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A TERTIARY CARE CENTRE STUDY OF MALIGNANT SINONASAL MASSES

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ABSTRACT

Background: The accurate diagnosis of sinonasal tract tumors is challenging as there is considerable overlapping between clinical features, radiology, histologic and immuno-phenotypic findings. Immunohistochemistry (IHC) aids in reaching a diagnosis. The objectives of the current study were to analyse the clinico-pathological, histomorphological and IHC characteristics of malignant sinonasal masses. **Materials and Methods:** This is a retrospective case series that included 268 cases of nasal mass. The clinico-pathological findings, histomorphology and IHC profile of all the malignant masses (n=25) were analysed. **Results:** The study included 268 non-neoplastic cases that were sinonasal polyps, fungal and granulomatous masses, angiofibroma, inverted papilloma etc. and 25 cases of malignant sinonasal mass. Based on the comprehensive histomorphological and IHC profile, 68% (17/25) cases were epithelial malignancies, 12 %(3/25) mesenchymal tumours, 16%(4/25) hematolymphoid malignancies and 4%(1/25) case was of malignant melanoma. The M: F ratio was 1.2:1.The maximum no. of cases 24% (6/25) were between the ages of 51-60 years with mean age of 45.84 years. The major complaint of the cases were nasal obstruction, intermittent epistaxis, rhinorrhoea, hyposmia, eye related symptoms, swelling over face and headache. **Conclusion:** Malignant sinonasal mass comprises histogenetically diverse entities with overlapping morphologic features. To reach the correct diagnosis histology with IHC must be combined with the imaging findings, and clinical findings, as there are significant differences in therapy and overall outcome.

INTRODUCTION

Malignancies of the nasal cavity and paranasal sinuses comprise only 0.2–0.8 percent of all malignant neoplasms[1] and because of the close anatomic proximity of the paranasal sinuses with the orbits and skull base, most include disease extension into these structures. Sinonasal malignancies most commonly arise in the maxillary sinus (60%), followed by the nasal cavity (20–30%), the ethmoid sinus (10–15%), and the sphenoid and frontal sinuses (<1%).[2] It is very challenging to reach the accurate diagnosis of sinonasal tract tumors as the biopsies are generally small and limited. They also show considerable overlapping between clinical features, radiology, histologic and immunophenotypic findings. A panel of immunohistochemical (IHC) markers should aid in reaching a definitive diagnosis. The objectives of the current study were to analyse the clinico-pathological, histomorphological and IHC characteristics of malignant sinonasal masses.

MATERIALS AND METHODS

This is a retrospective case series that included total 293 cases that were received as sinonasal mass in the department of pathology of a tertiary care centre, among which 25 cases were of malignant sinonasal mass and remaining 268 cases were non-neoplastic lesions and benign neoplasm. Lesions arising from nasopharyngeal region and external nose were not included in the study. The biopsy tissues were routinely processed for histopathological examination and were stained by Hematoxylin and Eosin (H&E) stain. Special stains were used wherever required. The clinical details and imaging studies were also obtained. Microscopic examination was done and the diagnosis was given. Neoplastic lesions were categorized as per the current WHO classification. IHC staining was performed on cases with diagnostic difficulties. The clinico-pathological findings, histomorphology and IHC profile of all the malignant cases (n=25) were analysed. IHC markers included known lineage-specific markers (Pan cytokeratin (AE1/AE3), p40, CD117, S100, HMB45, Desmin, and Myogenin), basal cell marker-P63, markers of neuroendocrine differentiation (Chrmogranin and Synaptophysin), markers for hematolymphoid lineage (leukocyte common antigen (LCA), CD20, CD3, CD56, Granzyme along with proliferation marker i.e. Ki67. The FLI1, product of chromosomal translocation between the FL1 gene and EWS gene, were considered for ancillary marker to confirm the diagnosis of Ewing/PNET. Markers were evaluated for cytoplasmic staining except for p40, P63, S100, FLI-1 and Ki67, which had positive

results for nuclear expression, and CD99, for which membranous staining was considered.

RESULTS

In the current study, total 293 cases, received as sinonasal mass, were included. Out of 293 cases, 25 cases were of malignant sinonasal mass and 268 cases were reported as non-neoplastic and benign lesions that included sinonasal polyps, fungal and granulomatous masses, angiofibroma and inverted papilloma etc. The male to female ratio (M: F) among malignant sinonasal masses was 1.2:1. The maximum number of cases 24% (n=6/25) were between the ages of 51-60 years with mean age of 45.84 years. The most common clinical complaint of the cases was nasal obstruction followed by intermittent epistaxis, rhinorrhoea, hyposmia, eye related symptoms, swelling over face and headache.

The malignant sinonasal masses were categorized according to epithelial, mesenchymal and hematolymphoid malignancy after comprehensive histomorphological and IHC immunostaining. 68% (n=17/25) cases were of epithelial malignancy, 16% (n=4/25) cases of hematolymphoid lineage, 12% (n=3/25) cases of mesenchymal malignancy, and one case was of mucosal malignant melanoma.

Epithelial malignancy: Adenoid cystic carcinoma 16% (n=4/25) and sinonasal undifferentiated carcinoma (SNUC) 16% (n=4/25) were the commonest among the epithelial malignancy followed by non-keratinising squamous cell carcinoma(SCC) 12% (n=3/25), and small cell undifferentiated neuro-endocrine carcinoma, malignant round cell tumour, epithelial myoepithelial carcinoma, SCC-small cell variant and adenocarcinoma-intestinal type with mucin production.(Figure 1-5)

Mesenchymal malignancy: Mesenchymal malignancy constituted 8% (n=2/25) of malignant sinonasal masses and reported as rhabdomyosarcoma and leiomyosarcoma. (Figure 8)

Hematolymphoid malignancy: 8% (n=2/25) cases were reported as Diffuse Large B-cell Lymphoma (DLBCL) followed by one case 4% (n=1/25) of Extranodal NK T cell Lymphoma (nasal type) and Peripheral T cell Lymphoma. Single case was reported as Ewing's sarcoma/PNET and one as mucosal melanoma. (Figure 6)

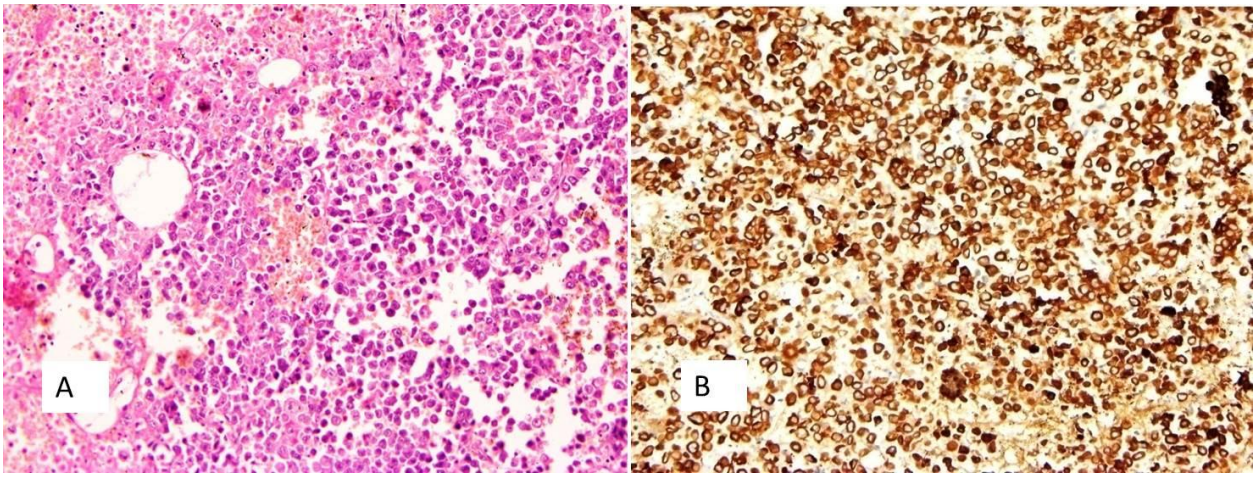

Fig.1: A: Sinonasal undifferentiated carcinoma (H&E X 100), B: Pan CK (DAB x100).

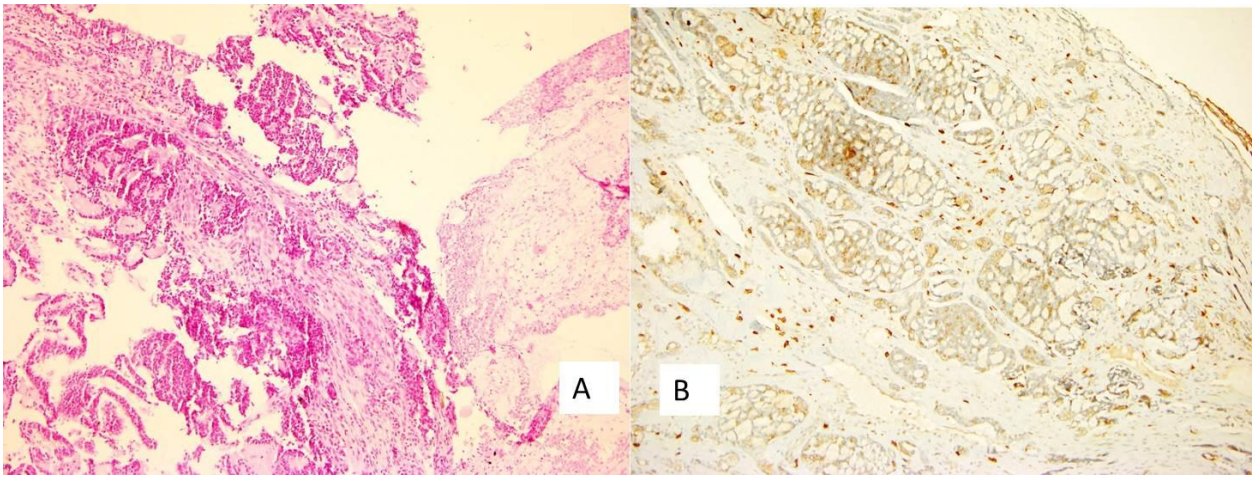

Fig.2: A: Adenoid cystic carcinoma (H&E X 100), B: CD117 (DAB x100).

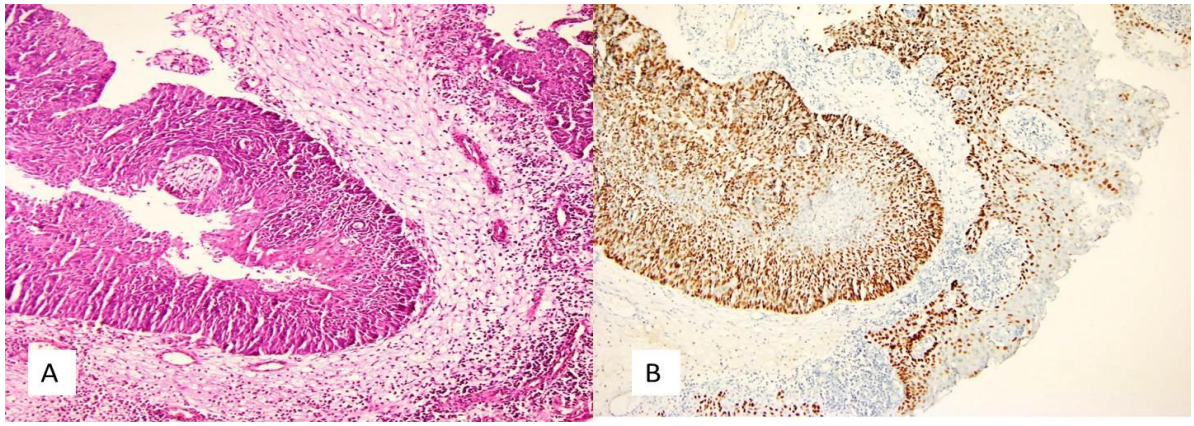

Fig.3: A: Non keratinizing squamous cell carcinoma (H&E X 100), B: p40 (DAB x100).

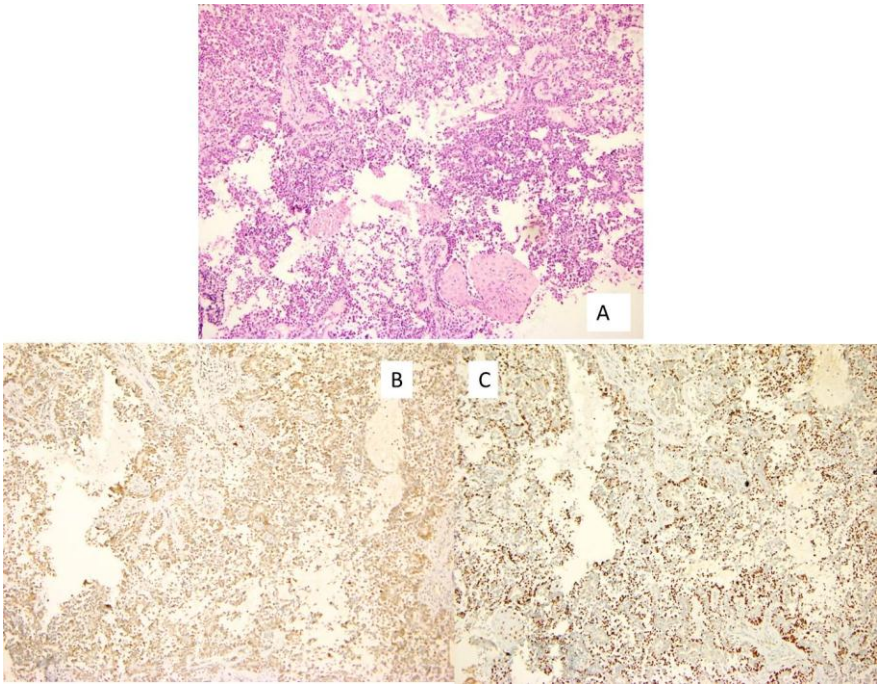

Fig.4: A: Epithelial myoepithelial carcinoma (H&E X 100), B: CD117(DAB x100), C: p63(DAB x100).

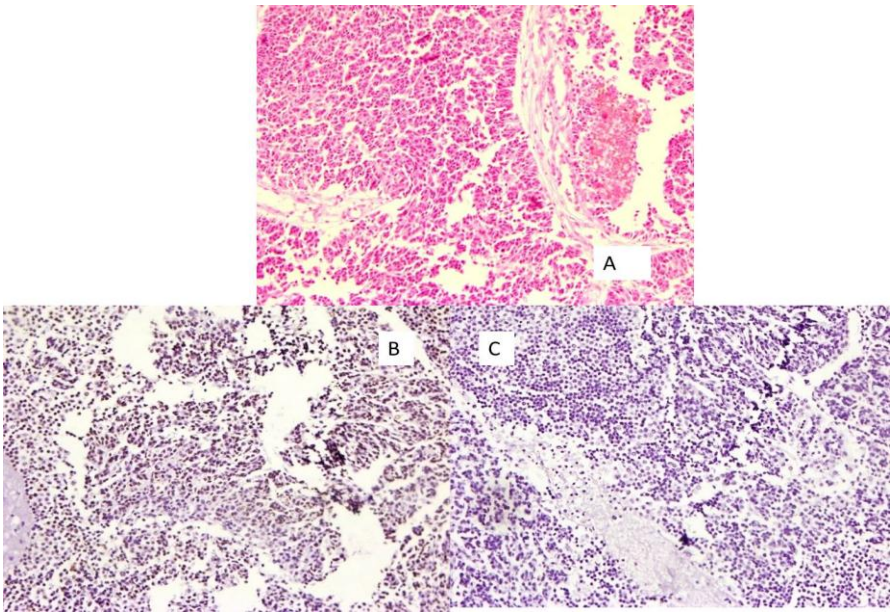

Fig.5: A: Squamous cell carcinoma-small cell varient(H&E X 100), B: p40(DAB x100), C: CD99 (DAB x100).

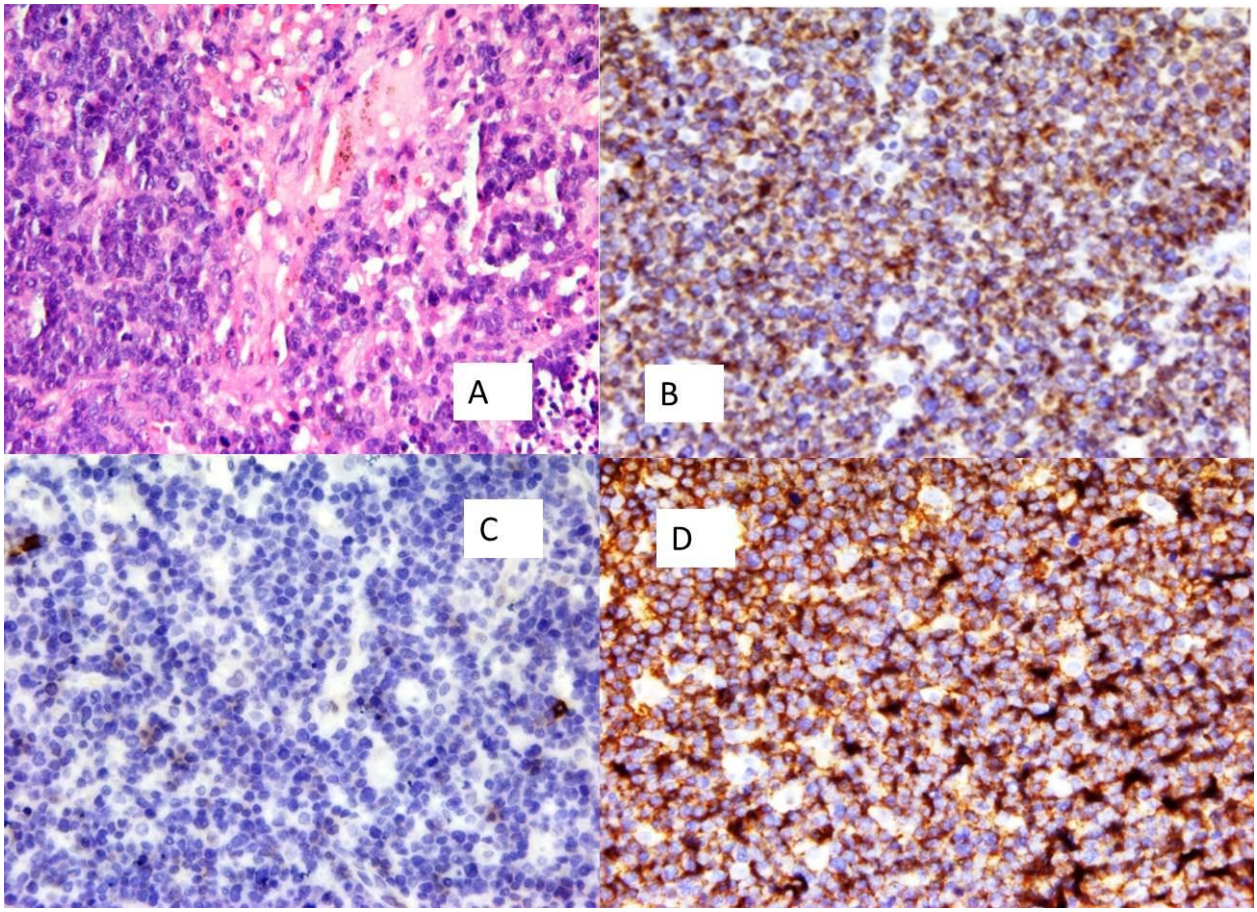

Fig. 6: A: Extranodal NK T cell Lymphoma (H&E X 100), B: CD 3 (DAB x100), C: CD 20 (DAB x100), D: CD 56 (DAB x100).

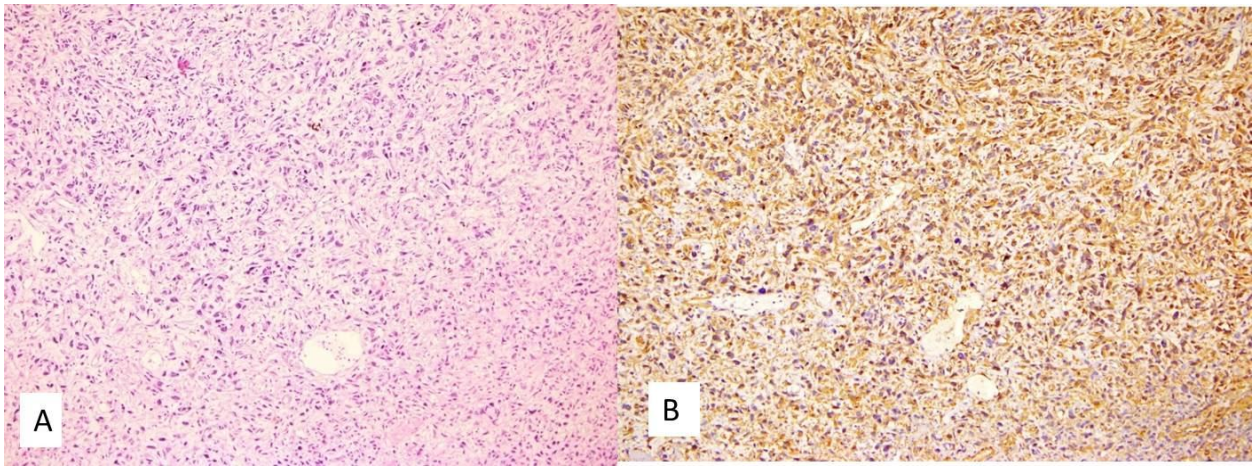

Fig.7: A: Leiomyosarcoma (H&E X 100), B: SMA (DAB x100).

DISCUSSION

The current study was carried out to evaluate the clinico-pathological, histomorphological and IHC characteristics of malignant sinonasal masses. All age groups and both sexes were affected except the first decade as there was no case seen of that age group. The study revealed predilection for males, demonstrating a male to female ratio of 1.2:1. It was higher (male-to female ratio of 1.7:1) in the study by Zafar et al[1], while a study from Nigeria[2] revealed an opposite ratio showing female preponderance (M:F ratio of 1:1.2).

The 2nd to 5th decades of life was found to be the most vulnerable period for development of sinonasal masses. Bakari et al.[2] had reported a peak incidence of 33 years, while for Zafar et al.[1], the mean age of presentation was 22.5 years. Malignancies have been reported generally after the fourth decade of life. All patients presented with different clinical complaints, but nasal obstruction (74.2%) was the most common presentation followed by intermittent epistaxis (71.3%), rhinorrhoea, hyposmia, eye related symptoms, swelling over face and headache. It was supported by the study conducted by Humayun et

al.[3] Radiological imaging was received in few cases and co-related.

Malignancies of sinonasal tract are rare.[5] The maxillary sinus is the most common site of origin[6], and the most common histological type is squamous cell carcinoma in most of the studies.[2,3,4] Whereas in our study sinonasal undifferentiated carcinoma(SNUC) and adenoid cystic carcinoma were the most common malignancy with 4 cases each (16%) followed by 2 cases of non-keratinising SCC. In a study by Kalpana et al[8], SNUC was comprised of 41% among all malignant tumors.

SNUC is a rare tumor that involves multiple sites of the sinonasal tract and often extends beyond the anatomic confines. It typically presents as a rapidly enlarging tumor mass. It lacks glandular or squamous features, and is not otherwise classifiable. Hence, it is a tumor of exclusion, comprising 3–5% of all sinonasal tract carcinomas.[9-12] It affects a wide age range, but is most common in 50–60 year olds, with men predilection. The most common clinical presentation is symptoms of nasal obstruction because of large, midline, widely destructive masses that arises from the nasal cavity but rapidly expanding into adjacent sites (60% have orbit or skull base extension).[9]

On histomorphological examination, these are cellular tumors, arranged in sheets, lobules, and trabeculae of atypical, but monomorphic polygonal cells, having round to irregular nuclei, and moderate cytoplasm (Figure 1). The nuclear chromatin is vesicular with prominent nucleoli. Fair number of mitoses and apoptosis are also seen. In few cases, surface dysplasia and rosettes may also be present. Some tumors that show basaloid growth and rhabdoid features, the lack of SMARCB1 (INI-1) protein by immunohistochemistry may suggest a different tumor type.[13]

The malignant cells are strongly positive for epithelial markers (AE1/AE3, CK7, EMA), p16 and CD117 and focal patchy positive for p63 and negative for CK5/6, p40, CEA, CD34, desmin, S100 protein, and calretinin. These tumors show overall poor prognosis.

Adenoid cystic carcinoma is a salivary gland tumor arises from upper aerodigestive tract and characterized by its biphasic ductal and myoepithelial differentiation, tubular / cribriform / solid architecture (Figure 2).[14] Clinically, it is characterized by frequent perineural invasion, high incidence of local and distant recurrence with poor long term prognosis. In the current study, 4 cases were reported as adenoid cystic carcinomas that show CK7 positivity in epithelial component and p63 in myoepithelial cells along with CD117 positivity. All the cases were middle aged except one, who presented at the age of 19 years.

Sinonasal squamous cell carcinomas involve most commonly the maxillary sinus.[15] Symptoms include nasal obstruction; epistaxis; rhinorrhea; pain; swelling of the nose or cheek or a palatal bulge; nasal mass; or, in advanced cases, proptosis, diplopia, or lacrimation.[15] We reported two cases of non- keratinizing squamous cell carcinoma both show positivity for p40 immunostain. We reported cases of Rhabdomyosarcoma, Leiomyosarcoma and Ewing's sarcoma/PNET with the help of appropriate immunohistochemical panel which is comparable to the observation of Bijjaragi et al.[6] 2 cases of Diffuse Large B-cell Lymphoma, one case each of Extranodal NK T cell Lymphoma and Peripheral T cell Lymphoma were also reported.

CONCLUSION

Malignant sinonasal masses comprise histogenetically diverse entities with overlapping morphologic features. Because of the limited initial biopsy tissue materials, differential diagnostic difficulties may arise, and as they have different management, exact diagnosis and classification are very important. To reach the correct diagnosis histology with IHC must be combined with the imaging findings, and clinical findings, as there are significant differences in therapy and overall outcome.

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