Clinico-Histopathological Spectrum of Sinonasal and Nasopharyngeal Lesions- A Two Years Study at a Tertiary Care Hospital in Eastern India

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ABSTRACT

BACKGROUND

Sinonasal tumours are highly heterogeneous group of tumours that account for less than one percent of all malignancies. Because of varied morphology & their undifferentiated nature, clinicoradiological & histopathological correlation along with ancillary studies is very much essential for a definite diagnosis. The aim of this study was to evaluate various lesions arising in the sinonasal tract and nasopharyngeal region with special reference to clinico-radiological correlation and ancillary studies for a definite diagnosis of sinonasal and nasopharyngeal tumours.

METHODS

A total 122 cases of non-neoplastic & neoplastic lesions occurring in sinonasal tract and nasopharynx were studied over a period of two years. All the paraffin embedded blocks of the cases were subjected to routine haematoxylin and eosin (H&E) stain, followed by special stain & immunohistochemistry (IHC) as per requirement.

RESULTS

The study showed 52 cases (42.62%) of non-neoplastic lesions of which inflammatory sinonasal polyp was the commonest; 21 cases (17.21%) were benign & 49 cases (40.16%) were malignant tumours. The commonest benign tumour was Schneiderian papilloma (33.32%) whereas among the malignant the commonest being nasopharyngeal carcinoma (NPC, 40.81%), small blue round cell tumours (SRBCT, 24.48%), squamous cell carcinoma (SCC, 20.40%) followed by sinonasal undifferentiated carcinoma (SNUC, 8.16%).

CONCLUSIONS

Tumours of the sinonasal and nasopharyngeal region are very much diverse & undifferentiated by histomorphology, hence pose a diagnostic challenge for a pathologist using conventional histopathologic approaches only. Thus, aid of ancillary techniques like IHC, molecular / cytogenetic studies are immensely helpful in establishing diagnosis for early intervention, in order to prevent significant morbidity & mortality especially in malignant tumours.

KEYWORDS

Inflammatory Sinonasal Polyps, Nasopharyngeal Carcinoma, Schneiderian Papilloma, Small Blue Round Cell Tumours, Sinonasal Undifferentiated Carcinoma.

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BACKGROUND

The nasal cavity and paranasal sinuses (PNS) are collectively referred to as sinonasal tract, which is anatomically and embryologically distinct from the nasopharynx, but forms a common functional unit. These tumours are rare and make up about 3% of tumours of upper respiratory tract.[1] These are twice as common in males than females and seen in 5th-6th decade of life.

Human papilloma virus (HPV) 6, 11, 16 & 18, allergens, air pollution, tobacco, industrial carcinogens predisposes to various neoplasms. They present with symptoms like nasal obstruction, congestion, headache or sometime epistaxis. The benign tumours includes epithelial tumours like squamous cell papilloma as well as vascular and mesenchymal tumours, some showing recurrence and cause local bone destruction.

The malignant tumours includes Squamous cell carcinoma (SCC), Nasopharyngeal carcinoma (NPC), Sinonasal undifferentiated carcinoma (SNUC) and small round blue cell tumour (SRBCT). Computer tomography (CT), magnetic resonance imaging (MRI) and endoscopies are done for clinical staging, to know the extension & check metastasis. Nasopharyngeal carcinoma incidence rises after the age of 30 years, peaks at 40-60 years & then declines.[2] The incidence of malignant tumours of nasal cavity & PNS is low in most of the western population (<1.5/100000 in men & <1.0/100000 in women) although higher incidence is seen in Japan & certain parts of China and India.[3,4]

One of the major groups of malignant tumours of sinonasal region are the SRBCTs and their early and accurate diagnosis is imperative for the patients to undergo appropriate therapy. Although definitive diagnosis of SRBCTs solely on H&E light microscopy is exceedingly difficult because of frequent absence of distinguishing features, lack of architecture & limited incisional biopsy; thus, aid of ancillary studies like IHC, molecular/cytogenetic studies is essential for the diagnosis.[5]

METHODS

A prospective study was conducted in the department of pathology for a period of two years from April 2018 to March 2020. Clinicoradiological data were archived from the hospital records. All the paraffin embedded blocks of the specimens (both endoscopic and radical type) were subjected to routine H&E stain and special stain like Ziel Neelson (ZN) stain, mucicarmine and Gomori methamine silver (GMS) wherever required. IHC was done in most of the malignant as well as benign neoplasm which includes cytokeratins, vimentin, Leucocyte common antigen (LCA), CD99, S-100, Synaptophysin, chromogranin, Neuron specific enolase (NSE), HMB45 CD34, desmin, EMA, Bcl6, MUM1, MyoD1, CD138. There was no ethical issue in this study.

RESULTS

A total of 122 cases of sinonasal & nasopharyngeal lesions were studied over a period of 2 years. Out of 122 cases, 52 cases (42.62%) were non neoplastic including inflammatory, fungal & heterotopias, while 70 cases were neoplastic out of which 21 (17.21%) were benign and 49 (40.16%) were malignant. Most of the non-neoplastic lesions and benign tumours were seen between 3rd to 4th decade of life with male sex predilection occurring predominantly in nasal cavity (80.76%,57.14% respectively) whereas the malignant tumours occurred mostly in 5th to 7th decade with male:female ratio of 1.5:1 arising mainly in paranasal sinus (42.85%) followed by nasopharynx (40.81%). The chief complaints of the patients were nasal obstruction, nasal mass and headache whereas those of malignant tumours were associated with epistaxis, nasal/nasopharyngeal mass, sometimes associated with visual disturbances and facial palsy. The non-neoplastic lesions included mostly inflammatory sinonasal polyp (80.76%), fungal sinusitis (17.29%) followed by nasal polyp with glial heterotopias (1.92%) (Table-1).

Type	No. of Cases (n, (%))	Mean Age (in Year)
Inflammatory Sinonasal Polyp	42 (80.76)	42.8
Fungal Sinonasal Mass		
Rhinosporidiosis	4 (7.69)	32.2
Mucormycosis	2 (3.84)	35
Aspergillosis	3 (5.76)	35.5
Nasal glial heterotopia	1 (1.92)	38

Table 1. Spectrum of Non-Neoplastic Nasal Masses (n=52 cases)

Type	No. of Cases (n, (%))	Mean Age (in year)
Schneiderian Papilloma		
Squamous	3 (14.28)	37.6
Inverted	4 (19.04)	47.5
Haemangioma	6 (28.57)	33.8
Juvenile Angiofibroma	3 (14.28)	12.7
Schwannoma	1 (4.76)	60
Angioleiomyoma	2 (9.52)	61
Hemangiopericytoma	1 (4.76)	19
Peripheral Ameloblastoma	1 (4.76)	50

Table 2. Spectrum of Benign Neoplastic Sinonasal Masses (n=21 Cases)

Schneiderian papillomas (33.32%) and haemangiomas (28.57%) constituted significant bulk of benign tumour. One case of peripheral extragnathic ameloblastoma was also included showing intra oral extension (Table -2).

The commonest malignant epithelial tumour was undifferentiated NPC (40.81%, (Figure 1) followed by SCC (well to moderately differentiated type, 20.40%) along with transitional cell carcinoma & Basaloid SCC (2.04% each) and 8.16% cases of SNUCs. No adenocarcinoma was reported in the study. SRBCT constitute another big category of malignant sinonasal tumours (n=12). Out of which majority was Non-Hodgkin's Lymphoma (10.20%) followed by olfactory neuroblastoma (ONB, 4.08%), Embryonal rhabdomyosarcoma (RMS, 4.08%), atypical Ewing's sarcoma/peripheral neuroectodermal tumour (EWS-PNET, 2.04%) (Figure 2 & 3), malignant neuroendocrine tumour & mucosal malignant melanoma constituted 2.04% each.

Type	Number of Cases [n, (%)]	Mean Age (in Years)	Immunohistochemistry	
Epithelial Malignancies			**Positive**	**Negative**
NPC-UDC	20 (40.81)	40.5	CK5/6	CK7
SCC-Keratinising type	10 (20.40)	55.8	CK5/6, P63	CK7
Basaloid SCC	1 (2.04)	78	CK7, P63	Synaptophysin
SNUC	4 (8.16)	42.5	CK7	CK5/6
Transitional cell carcinoma	1 (2.04)	42.5	P63, CK20, CK7	CK5/6
Small Blue Round Cell Tumours				
Lymphoid Malignancies				
DLBCL (ABC type)	2 (4.08)	65.2	LCA, CD20, MUM-1, Bcl2- 50% Ki67- 65%	CD3, CD10, CD30 Bcl6
NK/T cell lymphoma	2 (4.08)	59.5	LCA, CD5, CD56	PanCK, CD20, CD3, NSE, ALK-1, EMA,CD10,Bcl 6
Extramedullary plasmacytoma	1 (2.04)	60	CD138, Kappa chain	LCA, Lambda chain
Mesenchymal Malignancies				
Atypical Ewing's sarcoma	1 (2.04)	60	CD99, NSE PanCK, CK5/6	LCA, CK7, CD34, S100, Synaptophysin
RMS (Embryonal)	2 (4.08)	21.5	Desmin, MyoD1	NSE, PANCK, CK7
Malignant melanoma	1 (2.04)	70	HMB-45, S100	LCA, Synaptophysin
Olfactory neuroblastoma	2 (4.08)	26.5	NSE, S100, Chromogranin	LCA, CK5/6
Neuroendocrine carcinoma	1 (2.04)	65	NSE, PanCK, P63, Chromogranin	LCA, S100
Salivary Gland Neoplasm				
Adenoid cystic carcinoma	1 (2.04)	60	EMA, CK7, P63, CK5/6	CK20

Table 3. Spectrum of Malignant Lesions (n=49) with IHC

All cases of SRBCTs were subjected to IHC panel and molecular study as and when required. The diagnosis of atypical Ewing's sarcoma was established by CD99 positivity and EWSR1-FLI1 fusion by real time polymerase chain reaction (RT-PCR). Age incidence of these spectrum of diseases were varied showing high age incidence (6th to 7th decade) in malignant melanoma, extramedullary plasmacytoma and diffuse large B cell lymphoma (DLBCL). Whereas RMS and ONB were encountered among second decade. (Table-3)

DISCUSSION

The sinonasal tract is anatomically distinct from nasopharynx but forms a common functional unit & is lined by Schneiderian membrane.[6] In clinical practice a variety of non-neoplastic & neoplastic conditions involving the nasal cavity, paranasal sinus & nasopharynx are usually encountered.

Patients with sinonasal lesions present mainly in 4th to 5th decade of life showing male sex predilection. The clinical features with advanced imaging techniques provide us a presumptive diagnosis but histopathological examination remains the mainstay of the definitive diagnostic modality for reaching the correct diagnosis and timely intervention for the patient. About 60% of sinonasal tumours originate in the maxillary sinus, 20-30% in the nasal cavity, 10-15% in the ethmoid sinus followed by 1% in sphenoid & frontal sinus.[7]

The most common symptoms at the presentation was nasal obstruction (mostly unilateral), congestion, headache followed by epistaxis. Symptoms like severe epistaxis, bilateral nasal obstruction, anosmia, facial swelling & numbness favours more of malignant sinonasal tumour. Radiological investigations like CT scan-PNS or MRI helps to know the extent of the tumours and its association with the adjacent bone involvement. Not only malignant even the benign tumours had a tendency for local recurrence and bone destruction, thus many a times resulting in procuring only an incisional biopsy.

Inflammatory sinonasal polyp (80.76%) was the most common non neoplastic lesion (n=52) in the nasal cavity seen in our study corresponding to Bhattacharya et al[8]. There is no particular age or sex predilection,[9] but in our study male predominance was found. These patients were managed by non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids & endoscopy guided polypectomy. Rhinosporidiosis is a chronic granulomatous disease caused by fungus Rhinosporidium seeberi affecting mostly nasal mucosa and is prevalent in India & Srilanka. In our study we found 7.69% cases with male predominance which was similar to a study by Samaddar & Sen et al.[10]

Other fungal aetiology in the nasal tract included in our study were Aspergillus spp. (5.76%) in a HIV positive status patient followed by mucormycosis (3.84%) in a immunocompromised case (diagnosed case of Acute myeloid Leukemia). Both occurred in middle aged males.[11]

Sinonasal papilloma, inverted type are the most common papillomas in sinonasal region and frequently seen in 5th - 6th decade of life and twice common in males than females. Our study showed inverted papilloma (19.04%) as the predominant type of benign neoplastic condition with a more male sex predilection and one of these papillomata on recurrence showed features of transitional cell carcinoma.[12] Haemangiomas are common vascular tumour with a marked male preponderance (approximately 6:1). Our study showed capillary haemangioma (28.57%) was the commonest type followed by a case of pyogenic granuloma in a pregnant lady. The most common underlying cause are attributed to hormonal imbalance & excessive inflammatory response after local trauma. Similarly, juvenile angiofibroma (14.28%) presenting with chief complains of epistaxis occurred in adolescent males due to increased androgen activity correlating with other authors.[13]

Nasal haemangiopericytoma (HPC) is another vascular but rare tumour of uncertain malignant potential. WHO reclassified HPC as a fibroblastic/ myofibroblastic tumours. The incidence of these tumours in head & neck region is only 15% and most commonly seen in adults. In our study we had one case of sinonasal type of HPC in a 19-year-old male

having chief complaints of epistaxis, unilateral nasal obstruction & stuffiness. Diagnosis of HPC was established with the help of strong vimentin & CD34 immunopositivity.

Angioleiomyoma is a rare benign tumour formed by smooth muscles cells in the vascular wall. Less than 1% of all vascular leiomyoma occur in the nasal cavity.[14] There were 2 cases of elderly aged males having chief complaints of nasal mass with epistaxis and blockage diagnosed with angioleiomyoma in our study with strong smooth muscle actin and CD34 immunopositivity.[15]

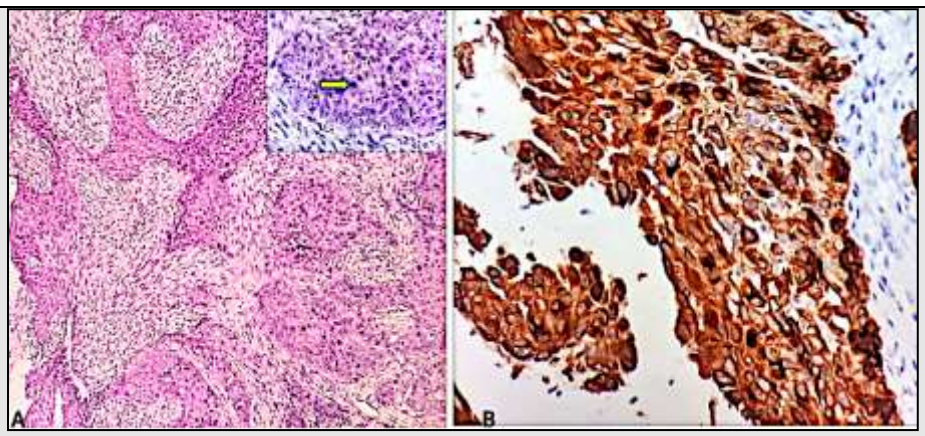

Figure 1A - Microphotograph of Undifferentiated NPC Showing Round to Polygonal Neoplastic Cells with Conspicuous Nucleoli & Atypical Mitoses (Arrowed) Arranged in Nest. (H & E 10X, Inset 40X). (1B). Strong CK5/6 Positivity (IHC 40X)

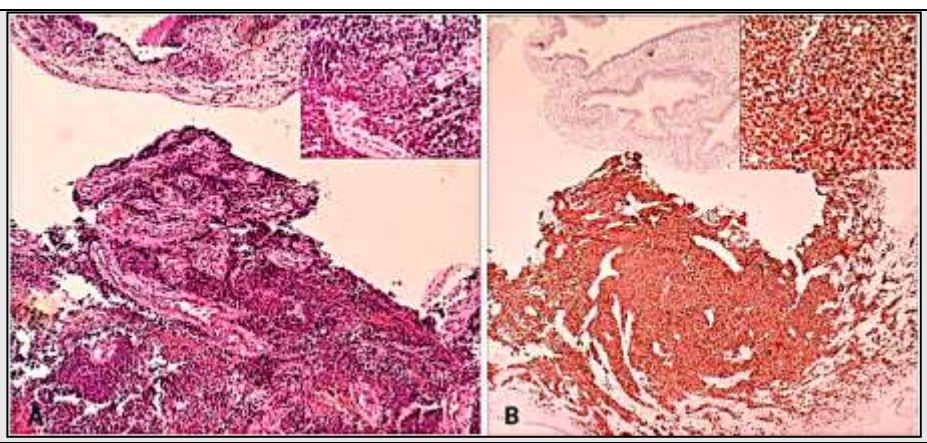

Figure 2A. Microphotograph of Embryonal RMS Showing Round to Elongated Cells with Hyperchromatic Nuclei Arranged Diffusely (H&E 10X, Inset 40X). (2B). Strong Desmin Positivity (IHC 10X, Inset 40X)

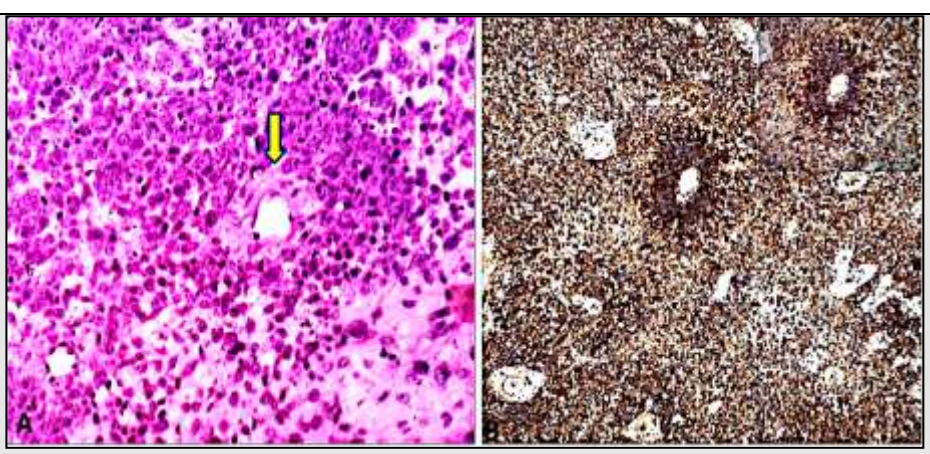

Figure 3A. Photomicrograph of Atypical EWS/PNET Showing Round Cells with Moderate Pleomorphism & Conspicuous Nucleoli Forming Pseudorosette (Arrowed). (H&E 40X) (3B). Intense CD99 Positivity (IHC 10X, Inset 40X)

Benign peripheral nerve sheath tumours like schwannoma are uncommonly encountered in the nasal cavity & PNS and constituted 4.76% in our study.[16]

Sinonasal ameloblastoma is a locally aggressive borderline tumour with high propensity for recurrence. A large review found ameloblastomas to comprise approximately 0.11% (n=19,658) of all sinonasal tract tumours.[17] They primarily occur in mandible but peripheral (extragnathic) type of ameloblastomas occurring primarily in sinonasal tract is extraordinarily uncommon. Our study

reported a case of peripheral ameloblastoma of acanthomatous variant in a 50-year-old female with complaints of nasal blockage. Non contrast CT scan revealed a solid mass with bony destruction of frontal process of maxilla with an intraoral extension.

Nasal glial heterotopia a rare developmental abnormality seen in a wide age group but typically present in early childhood. Failure to recognise this rare entity has diagnostic difficulty as the patient present with sinonasal polyp. In our study we had a case of inflammatory sphenoidal polyp with glial heterotopias with predominant glial cells showing strong immunoreactivity for GFAP and S-100.[18]

NPC particularly SCC includes Keratinising, non-keratinising and undifferentiated subtype and are commonest malignant tumours arising from paranasal sinuses and nasopharynx. But these tumours are least common in head and neck region. The common subtype was keratinising type of SCC followed by adenocarcinoma, transitional and undifferentiated type. It is endemic in Southern china, Southeast Asia, Northafrica.[19] High risk HPV is most frequently associated with non-keratinising SCC whereas Epstein Barr virus (EBV) are seen in undifferentiated carcinoma[20] .There were 20.40% cases of SCC, 2.04% case of basaloid SCC and transitional cell carcinoma, 40.81% cases of Nasopharyngeal carcinoma of undifferentiated subtype. Among total 49 malignant sinonasal tumours with age group ranging from 40-78 years, all were treated with neoadjuvant therapy.

SNUC is an undifferentiated carcinoma without glandular or squamous differentiation; extremely rare and occurs in a wide range of age (average-50-60 years) with a more male sex predilection. They are highly aggressive malignancy with nodal involvement and distant metastasis with very poor prognosis.[21] There were 8.16% cases of SNUC in our study and two cases presented at stage T3/T4 similar to a study by Gallo et al.[22] Patients mostly presented with nasal obstruction, epistaxis, diplopia, proptosis, facial pain. CT/MRI scan showed extensive bony destruction with the irregularity of margin of tumour.

The tumours were surgically resected with a tumour free surgical margins & orbital exenteration. To ascertain the origin of undifferentiated carcinoma in sinonasal or nasopharyngeal region, IHC markers like CK7 was positive in SNUC while CK 5/6 was positive in NPC were immensely helpful.[15]

SRBCT constitute heterogenous group of malignant neoplasm characterised by monotonous population of undifferentiated cells with relatively small sized hyperchromatic nuclei & scant neoplasm. Definite diagnosis usually not possible by morphology alone, but with the support of panel of antibodies like Cytokeratin, CD99, LCA, Epithelial membrane antigen (EMA), desmin, vimentin along with molecular/cytogenetic study is essential to reach at diagnosis[5]. In our study we had predominantly Non-Hodgkin's Lymphoma (10.2%), olfactory neuroblastoma (ONB, 4.08%), embryonal RMS (4.08%), 2.04% cases of high-grade neuroendocrine carcinoma, Atypical Ewing's sarcoma, and mucosal malignant melanoma each, all of which were immunohistochemically established. ONB (1-5%) is an uncommon neoplasm originating in the olfactory epithelium of nasal fossa. Misdiagnosis often occurs due to marked crushing artefact or divergent differentiation. But the diagnostic criteria include cell heterogeneity, Homerwright rosettes and S100 positive sustentacular cells.[23] Atypical EWS/PNET was most challenging and the differential diagnosis included were other SRCT of bone & soft tissue, aesthesioneuroblastoma as well as SNUC.[24]

The criteria used for these histological subtypes include the high degree of cell heterogeneity, the existence of unusual patterns or the presence of pseudo vascular rosettes along with IHC CD99 positivity and further cytogenetic studies for confirmation. Mucosal malignant melanoma is more aggressive than cutaneous melanoma and commonly presents with epistaxis. They have to be distinguished with other high-grade malignancies by demonstration of HMB45, S-100, vimentin as well as detectable melanin pigments under light microscopy.[25]

Malignant lymphoma of the sinonasal tract are uncommon malignancies representing 3-5% of all malignancies; NHL accounts for 60% of all the lymphomas occurs exclusively in nasal cavity as a homogenous polypoid mass. In a study by Chalastras et al The most common type was the diffuse large B cell lymphoma.[26] But in a study in japan reported angiocentric T cell lymphoma (35.9%) was predominant followed by B cell lymphoma (22.6%) as the predominant histological types in Japan.[27] We had equal numbers of (4.08% cases) of DLBCL of activated B cell type & extranodal NK/T cell lymphoma nasal type showing angiocentricity, necrosis and was immunohistochemically CD56 positive and CD3 negative. The patient underwent transnasal endoscopic orbital decompression with excision of mass was performed.

Poorly differentiated tumours (plasmacytoma) are the most difficult to recognize and may result in diagnostic confusion with other sinonasal SRBCTs. Our study had a case of extramedullary/extraosseous plasmacytoma (2.04%) in nasal cavity in an elderly male patient presented with a progressive unilateral nasal obstruction & epistaxis, without history of multiple myeloma which is a very unusual solitary tumour in sinonasal tract.[28]

Salivary gland tumour like Adenoid cystic carcinoma (ADCC) is the second most common salivary gland tumour in the sinonasal tracts and usually invades the lateral wall of nose sometimes showing intracranial extension due to trigeminal nerve involvement.[29] It constituted only 2.04% of all malignant tumours of sinonasal tract in our study similar to study by Manning & Batsakis.[30]

Different modalities of treatment are used for different sinonasal tumours. For most cases the treatment option is wide surgical excision followed by precision radiotherapy in cases of invasion and metastases. Chemotherapy is particularly beneficial in haematolymphoid malignancy.

CONCLUSIONS

Sinonasal and nasopharyngeal tumours usually present with vague complaints of nasal obstruction, congestion and headache which often delay the diagnosis at the time of presentation. This delay in diagnosis sometimes causes invasion & local destruction even in benign tumours. Malignant tumours have very poor prognosis and sometimes extremely difficult to categorise because of the undifferentiated histomorphology. Thus, accurate clinicoradiological correlation as well as early histopathological diagnosis supplemented with immunohistochemistry and other molecular markers are immensely important as they present in advanced stage because of its proximity to the vital structures like skull base and orbit.

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