few such as olfactory neuroblastoma are unique to this site [3].

### Materials and Methods

The surgical specimens received in the Institute of Pathology, Madras Medical College, Chennai from the Upgraded Institute of Otorhinolaryngology, Government General Hospital, Chennai for the period of five years formed the material for this study. Small biopsy specimens and excision biopsy specimens and resection specimens were included. Inadequate or unrepresentative biopsy material was excluded from the study. Informed written consent from the patient was obtained. Ethical committee clearance was obtained.

The clinical features such as age and sex of the patient, site of lesion and type of surgery done were noted.

The tissues were routinely processed and paraffin blocks were made and histological sections of 5 to 6 micrometer were taken in Leica microtome and routinely stained with hematoxylin and eosin stains. Microphotographs were taken.

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(Received on 24.05.2017, Accepted on 13.06.2017)

The microscopic analyses were done from all the available slides. These included the histological pattern, cellular features, vascularity and secondary changes. Diagnosis was made and the malignant tumors were classified.

## Results

We encountered 107 cases of malignant tumors with an incidence of 0.24%. Malignant tumors occurred in patients with a mean age of 52.05 years and the male to female ratio was 2.3:1. Among malignant tumors, epithelial tumors (97 cases) constituting 90.65% predominated over non epithelial tumors (10 cases) constituting 9.35% with a ratio of 9.7:1.

The age range varied from second to ninth decade of life but the peak age of presentation was 5<sup>th</sup> decade followed by 7<sup>th</sup> decade as shown in Table 2.

Males showed a higher incidence than females with a male to female ratio of 2.3:1 as shown in Table 3.

Out of the 107 cases 58 tumors involved the nasal cavity (54.21%) and 49 involved paranasal sinuses

(45.79%). Amongst paranasal sinuses, maxillary sinus was the commonest site in our study as shown in Table 4.

The most common malignant tumor encountered was squamous cell carcinoma-60 cases (56.07%), followed by Sinonasal undifferentiated carcinoma (SNUC) 10 cases (9.35%).

The other malignant lesions that involved the region were adenoid cystic carcinoma, adenocarcinoma, mucoepidermoid carcinoma, sinonasal neuroendocrine carcinoma, olfactory neuroblastoma and ameloblastic carcinoma. We also encountered rarer tumors like mucosal malignant melanoma, plasmacytoma, PNET, fibrosarcoma and clear cell metastatic deposits as shown in Table 5.

The most common clinical presentation in our study was mass in the nose which constituted cases (94.39%) as shown in Table 6.

In our study we had 15 cases of undifferentiated carcinoma for which we employed a panel of immunohistochemical markers that included cytokeratin, NSE, synaptophysin, vimentin, desmin, S100, CD99 and CD45. 10 cases were finally diagnosed

**Table 1:** Distribution of malignant tumors of nasal cavity, paranasal sinuses according to the incidence, sex ratio, age and site of presentation

Diagnosis	No. of Cases	%	M:F	Peak Age(decade)	Nasal cavity		PNS	
					No	%	No	%
	Malignant tumors			107				
Adenocarcinoma	5	4.67	M only	7	3	5.17	2	4.08
Adenoid cystic Carcinoma	8	7.48	1.6:1	7	5	8.62	3	6.12
Ameloblastic Carcinoma	2	1.87	M only	5&7		0	2	4.08
Hemangioendotheloma	1	0.93	M only	7	1	1.72		0
Melanoma	2	1.87	M only	4&6	2	3.44		0
Mucoepidermoid Carcinoma	5	4.67	1:1.5	5	1	1.72	4	8.16
Olfactory Neuroblastoma	2	1.87	1:1	2&5	1	1.72	1	2.04
Fibrosarcoma	1	0.93	M only	4		0	1	2.04
Plasmacytoma	2	1.87	1:1	5&7	2	3.44		0
SNUC	10	9.35	4:1	5	7	12.06	3	6.12
SNEC	6	5.61	1.5:1	3&5	5	8.62	1	2.04
PNET	2	1.87	M only	2	1	1.72	1	2.04
Squamous cell carcinoma	60	56.07	2.7:1	7	30	51.72	30	61.22
Metastasis	1	0.93	F only	5		0	1	2.04

Abbreviations: SNUC-Sinonasal Undifferentiated Carcinoma SNEC- Sinonasal Neuroendocrine Carcinoma PNET-Primitive Neuroectodermal tumor

**Table 2:** Age distribution of malignant neoplasms

Age group (years)	Number	Percentage
<10	0	0
10 to 20	4	3.74
21 to 30	4	3.74
31 to 40	15	14.02
41 to 50	28	26.17
51 to 60	22	20.56
61 to 70	27	25.23
71 to 80	6	5.61
81 to 90	1	0.93
Total	107	100

**Table 3:** Sex distribution of malignant neoplasms

Sex	Number	Percentage
Male	75	70.09
Female	32	29.91
Total	107	100

**Table 4:** Site of malignant neoplasms

Site	Number	Percentage
Nasal cavity	58	54.21
Maxillary sinus	38	35.51
Ethmoid sinus	4	3.74
Frontal sinus	2	1.87
Sphenoid sinus	5	4.67
Total	107	100

**Table 5:** Histological diagnosis of malignant neoplasms

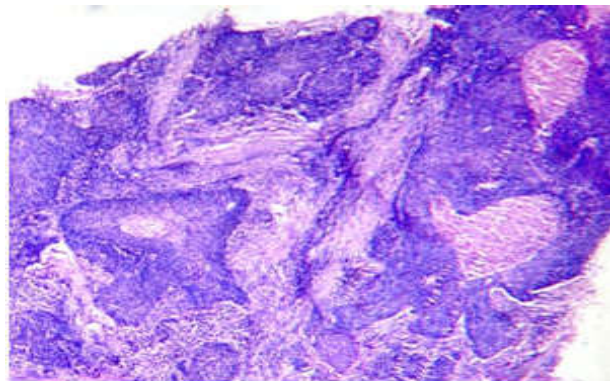
Types	Frequency	Percentage
Adenocarcinoma	5	4.67%
Adenoid cystic carcinoma	8	7.48%
Ameloblastic carcinoma	2	1.87%
Hemangioendothelioma	1	0.93%
Melanoma	2	1.87%
Mucoepidermoid carcinoma	5	4.67%
Olfactory Neuroblastoma	2	1.87%
Fibrosarcoma	1	0.93%
Plasmacytoma	2	1.87%
SNUC	10	9.35%
SNEC	6	5.61%
PNET	2	1.87%
Squamous cell carcinoma	60	56.07%
Metastasis	1	0.93%
Total	107	100.00%

**Table 6:** Clinical presentation

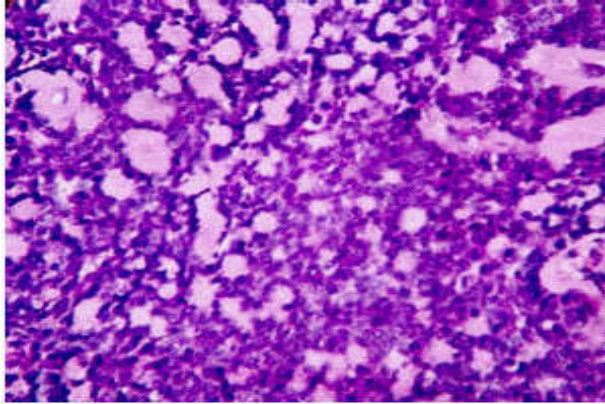
Clinical Presentation	Frequency	Percentage
Mass in the nose	101	94.39
Polyp	1	0.93
mass & epistaxis	2	1.87
epistaxis & nasal obstruction	1	0.93
Mass & proptosis	1	0.93
mass & headache & blurr. vision	1	0.93
Total	107	100%

**Squamous Cell Carcinoma**

**Fig. 1:** Maxillectomy specimen with an irregular infiltrating grey white growth.

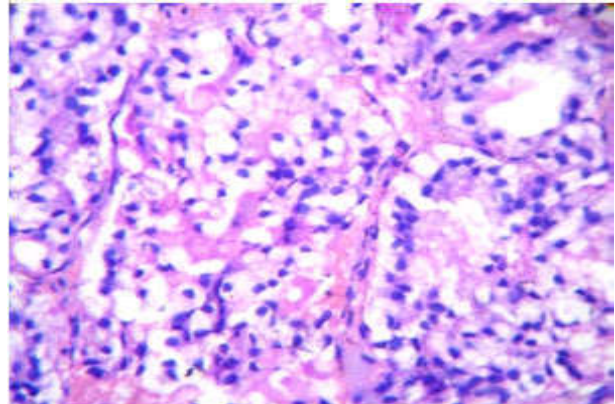
**Basaloid Squamous Cell Carcinoma**

**Fig. 2:** Lobules and nests of basaloid cells with comedo necrosis (H&E 100x)



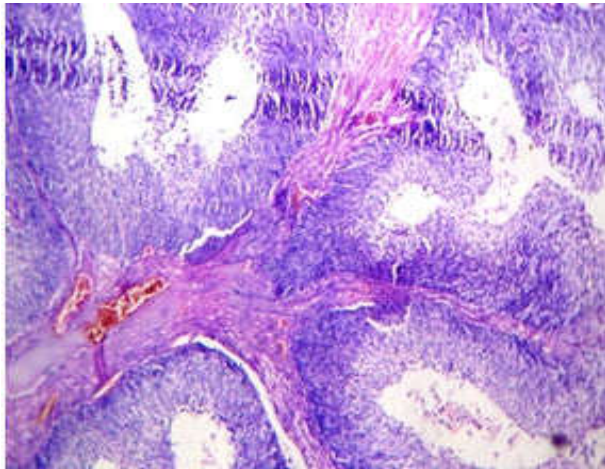
#### Adenoid Cystic Carcinoma

Fig. 3: Cribriform configuration of neoplasm composed of basaloid cells with eosinophilic basement membrane material in the lumen (H&E400x)



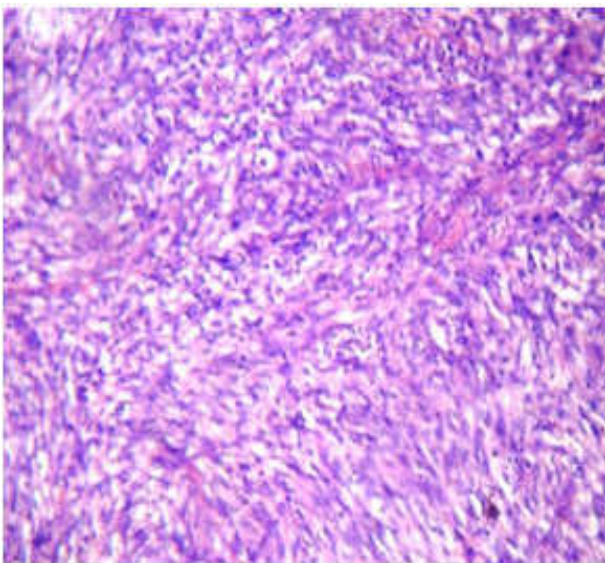
#### Metastatic Clear Cell Carcinoma

Fig. 6: Neoplasm in solid tubuloalveolar pattern composed of clear cells with round nuclei (H&E400X).



#### Papillary Adenocarcinoma

Fig. 4: Papillary configuration of tumour lined by malignant columnar epithelial cells with nuclear stratification (H&E100x)



#### Fibrosarcoma

Fig. 5: Fascicles and herringbone pattern of spindle shaped cells with mild cellular pleomorphism (H&E100X)

as Sinonasal undifferentiated carcinoma (SNUC). 5 cases were finally categorized as Sinonasal neuroendocrine carcinoma (SNEC).

We had 5 cases of small round cell tumor (SRCT) for which the same immunohistochemistry panel was employed. Among them 2 cases were finally diagnosed as esthesioneuroblastoma(ENB). Among the other 3 cases, 2 cases were diagnosed as PNET and 1 case was diagnosed as SNEC.

### Discussion

The present clinicopathological study of sinonasal tumors includes 107 malignant tumors of nasal cavity and paranasal sinuses for a period of five years. During the above period 44730 specimens were received at the general surgical pathology laboratory of our institute. Out of which 107 were malignant sinonasal tumors with incidence of malignant sinonasal tumors representing 0.24%. The rare nature of the tumors is almost a universal finding [4-13]. Epithelial tumors (97 cases) predominated with a 90.65% over nonepithelial tumors (10 cases) with a 9.35%. The ratio of epithelial to nonepithelial tumors was 9.7:1. Male to female ratio was 2.3:1 similar to other studies [8]. Age range was 10 to 90 years with an average of 52.05 years. The maximum number of cases were present in nasal cavity (54.21%) followed by paranasal sinuses (45.79%). Among the paranasal sinuses maxillary sinus (35.51%) was the commonest site of presentation. Mass in the nose (94.39%) was the most common clinical presentation in our study. Both sides (Right & Left) involved with equal frequency (50%).

While reviewing literature of tumors of nasal cavity and paranasal sinuses, it was found that various

authors have studied these tumors in different aspects, such as epithelial tumors, non epithelial tumors and malignant neoplasms [9-13]. Some have studied specific tumor entities like fibro osseus tumors and minor salivary gland tumors. Some others have included tumors of nasopharynx while studying tumors of nasal cavity and paranasal sinuses [8].

Among the 107 malignant tumors it was found that the majority were squamous cell carcinomas. Studies on the incidence of squamous cell carcinoma by various authors also reveal similar findings. Ghosh et al noted the incidence of 72.70%. The incidence of squamous cell carcinoma in the present study was 56.07%. Several authors have analysed the age incidence of squamous cell carcinoma and the average peak was noted between 50-70 yrs of age.

Our study revealed that most of the cases were in the age range of 51 to 60 years. Males predominated over females in studies by several authors. Our study also revealed a male preponderance with a ratio of 2.69:1. The nasal cavity was slightly preponderant site of involvement in our study over paranasal sinuses. In the paranasal sinuses maxillary sinus was the predominant site of occurrence. Sagar et al and other authors have noted a predilection for paranasal sinus over nasal cavity.

Gupta et al and Panchal et al (2005) [9] observed that moderately differentiated squamous cell carcinoma was most commonly encountered. We also observed that moderately differentiated squamous cell carcinoma predominated in our study similar to other authors. We had 10 cases of poorly differentiated squamous cell carcinoma and all the cases showed immunoreactivity for cytokeratin. We encountered uncommon & high grade variants of squamous cell carcinoma like 2 cases of basaloid variant [14], 1 case each of acantholytic, adenosquamous, spindle cell variants. Microscopy of basaloid variant showed lobular arrangement of basaloid cells with areas of comedo necrosis admixed with focal areas of squamous differentiation (Figure 2). The acantholytic variant showed the neoplasm in pseudoglandular pattern. Spindle cell squamous carcinoma was confirmed by showing positive immunoreactivity for cytokeratin and negativity for mesenchymal markers. In our study we did not encounter any case of metastatic squamous cell carcinoma. We noted that one case was a recurrent tumor which involved the maxilla of a 46 year old male.

Among 107 malignant tumors we encountered 10 cases of sinonasal undifferentiated carcinomas with a peak incidence in the 5th decade. Males dominated over females in our analysis.

The commonest site in our study was nasal cavity. Histopathology showed either small or large tumor cells and was predominantly arranged in nests, ribbons thick trabeculae or sheet like pattern and had coarse chromatin, prominent nucleoli and necrosis.

We had 8 cases of adenoid cystic carcinoma with an incidence of 7.48% and slight preponderance in females, in the age range of 40 to 70 yrs with the peak in 7th decade similar to other studies. 5 cases involved the nasal cavity and 3 cases involved the maxilla [15]. Histopathology showed basaloid cells with scant cytoplasm and round to oval hyperchromatic nuclei arranged in tubular and cribriform pattern (Figure 3). Among our cases four were grade II and grade I.

Adenocarcinoma of the sinonasal tract was observed in 5 out of 107 malignant tumors with an incidence of 4.67%. Several authors have analysed the incidence of adenocarcinoma and found it was widely variable ranging from 4% [Lopez et al (1990)] to 42.86% [Tandon and Bahadur et al (1992)]. The mean age of presentation was 57.6 years. All our five cases were males similar to studies by Lopez et al (1990). The nasal cavity was the predominant site. Barbeiri et al (2003) and others noted a preponderance of paranasal sinus involvement [18,20], while Tandon et al (1992) noted an increased incidence in the nasal cavity.

Lopez et al (1990) observed Tubulopapillary variant of Intestinal type adenocarcinoma as the most common variant (83.33%). Urso et al (1993) observed that moderately differentiated intestinal type adenocarcinoma was the most common histologic type (27.78%). Abecasis et al (2004) [19] observed that 10 out of 14 cases were high grade Intestinal type adenocarcinoma and 2 out of 14 cases were low grade Intestinal type adenocarcinoma. The papillary variant of adenocarcinoma predominated in our study and 2 tumors were moderately differentiated and 2 tumors were well differentiated. Microscopy showed a papillary architecture lined by malignant epithelial cells with nuclear stratification and mild atypia (Figure 4) [15,16,17]. We noted that one case was a recurrent tumor involved a nasal cavity of male in the 5th decade. We did not encounter any case of metastatic adenocarcinoma.

We encountered 5 cases of mucoepidermoid carcinoma with an incidence of 4.67%. The peak incidence was in 5th decade with a male to female ratio of 1.5:1. Paranasal sinus was the commonest site in our study. Histopathology revealed islands of malignant squamous cells admixed with mucous secreting cells. 4 cases were high grade and 1 case was low grade. 2 cases of plasmacytoma were reported with an incidence of 1.87%. Both cases presented in the

nasal cavity with an equal sex incidence and occurred in 5 & 7<sup>th</sup> decade respectively similar to Roberta De Paula Araujo et al (2008) except that they found male preponderance in their study. Histopathology showed plasma cells in diffuse sheets with varying degrees of maturation, round eccentrically placed nucleus with paranuclear clear zone and clock face chromatin. Our cases did not show evidence of multiple myeloma elsewhere [22].

We noted 2 cases of ameloblastic carcinoma which presented in the maxilla of two males in the 5<sup>th</sup> decade and 7<sup>th</sup> decade respectively with a incidence of 1.87%.

We had 1 rare case of spindle cell sarcoma involving a maxilla of a 38 year old male with an incidence of 0.93%. Histopathology showed spindle shaped cells in fascicles and herring bone pattern with mild cellular pleomorphism provisionally diagnosed as fibrosarcoma-low grade (Figure 5). This was supported by immunohistochemistry by vimentin reactivity and cytokeratin negativity similar to G.plaza et al. (2006) [23]. We had one case of hemangioendothelioma which presented in the nasal cavity of a 65 year old male with a incidence of 0.93%. Histopathology showed rounded epithelioid tumor cells with intracytoplasmic lumina arranged in nests and strands with angiocentric growth pattern similar to study by Chih -Chieh Tseng et al (2005)[24].

One case of metastatic clear cell carcinomatous deposits was encountered involving the sphenoid sinus of a 45 year old female with an incidence of 0.93%. Histopathology showed solid tubuloalveolar pattern of clear cells with round nuclei (Figure 6). PAS stain showed positivity in the cytoplasm of tumor cells [25,26,27]. We had 2 cases of malignant melanoma with a incidence of 1.87%. Both cases presented in the nasal cavities of males aged 40 and 54 years respectively similar to Zafer et al(2008) [8].Histopathology showed features similar to other undifferentiated neoplasms of sinonasal tract showing malignant epithelioid and spindle cells with pleomorphic nuclei and eosinophilic nucleoli with evidence of melanin deposition. Masson Fontana stain showed positivity in the cytoplasm of tumor cells. Immunostaining revealed tumor cells which were positive for markers HMB45, S100 confirming the diagnosis of melanoma.

### Conclusion

We encountered a heterogenous and a wide variety of neoplasms. Squamous cell carcinoma was the most common in our study. Rare entities like malignant melanoma, fibrosarcoma, metastatic clear cell

carcinoma, esthesioneuroblastoma, sinonasal undifferentiated carcinoma, neuroendocrine carcinoma were encountered.

Tumours of the nasal cavity and paranasal sinuses are rare pathologies with extremely varied behavior. The symptoms of the neoplastic processes are essentially similar to inflammatory pathology of the sinonasal tract with resultant delay of diagnosis. Definite diagnosis requires histopathological examination as most of the lesions are inaccessible for fine needle aspiration or FNAC is not recommended because of fear of haemorrhage.

To conclude, categorizing the malignant sinonasal tumours according to histopathological features into various types helps us to understand the clinical presentation, treatment, clinical outcome and prognosis. The key in the diagnosis and treatment of malignant sinonasal tumours remains a high index of suspicion and early diagnosis as late presentation and delay in early diagnosis are major constraints to favourable outcome of treatment.

### Acknowledgement

Nil

*Conflict of Interest:* Nil

### Key Messages

The malignant sinonasal tumours encompass an entire range of both epithelial and non-epithelial tumours. The clinical and radiological features are overlapping. Definite diagnosis of sinonasal tumors requires histopathological examination.

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