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Pathology Section

Histomorphological and Immunohistochemcial Evaluation of Sinonasal Masses: A Cross-sectional Study from Uttar Pradesh, India

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ABSTRACT

Introduction: Masses arising in the nasal cavity and paranasal sinuses constitute a heterogeneous group of lesions, ranging from non-neoplastic inflammatory polyps to a wide spectrum of benign and malignant neoplasms. Clinically, these entities often present with overlapping features and are frequently misdiagnosed as nasal polyps. Histomorphological evaluation remains the cornerstone for diagnosing sinonasal masses; however, in certain poorly differentiated tumours, Immunohistochemistry (IHC) becomes essential for accurate classification.

Aim: The study aimed to evaluate the histomorphological and IHC profile of sinonasal masses.

Materials and Methods: The present prospective cross-sectional study included all consecutive patients presenting to the Ear, Nose and Throat (ENT) Department of a Tertiary Care Hospital in Lucknow, Uttar Pradesh, India from September 2021 to October 2022. Eighty biopsy specimens were originating from the sinonasal tract and received in the histopathology section were processed routinely with haematoxylin and eosin staining for histomorphological assessment. The parameters studied included patient's demographics (age, sex), clinical presentation, anatomical site of the lesion, gross features, and microscopic characteristics. Lesions were classified into benign and malignant categories based on established histopathological criteria. IHC was applied selectively in diagnostically challenging cases using a targeted panel comprising Pan-CK, p63, p40, S-100, Synaptophysin, LCA (CD45), HMB-45, Vimentin, CD117, and additional markers as required. The data were analysed descriptively, and results were expressed as frequencies, percentages, and mean values where applicable. Associations between categorical variables were evaluated using the Chi-square test. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were carried out using Statistical Package for Social Sciences (SPSS) software (version 26.0) and advanced Microsoft Excel tools.

Results: Of the 80 cases studied, 59 (73.75%) were benign and 21 (26.25%) were malignant. Most patients presented in the third to fourth decades 17 (21.20%), with a mean age of 38.4±2 years, and a male-to-female ratio of 1.4:1. Nasal obstruction was the most common symptom 72 (90%). Among the benign lesions, inflammatory polyps were most frequent 25 (42.38%), followed by inverted papilloma 6 (10.16%). Adenoid cystic carcinoma was the commonest malignant tumour 9 (42.87%). IHC aided diagnosis in seven morphologically challenging malignant cases.

Conclusion: Histopathological examination remains the gold standard for diagnosing sinonasal masses, many of which present clinically as polypoidal lesions. In cases of poorly differentiated tumours, IHC plays a vital role in achieving accurate and definitive diagnosis.

Keywords: Diagnostic challenges, Nasal polyps, Nasal cavity, Paranasal sinuses

INTRODUCTION

Masses arising in the nasal cavity and paranasal sinuses constitute a heterogeneous group of non-neoplastic and neoplastic lesions, including inflammatory polypoidal conditions [1]. These lesions often present with overlapping clinical features and are frequently misdiagnosed as nasal polyps. Patients typically present with symptoms such as nasal obstruction, epistaxis, rhinorrhoea, facial swelling, and anosmia [2]. Owing to their varied clinicopathological presentations, lesions of the sinonasal region pose significant challenges in diagnosis, prognostication, and management [3]. Neoplastic lesions of the nasal cavity and paranasal sinuses frequently mimic chronic inflammatory conditions, further complicating clinical evaluation.

Among neoplastic sinonasal lesions, benign tumours are more common than malignant ones. Schneiderian papilloma is the most frequent benign tumour, whereas Squamous Cell Carcinoma (SCC) predominates among malignancies. Cancers of the nasal cavity and paranasal sinuses account for only 0.2-0.8% of all malignant neoplasms, and SCC represents approximately 3% of all head and neck cancers [4]. The global incidence of sinonasal SCC is approximately one per 100,000 population. Although rare, malignant tumours of this region tend to have a prolonged clinical course and are associated with high morbidity due to frequent local recurrences.

Diagnosing sinonasal masses can be challenging due to their diverse morphological patterns, unique histopathological features, and complex embryologic origins. In such cases, IHC becomes indispensable for accurate diagnosis [5]. Clinical, radiological, and endoscopic assessments alone cannot reliably differentiate simple nasal polyps from neoplastic polypoidal lesions. Thus, histopathological examination remains the gold standard for definitive diagnosis [6]. It is therefore essential that all polypoidal lesions of the sinonasal tract be submitted for histopathological evaluation, with special stains and IHC applied when required.

The present study highlighted the diagnostic value of a selective, targeted IHC panel applied only to morphologically challenging sinonasal lesions, demonstrating that even limited IHC use can substantially improve diagnostic accuracy in resource-constrained settings. By evaluating detailed histomorphology with selective IHC, the study provides practical evidence on distinguishing aggressive

malignancies from benign mimickers, a challenge frequently encountered in routine pathology. Thus the present study aimed to evaluate the histomorphological spectrum of sinonasal masses and determine the diagnostic utility of selective IHC markers, particularly in lesions with undifferentiated or poorly differentiated morphology.

MATERIALS AND METHODS

The present prospective cross-sectional study was conducted on all 80 consecutive cases diagnosed with sinonasal masses in the ENT Department of a tertiary care hospital in Lucknow, Uttar Pradesh, India. The study was carried out prospectively over a period of 14 months from September 2021 to October 2022 following approval from the Institutional Human Ethics Committee (HIMSB/MD/MS(20)/RD-4057/2022).

Inclusion and Exclusion criteria: The study included all biopsy specimens originating from the sinonasal tract and received in the histopathology section of the Department of Pathology. Specimens were excluded if the lesion represented an extension into the sinonasal region from neighbouring anatomical structures, if the mass was a recurrent lesion, or if the biopsy material was deemed inadequate or non-representative for reliable interpretation.

Study Procedure

For each patient, all relevant demographic and clinical data- including age, gender, duration of symptoms, presenting complaints, aggravating and relieving factors, and pertinent past history- were collected from medical records. Radiological details and additional information provided on histopathology requisition forms were also incorporated to ensure comprehensive documentation.

Biopsy specimens obtained from the nasal cavity were fixed in 10% neutral buffered formalin and processed using standard histopathological techniques. A detailed gross examination was performed, noting the number of tissue fragments received (single or multiple) and recording precise measurements in three dimensions. After routine tissue processing and paraffin embedding, sections were cut and stained with Haematoxylin and Eosin (H&E). Microscopic evaluation of these slides was undertaken systematically, and findings were recorded in detail. Special stains, particularly the Periodic Acid Schiff (PAS) stain, were employed when fungal aetiologies such as *Aspergillus*, *Mucor*, or *Rhinosporidiosis* were clinically or histologically suspected. The IHC was applied selectively in diagnostically challenging cases using a targeted panel comprising Pan-CK, p63, p40, S-100, Synaptophysin, LCA (CD45), HMB-45, Vimentin, CD117, and additional markers as required.

STATISTICAL ANALYSIS

For statistical analysis, categorical variables were summarised as frequencies and percentages, whereas continuous variables were expressed as mean values with corresponding standard deviations. Associations between categorical variables were evaluated using the chi-square test. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were carried out using SPSS software (version 26.0) and advanced Microsoft Excel tools.

RESULTS

A total of 80 sinonasal masses were evaluated over a period of 14 months. Of these, 59 cases (73.75%) were benign and 21 cases (26.25%) were malignant [Table/Fig-1]. The largest proportion of patients 17 (21.20%) presented in the third to fourth decade of life, with a mean age of 38.4±2 years and a male predominance 47 (58.80%). The male-to-female ratio was 1.4:1. Nasal obstruction or a visible nasal mass 72 (90%) was the most frequent presenting symptom, followed by epistaxis 31 (38.70%). Right-sided lesions were slightly more common 41 (51.30%) compared to left-sided lesions 35 (43.70%). Radiological evaluation was available in 46 cases (57.50%), including CT in 28 cases (35%) and MRI in 18 cases (22.50%). Most cases showed overlapping features [Table/Fig-2].

Benign lesion (n=59)	No. of cases and percentage	Malignant lesion (n=21)	No. of cases and percentage
Inflammatory polyp	n=25 (42.38%)	Adenoid cystic carcinoma	n=9 (42.87%)
Inverted papilloma	n=6 (10.16%)	Olfactory neuroblastoma	n=3 (14.29%)
Granulomatous inflammation	n=6 (10.16%)		
Haemangioma	n=6 (10.16%)	Malignant melanoma	n=2 (9.52%)
Allergic polyp	n=5 (8.48%)	Lymphoma	n=2 (9.52%)
Fungal diseases	n=4 (6.78%)	Undifferentiated CA	n=1 (4.76%)
Angiofibroma	n=4 (6.78%)	Osteoblastic osteosarcoma	n=1 (4.76%)
Neurofibroma	n=1 (1.70%)	Small round cell neoplasia	n=1 (4.76%)
Meningioma	n=1 (1.70%)	Squamous Cell Carcinoma (SCC)	n=1 (4.76%)
Vestibular verruca vulgaris	n=1 (1.70%)	Non-keratinising poorly diff malignancy	n=1 (4.76%)

[Table/Fig-1]: Distribution of benign and malignant cases on histomorphology.

CT scan finding (n=28)*			MRI finding(n=18)*		
Features	Number	Percentage	Features	Number	Percentage
Hyperdense, Homogenous mass	3	10.71%	Heterogenous	6	33.33%
Hyperdense, Heterogenous mass	5	17.85%	Homogenous	1	5.55%
Hypodense, Homogenous mass	2	7.14%	T2-Hypointense	5	27.77%
Hypodense, Heterogenous mass	1	3.57%	T2-Hyperintense	5	27.77%
Non-enhancing	5	17.85%	T1-Hypointense	3	16.66%
Contrast enhancing	3	10.71%	TI-Isointense	3	16.66%
Minimal enhancing	2	7.14%			

[Table/Fig-2]: Distribution of cases on the basis of radiology.
* Radiology was available in only 46 cases with CT performed in 28 cases and MRI in 18 cases. (Multiple radiological features were observed in individual cases; therefore, percentages do not total 100%)

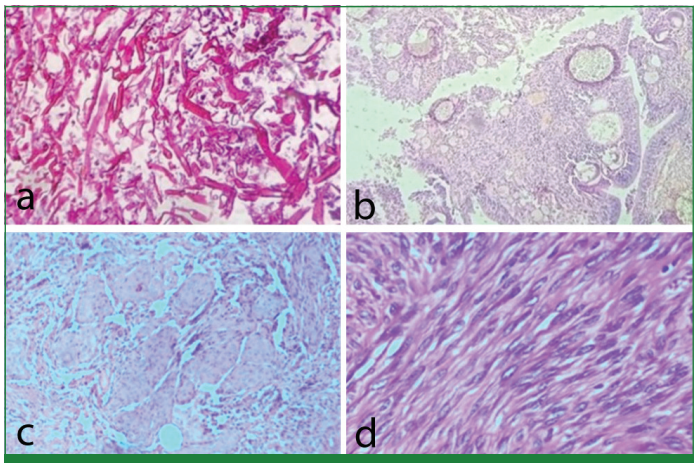
Amongst the 59 benign cases, inflammatory polyps accounted for the largest proportion 25 (42.38%), followed by granulomatous lesions 6 (10.16%), inverted papilloma 6 (10.16%), haemangioma 6 (10.16%), allergic polyps 5 (8.48%), fungal infections 4 (6.78%), angiofibroma 4 (6.78%), neurofibroma 1 (1.70%), meningioma 1 (1.70%), and vestibular verruca vulgaris 1 (1.70%) [Table/Fig-3,4]. Benign lesions commonly presented in the third to fourth decade of life 26 (44%) with a male predominance 35 (59%), and nasal mass 55 (93%) remained the leading complaint. The size of the lesions ranged from 0.8 to 3 cm.

Amongst the 21 malignant cases, adenoid cystic carcinoma was the most frequent diagnosis 9 (42.87%), followed by olfactory neuroblastoma 3 (14.29%), malignant melanoma 2 (9.52%), lymphoma 2 (9.52%), SCC 1 (4.76%), non-keratinising epithelial malignancy 1 (4.76%), undifferentiated carcinoma 1 (4.76%), osteoblastic osteosarcoma 1 (4.76%), and small round cell neoplasia 1 (4.76%). Malignant lesions predominantly occurred in the fifth decade of life, again showing male predominance. Tumour sizes ranged from 0.3 to 4.4 cm.

Of the 80 total cases, histomorphology alone provided a definitive diagnosis in 73 cases, whereas IHC was required in seven diagnostically challenging cases only [Table/Fig-3]. Application

of tailored IHC panels facilitated differentiation of morphologically overlapping entities. Sinonasal Undifferentiated Carcinoma (SNUC) was distinguished from nasopharyngeal carcinoma and epithelial malignancy using Pan-CK and p40, both of which were positive, supporting a diagnosis of SCC. Poorly differentiated SCC was confirmed with p63 and Pan-CK positivity [Table/Fig-5]. Olfactory neuroblastoma was identified by synaptophysin and S100 positivity with negative Pan-CK [Table/Fig-6]. Malignant melanoma was confirmed by HMB-45 positivity. High-grade adenoid cystic carcinoma was supported by CD117 positivity with negative Pan-CK. For small round cell neoplasms, CD45 positivity identified non-Hodgkin lymphoma, whereas Pan-CK positivity confirmed SCC in another case. Following IHC evaluation, three poorly differentiated epithelial malignancies were reclassified as SCC, increasing the total SCC cases to four 4 (19%).

When benign and malignant sinonasal masses were compared with age, gender, and site, the p-values were >0.05, indicating no statistically significant association. However, when association with clinical presentation was evaluated, the p-value was <0.05, indicating a statistically significant relationship [Table/Fig-7].



[Table/Fig-3]: a) Micrograph of mucormycosis with numerous broad aseptate hyphae (H&E, 100X); b) Micrograph of rhinosporidiosis showing many thick walled sporangia (H&E, 100X); c) Micrograph showing classical nests of meningothelial cells (H&E, 100X); d) Micrograph showing spindle shaped cells with wavy nuclei (H&E, 100X).

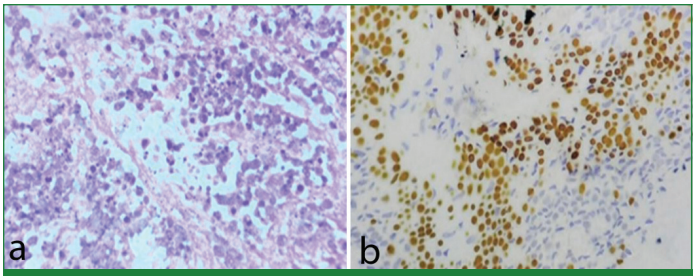
DISCUSSION

A total of 80 sinonasal lesions, including nasal endoscopic biopsies and maxillectomy specimens, were examined histopathologically. Of these, 73.75% (n=59) were benign and 26.25% (n=21) were malignant, a distribution very similar to that reported by Bhattacharya J et al., Regmi S et al., and Mukherjee T et al., [7-9]. These consistent findings across studies highlight that benign lesions continue to constitute the majority of sinonasal masses encountered in routine clinical practice. The mean age in our cohort was 38.4±2 years, with the highest frequency in the third to fourth decade, and males outnumbered females (ratio 1.4:1), reflecting demographic patterns described in earlier studies by Agarwal P et al., and Kulkarni A et al., [6,10]. The absence of statistically significant associations between demographic variables and lesion type (p=0.27, p=0.93) suggests that age and gender are poor predictors of biological behaviour in sinonasal pathology.

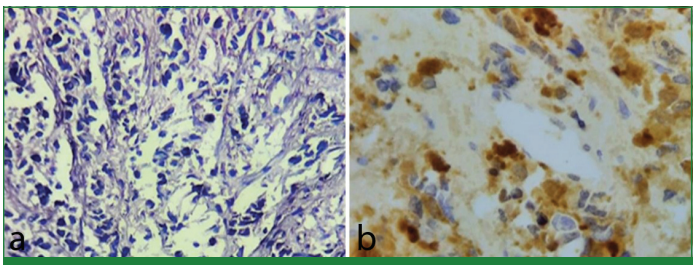
Clinically, nasal obstruction or mass was the most frequent presenting symptom (90%), followed by epistaxis (38.70%) and rhinorrhoea (26.20%), findings corroborated by Mukherjee T et al., Bakari A et al., and Lathi A et al., [9,11,12]. The significant association between symptoms and lesion type (p=0.0009) is biologically plausible, malignant tumours tend to present with epistaxis, rapid obstruction, or pain due to their infiltrative growth, while benign lesions usually exhibit indolent progression. Although right-sided lesions were slightly more common (51.30%), followed by left-sided (43.70%), laterality did not significantly correlate with lesion type (p=0.14). Divergent patterns reported in other studies, such as the bilateral predominance seen by Bakari A et al., or the left-sided preference noted by Bist SS et al., likely arise from population differences, referral patterns, and sample heterogeneity rather than genuine biological variation [2,11]. Larger mean sizes were observed in inverted papilloma (3 cm), allergic polyps (2.5 cm), and angiofibromas (2.5 cm), reflecting their expansile or vascular nature and explaining their presentation with obstruction or bleeding. Fungal lesions and haemangiomas showed moderate sizes (2.1 cm), consistent with their limited but clinically significant growth. Inflammatory polyps (1.7 cm) and granulomatous diseases (0.8 cm) were smaller, aligning with their more localised, chronic inflammatory behaviour and earlier detection. Rare lesions such as neurofibroma, meningioma, and verruca vulgaris showed variable

S. no.	Histopathological diagnosis	Morphology	IHC	Final diagnosis
1.	Sinonasal undifferentiated carcinoma/Nasopharyngeal carcinoma/ epithelial malignancy/Basaloid SCC	-Large round to oval polygonal cells -lobular pattern -brisk mitotic activity -extensive necrosis and apoptosis	Pan-CK+ve P40+ve	SCC-Poorly differentiated
2.	Olfactory Neuroblastoma/ Epithelial malignancy	-Nest of tumour cells -fibrillary stroma -necrosis present	SYN+ve S100+ve Pan-CK-ve	Olfactory neuroblastoma
3.	Spindle cell malignancy/ malignant melanoma	-sheets and fascicles of spindle cells, bizarre nuclei -foci of lymphoid aggregate	Vimentin+ve HMB45+ve	Malignant Melanoma
4.	Adenoid cystic carcinoma/ HPV associated sinonasal carcinoma	-Solid island and trabeculae of basaloid cells -Frequent mitosis -Focal necrosis -Cribriform pattern -Perineural invasion	CD117-+ve Pan-CK-ve P16-ve	Adenoid cystic carcinoma
5.	Poorly differentiated malignancy/SNUC/Others	-polygonal appearing cells -Necrosis	P63 +ve Pan-CK +ve	SCC-Poorly differentiated
6.	Small round cell neoplasia/ NHL/Neuroblastoma / Poorly differentiated malignancy	-diffuse round blue cell --vague nodule	CD45 +ve PCK-ve HMB45-ve S100-ve	Non-hodgkin's lymphoma
7.	Small round cell/Epithelial Malignancy/SNUC	-Nest and sheet of small round cell -Lobular pattern -Occasional clear cell	Pan-CK+ve CD45-ve P63-ve S100-ve	SCC-Poorly differentiated

[Table/Fig-4]: Expression of Immunohistochemistry (IHC) in seven troublesome malignant cases.



[Table/Fig-5]: a) Micrograph showing poorly differentiated tumour cells arranged in diffuse sheets (H&E, 100X). b) Micrograph showing p40 nuclear positivity in the poorly differentiated tumour cells (H&E, 100X).



[Table/Fig-6]: a) Micrograph of olfactory neuroblastoma showing monotonous tumour cells with rounded nuclei, indistinct nucleoli and scanty cytoplasm (H&E, 100X). b) Micrograph of olfactory neuroblastoma showing sustentacular cells highlighted by S100 (IHC, 100X).

Parameters	Benign	Malignant	Chi -square test (χ^2 value)	p-value	Degree of freedom (df)
Age (years)					
0-40	37	12	2.578	0.27	2
41-60	16	4			
61-80	6	5			
Gender					
Male	34	13	0.007	0.93	1
Female	25	8			
Site					
Right	34	7	3.932	0.14	2
Left	22	13			
Bilateral	3	1			
Clinical presentation					
Nasal mass	53	19	24.54	p=0.0009, statistically significant	7
Epistaxis	18	13			
Rhinorrhoea	17	4			
Nasal congestion	13	3			
Hyposmia/anosmia	12	1			
Headache/pain	8	5			
Facial swelling	0	5			
Visual disturbances	0	2			

[Table/Fig-7]: Association between the clinical parameters with benign and malignant sinonasal mass.

but generally modest sizes, corresponding to their slow-growing nature. Overall, lesion size helped differentiate expansile neoplastic processes from smaller inflammatory or granulomatous conditions.

Amongst the benign lesions, inflammatory polyps were the most prevalent (42.38%), consistent with findings from Garg D and Mathur K [13]. These lesions exhibited typical features of stromal oedema, sparse collagen, and chronic inflammatory infiltrates, reaffirming their pathogenesis as a chronic mucosal inflammatory response [14]. Granulomatous diseases accounted for 10.16% of benign cases and included rhinoscleroma, rhinosporidiosis, and one nonspecific granulomatous lesion. Rhinoscleroma cases demonstrated classical Mikulicz cells and plasma cell-rich infiltrates, matching descriptions by Modh SK et al., while rhinosporidiosis cases displayed large sporangia with endospores, consistent with the established pathology described in earlier reports [15-17]. The relatively younger age distribution observed in these cases likely reflects regional epidemiological differences.

Allergic polyps constituted 8.48% of benign lesions and showed characteristic goblet cell hyperplasia, basal lamina thickening, and eosinophilic infiltrates, supporting their immunoallergic aetiology as described by Dasgupta A et al., and others [18,19]. Fungal lesions, mainly mucormycosis (6.78%), were seen predominantly in older patients and showed broad aseptate hyphae with angioinvasion, aligning with reported patterns by Parmar NJ et al., [20] and reflecting the tissue-destructive nature of mucor species [21,22].

Inverted papilloma (10.16%) exhibited typical endophytic epithelial proliferation and myxoid stroma [23,24]. Their known association with smoking-related epithelial dysregulation and potential for malignant transformation, particularly in smokers (24.60%), reinforces the necessity for strict follow-up. Haemangiomas (10.16%) showed lobular capillary architecture and commonly presented with epistaxis, a feature explained by their vascular nature [25,26]. Angiofibromas (6.78%) demonstrated fibrovascular stroma with slit-like blood vessels, corroborating classical histopathological criteria described in the literature [27,28]. Rare benign lesions-neurofibroma, meningioma, and verruca vulgaris-were also identified, each displaying classic microscopic features known for these uncommon sinonasal entities [29-32].

Malignant tumours accounted for 26.25% of all cases. Unlike several earlier studies, Regmi S et al., Kulkarni A et al., Devi CP et al., that identified SCC as the predominant malignancy, adenoid cystic carcinoma was the most common in our study (42.87%) [8,10,33]. This difference is likely attributable to our exclusion of nasopharyngeal lesions, where SCC is more frequently encountered. IHC was indispensable in seven challenging malignant cases, highlighting its vital role in differentiating morphologically overlapping entities.

Adenoid cystic carcinoma cases exhibited the expected cribriform, tubular, and solid patterns. The solid subtype showed necrosis, nuclear atypia, and frequent mitoses, consistent with its known aggressive behaviour and poorer prognosis. CD117 positivity helped distinguish these tumours from certain HPV-associated sinonasal carcinomas, underscoring the importance of ancillary testing. Although only one case of moderately differentiated SCC was identified morphologically, three additional cases required IHC confirmation using Pan-CK, p63, and p40, highlighting the diagnostic complexity of poorly differentiated sinonasal malignancies and supporting observations by Bhattacharya J et al., and Kulkarni A et al., [7,10].

Olfactory neuroblastoma cases occurred exclusively in young males and showed classic lobular architecture with fibrillary neuropil. Synaptophysin and S100 positivity were crucial for diagnosis and differentiation from small round cell mimickers. Malignant melanoma cases exhibited typical spindle or epithelioid morphology with prominent nucleoli and intense HMB45 and S100 positivity, consistent with their aggressive clinical course noted in previous studies [34]. Lymphomas displayed angioinvasion and necrosis, with CD45 confirming their haematolymphoid origin, and their features correlated well with extranodal NK/T-cell or B-cell lymphomas described earlier [35,36]. The single osteoblastic osteosarcoma showed copious malignant osteoid and pleomorphic cells, an exceedingly rare presentation consistent with previously documented cases [37].

Overall, the study reinforces the central role of histopathology-supplemented by targeted IHC-in accurately diagnosing sinonasal masses. While radiology delineates anatomical extent, only microscopic evaluation can reliably differentiate inflammatory, benign neoplastic and malignant processes. Treatment decisions hinge on precise histological classification, as benign lesions often require surgical removal, whereas malignant tumours necessitate a multimodal approach. The generally poor prognosis associated with sinonasal malignancies arises from their nonspecific early symptoms,

complex anatomical constraints, and limited responsiveness to adjuvant therapies. These findings highlight the need for early clinical suspicion, thorough histopathological assessment, and incorporation of ancillary techniques to improve diagnostic accuracy and patient outcomes.

Limitation(s)

The present study is limited by its small sample size and single-centre design, which may reduce generalisability. The one-year duration may not reflect long-term trends in sinonasal pathology. Radiological correlation and clinical follow-up were not uniformly available, limiting assessment of tumour behaviour and outcomes.

CONCLUSION(S)

Sinonasal masses encompass a wide spectrum of benign and malignant lesions, often presenting with overlapping clinical and radiological features that pose diagnostic challenges. In this study, benign lesions predominated, with inflammatory polyps being the most common entity, whereas adenoid cystic carcinoma was the leading malignancy. Histopathology remained the cornerstone of diagnosis; however, IHC played a crucial role in resolving difficult or ambiguous cases and ensuring accurate tumour classification. The significant association between clinical presentation and lesion type further highlights the importance of integrated clinicopathological evaluation. Early and precise diagnosis-supported by targeted IHC panels where necessary- can facilitate appropriate therapeutic decision-making and improve patient outcomes.

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