Original Article

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Pathology Section

Histopathological and Immunohistochemical Features of Nasal and Paranasal Sinus Neoplastic Lesions- A Cross-sectional Study

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ABSTRACT

Introduction: Majority of nasal and paranasal sinus lesions clinically present as polypoidal lesions, complicating the diagnosis for the physician which inturn hampers the patient prognosis and in few cases survival of patient, so histopathology is imperative to arrive at the diagnosis. Carcinoma of the paranasal sinus cavity is rare representing 3-4% of head and neck tumours and less than 1% of all malignancies.

Aim: To examine the histopathological patterns of neoplastic nasal and paranasal sinus lesions, to categorise neoplastic lesions into benign and malignant types, to find the relation of these lesions with age and sex and also to find the utility of Immunohistochemistry (IHC) in differentiating morphologically suspicious lesions.

Materials and Methods: The present cross-sectional study was carried out between January 2020-January 2021. A total of 22 cases were taken for the study, which were received as nasal and paranasal sinus lesions in histopathology. All the lesions received were processed according to standard protocol and diagnosed histopathologically and confirmed by relevant special stains and immunohistochemical analysis (CD99, CD56 etc.).

Results: Out of 22 cases, 16 were benign and six were malignant. The lesions were commonly detected between fourth to sixth decades. Male to female ratio was 1.4:1. The ratio of benign to malignant lesion was 2.67:1. The most common benign lesion encountered was capillary haemangioma (seven cases) and malignant lesion seen was squamous cell carcinoma (three cases), comparable to other similar studies. The IHC was done in malignant lesions for accurate diagnosis.

Conclusion: In the present study, the cases are divided into benign and malignant lesions with the help of histopathological examination. Cases showing features of malignancy were further subjected to immunohistochemical examination as to diagnose the cases precisely and thus help in patient treatment and prognosis.

Keywords: Capillary haemangioma, Diffuse large B cell lymphoma, Ewing sarcoma, Squamous cell carcinoma

INTRODUCTION

The upper respiratory tract is a complex association of nasal cavity and paranasal sinuses. This region is made up of diverse type of elements such as epithelial, glandular, lymphoid, cartilage and bone and is subjected to a variety of infections, tumour-like and true neoplastic conditions [1]. Nasal cavity and paranasal sinus are the site of diverse group of tumours due to their varied histology. The tumours include neoplasms derived from mucosal epithelium, seromucinous glands, soft tissues, bone, cartilage, neural/neuroectodermal tissue, haematolymphoid cells and the odontogenic apparatus [2]. In 2017, World Health Organisation (WHO) has classified sinonasal tumours into malignant epithelial tumours, benign epithelial tumours, soft tissue tumours, tumours of bone and cartilage, haemotolymphoid tumours, neuroectodermal, germ cell tumours and secondary tumours [2].

The most frequent lesion of the nasal cavity is nasal polyps which are either allergic or inflammatory in nature. The incidence of nasal polyp in India is reported to involve 4% of the population. Inverted papilloma is a very common non neoplastic lesion of the sinonasal region. Carcinoma of the paranasal sinus cavity is rare representing 3-4% of head and neck tumours and less than 1% of all malignancies. An 80% of these tumours are squamous cell carcinoma with adenocarcinoma and adenoid cystic carcinomas accounting for 10%. The maxillary sinus is most commonly involved with tumour, followed by the nasal cavity, the ethmoidal sinus and then the frontal and sphenoid sinuses [3].

Nasal obstruction is the most frequent presenting complaint, followed by rhinorrhoea, hyposmia, intermittent epistaxis, headache, facial swelling and eye related symptoms [4]. Males are twice more commonly affected than females and adults more than children. The incidence of nasal and paranasal sinus tumours is on rise due to innumerable reasons. Allergens, air pollution and industrial carcinogens predispose to the development of benign lesions. Tobacco, alcohol and occupational exposure to heavy metal particles such as nickel and chromium, particularly for workers in the leather, textile, furniture and wood industries predispose to the development of malignancies [3].

The presentation of gross appearance of various nasal and paranasal sinus lesions is very similar, with many of the lesions presenting as polypoidal lesions. Histopathological examination thus plays an important role in diagnosis along with imaging studies. Staging of carcinomas is effectively done using histopathological examination. Lesions with overlapping features are further diagnosed with the help of IHC [5]. The objective of the present study was to examine the histopathological patterns of neoplastic nasal and paranasal sinus lesions. To categorise neoplastic lesions into benign and malignant types. To relate these lesions with age and sex and to utilise IHC in differentiating morphologically suspicious lesions.

MATERIALS AND METHODS

The present cross-sectional study was done on 22 cases from lesions of nasal cavity and paranasal sinuses for a period of one year from January 2020-January 2021 received in surgical pathology laboratory from the department of ENT in a tertiary care hospital. The Institutional Ethics Committee (IEC 612), approved the study.

Inclusion criteria: All benign and malignant neoplastic nasal and paranasal sinus lesions.

Exclusion criteria: Metastasis to nasal and paranasal sinus region, Lesions arising due to injury, Autolytic specimens/specimens with autolytic changes.

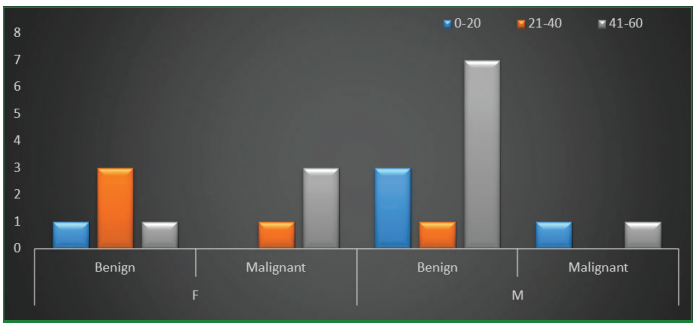
All tissues were fixed in 10% neutral buffered formalin and processed and then stained with Haematoxylin and Eosin (H&E). The histopathological features were studied and IHC was performed, wherever needed to arrive at an accurate diagnosis.

STATISTICAL ANALYSIS

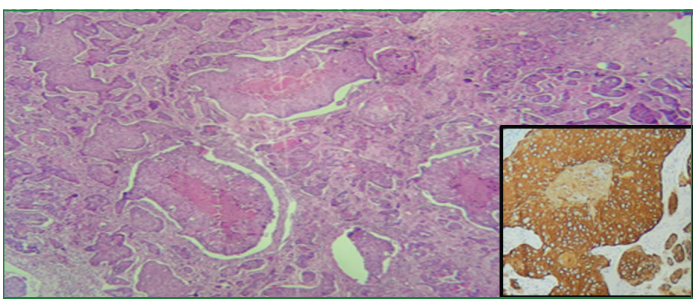
The statistical software Statistical Package for the Social Sciences (SPSS) version 22.0 was used for analysis of data in Microsoft Excel spread sheet generate tables, graphs. Proportions were described as percentages.

RESULTS

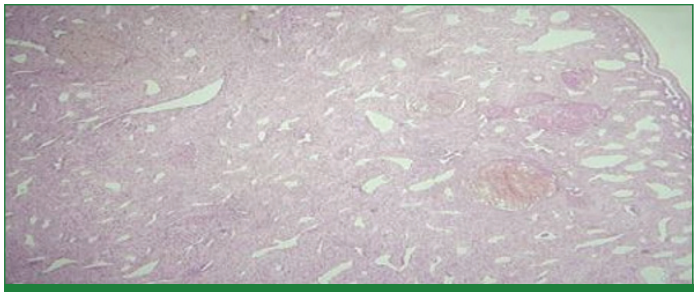
The neoplastic lesions of nasal cavity and paranasal sinuses were classified as benign and malignant masses. In this study, patients age were in range of 16-57 years. Majority of cases were in age group of 41-60 years with mean age being 36.5 years. There was a male preponderance with 13 patients being male and nine patients being female [Table/Fig-1]. On histopathological examination, there were 16 benign neoplastic lesions and six malignant lesions. The most common benign lesion encountered was capillary haemangioma (seven cases) and malignant lesion seen was squamous cell carcinoma (three cases) [Table/Fig-2]. Four cases of angiofibroma [Table/Fig-3], four cases of inverted papilloma [Table/Fig-4] and one case of Schwannoma seen [Table/Fig-5]. Other malignant lesions seen were one case of Ewing sarcoma [Table/Fig-6]. IHC was done on the malignant lesions and the results is shown in the [Table/Fig-7]. Two of the malignant cases showed ambiguity in their histopathological diagnosis and were diagnosed as sinonasal undifferentiated carcinoma. The lesions were put under immunohistochemical panel, the initial panel was inconclusive, and the second panel of IHC diagnosed one of the lesion as Diffuse Large B Cell Lymphoma (DLBCL) [Table/Fig-8] and the other as NK-T cell lymphoma [Table/Fig-9].



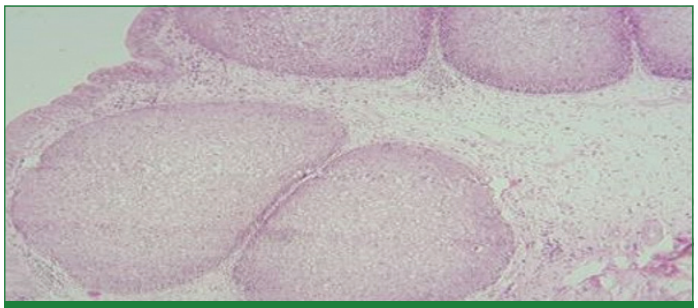
[Table/Fig-1]: Graph showing distribution of benign and malignant lesions in different age groups in males and females.



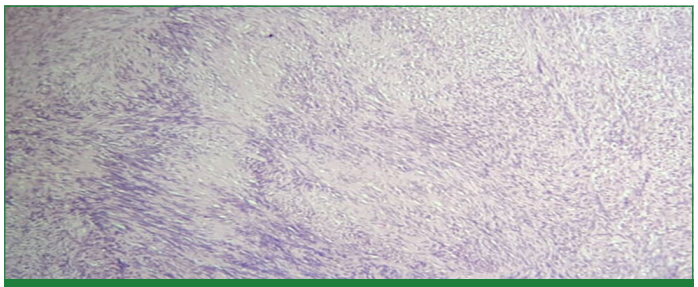
[Table/Fig-2]: H&E slide showing nests of tumour cells with eosinophilic cytoplasm in squamous cell carcinoma (mag: 100x). Inset shows positivity of tumour cells for Ck 5/6 (mag: 100x).



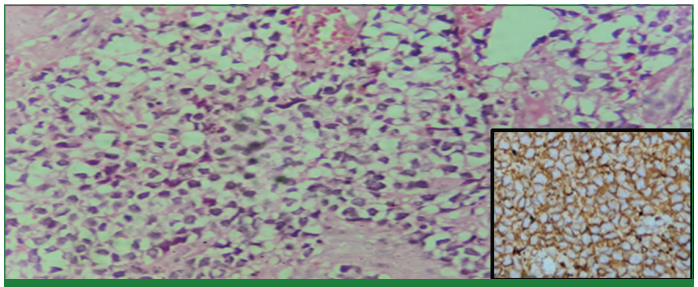
[Table/Fig-3]: H&E slide shows vascular space of different sizes ranging from dilated blood vessels to slit-like capillaries (mag 100x).



[Table/Fig-4]: H&E slide shows endophytic growth pattern epithelial cell nests (mag: 100x).



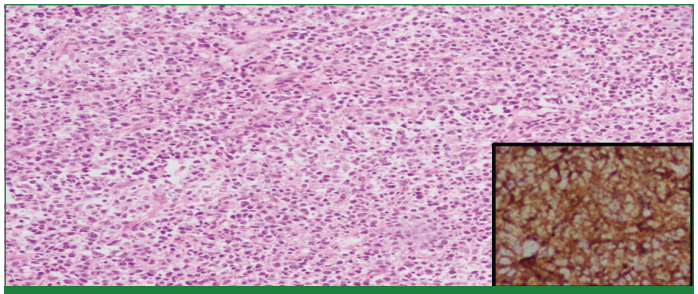
[Table/Fig-5]: H&E slide shows biphasic pattern with Antoni A Antoni B areas. Verocay bodies (Nuclear palisading around fibrillary process) also seen (mag 100x).



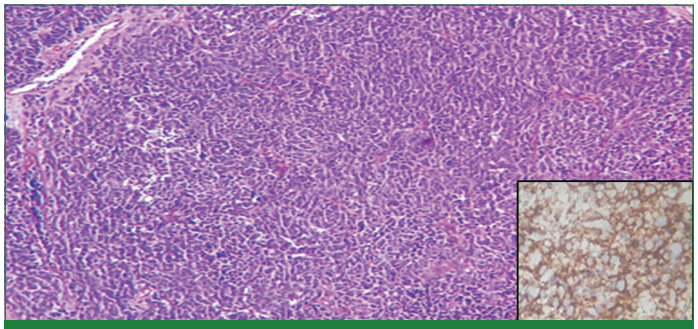
[Table/Fig-6]: H&E shows tumour cells with clear cytoplasm, round nuclei and inconspicuous nucleoli (mag:400x). Inset shows CD99 membranous positivity (mag:400x).

Age group (years)	No of cases	Benign	Age group (years)	No of cases	Malignant	IHC
0-20	2	Angiofibroma	0-20	1	Squamous cell carcinoma	CK5/6
	2	Capillary haemangioma				
21-40	1	Angiofibroma	21-40	1	DLBCL	CD20, Bcl2
	3	Capillary haemangioma				
41-60	1	Angiofibroma	41-60	1	Ewing's sarcoma	CD99
	1	Schwannoma		1	NK- T cell lymphoma	CD56
	2	Capillary haemangioma		2	Squamous cell carcinoma	CK5/6
	4	Inverted papilloma				

[Table/Fig-7]: Table showing all the benign and malignant lesions with Immunohistochemistry panel.



[Table/Fig-8]: H&E slide showing sheets of atypical lymphocytes admixed with large cells in DLBCL (mag: 100x). Inset shows positivity for CD 20 (mag:400x).



[Table/Fig-9]: H&E slide showing sheets of pleomorphic cells with hyperchromatic nuclei (mag: 100x). Inset:Tumour cells showing positivity for CD 56 (mag 400x).

DISCUSSION

The majority of nasal and paranasal lesions presented in the clinically as nasal polyp, leading to ambiguity in diagnosis and consequently affecting the treatment and prognosis of the patient. Histopathological examination plays a vital role to distinguish to lesions and aid in diagnosis and treatment [6].

The incidence of sinonasal malignancies is 0.83 per 100,000 people and males are commonly affected [7]. In present study, malignant lesion presented most commonly between 41-60 years which was comparable to study done by Maru A et al., which had maximum malignant cases after 40 years of age [8]. A study done by Banerjee A and Ghosh S, showed maximum cases after 50 years of age [9]. In present study, the males were commonly affected compared to females with M:F being 1.4:1 which was comparable to other studies done by Parmar N et al., and Pushpalatha K et al., [10,11].

The most common benign lesion diagnosed in present study was capillary haemangioma with seven cases which was similar to study done by Banerjee A et al., the cases of capillary haemangioma were seen most commonly in patients less than 40 years of age [9]. Histopathology of capillary haemangioma showed lobules of capillaries intermixed with fibromyxoid stroma. The thin walled capillaries are lined by plump endothelial cells. Clinically, the lesions present with nasal obstruction and with two of cases presenting with nasal obstruction with epistasis.

Beyond 40 years, the most common benign lesion diagnosed was inverted papilloma, with four cases comprising 18% of neoplastic lesions. A study done by Garg D, showed the most common lesion to be inverted papilloma (45.46% of all benign neoplastic lesion) [12]. Clinically, the lesions present as nasal polyps. Microscopically, the lesions present as squamous cell proliferation with scarce columnar cells showing endophytic proliferation. The cells appear bland with no atypical mitotic figures. One of the case shows neutrophilic microabscesses dispersed between the epithelial proliferation.

Four cases of angiofibroma was diagnosed and comprising of 18% of all neoplastic lesions which was comparable to studies done by Banerjee A et al., (14.2%) and Garg D et al., (18.1%) [9,12]. Study by Pushpalatha K et al., showed angiofibroma constituting 9.09% of all benign neoplastic lesions [11]. Clinically, the lesion presented with epistasis and rhinorrhoea. Grossly, presented with large grey white polypoidal mass with cut surface showing grey white areas admixed with haemorrhagic specks. Microscopically, the lesion showed fibrocollagenous stroma admixed with varying sized blood vessels ranging from dilated blood vessels containing thrombi to small slit like blood vessels. Centrally, the tumour shows numerous fibroblasts.

One case of schwannoma was diagnosed in a male patient of 41 years, comprising of 4.5% of all neoplastic lesions. Study done by Garg D et al., showed Schwannoma in 18.18% of benign neoplastic lesions [12]. Clinically, Schwannoma presented as nasal obstruction. Grossly presented as polypoidal mass which on cut section appeared grey white. Microscopically, characteristic Antoni A and Antoni B areas were seen. Verocay bodies were also observed at Antoni A areas.

In this study, the most common malignant lesion seen was Squamous cell carcinoma, of 3 cases. This finding coincided with study done Garg D, and Vohra G et al., but deviation was seen in study done by Banerjee A et al., showed the most common malignant lesion to be olfactory neuroblastoma [9,12,13].

Overall, squamous cell carcinoma is still the most common malignant lesion encountered in the nasal and paranasal sinus region. Clinically, the patient presented with nasal obstruction, epistasis. One of the patient showed gross hemi facial swelling. One patient was in the age range 0-20 years and two other patients were above 40 years of age. Grossly, the lesion appeared as irregular grey brown to grey black lesions which on cut sections showed grey brown areas. Microscopically the lesions showed nests of malignant cells showing large eosinophilic cytoplasm with increased nuclear cytoplasmic ratio and prominent eosinophilic nucleoli. All the cases showed scant to few keratin pearls. To conclusively arrive to diagnosis, IHC was done by using CK5/6, which showed diffuse cytoplasmic staining for all the tumour cells.

In present study, there was a case with clinical findings of nasal obstruction, epistasis and facial pain of short duration. Grossly, the lesion showed multiple irregular grey brown pieces of tissue. Microscopically, the lesion showed high grade pleomorphic cells arranged in sheets and nests. The individual cells showed high nuclear cytoplasmic ratio with clumped chromatin inconspicuous nucleoli and eosinophilic cytoplasm. The initial markers were inconclusive and the second line markers showed CD56 positivity, diagnosing the case as NK-T cell lymphomas. NK-T cell lymphomas are rare aggressive malignancies comprising of 1.16% of all NHL in south India [14]. Study done by Saldanha SC et al., showed the age of presentation to be between 31-60 years. Study done by Metgud R et al., presented a male patient aged 60 years which coincided with present study with male patient of 57 years, most commonly seen in nasal cavity and may also include the skin, GIT, testis, kidney, upper respiratory tract and rarely the eye/orbit [15,16].

A case of Ewing sarcoma, in a 45-year-old female was diagnosed in present study. Ewing sarcoma presenting in head and neck are unusual, constituting only 4-9% of overall Ewing sarcomas [17]. Studies done by Hamid I et al., and Suzuki T et al., showed Ewing sarcoma in males between 20-30 years [17,18]. In present study, the patient presented clinically with pain and epistasis. Radiology of the patient showed soft tissue lesion in maxillary sinus extending into the nasal cavity with bony destruction. Grossly, two grey black bits of tissue were received. Microscopic examination showed tumour cells arranged in nests and sheets admixed with areas of haemorrhage. The individual tumour cells were small, round with vacuolated cytoplasm, resembling small round blue cell tumour. IHC of CD99 showed diffuse membranous positivity for tumour cells narrowing the diagnosis to Ewing sarcoma.

In the present study, a case of DLBCL was also diagnosed in a 33-year-old female, originating at maxillary sinus. A study done by Hao S et al., showed DLBCL in nasal cavity in a 62 female and a study done by Varelas A et al., showed mean age of presentation in men (65.3) and women (71.1) [18,19]. In sinonasal region the most

common site of presentation of primary DLBCL is maxillary sinus (36.1%) and nasal cavity (34.5%) [19,20]. The clinical findings were similar to other malignant tumours, facial swelling, nasal obstruction and pain. Grossly, the lesion showed multiple grey brown to grey black tissue. Microscopic representation showed pleomorphic cells arranged in sheets admixed with few large cells. Assistance of IHC was taken and the lesion showed positivity for CD20, BCL2 conclusively proving the lesion to be DLBCL. [Table/Fig-10] shows the comparison of present study and different studies in terms of benign and malignant lesions [4,5,8,9,11-13,21,22].

Study (Publication year)	Benign	Malignant	Ratio
Present study, (2022)	16	6	2.67
Pushpalatha K et al., (2017) [11]	44	11	4.00
Vohra G et al., (2019) [13]	13	6	2.16
Maru A et al., (2015) [8]	14	6	2.30
Raj JA et al., (2013) [5]	12	8	1.50
Bajaj D and Kanoriya D (2017) [21]	34	6	5.60
Lathi A et al., (2011) [4]	19	13	1.40
Kumar A et al., (2017) [22]	22	31	0.70
Garg D, (2014) [12]	11	13	0.80
Banerjee A and Ghosh S (2017) [9]	42	14	3.00

[Table/Fig-10]: Comparison of benign and malignant lesions between different studies [4,5,8,9,11-13,21,22].

Limitation(s)

The present study shows the incidence pattern according to age and gender, and this is analogous to presentation in other similar studies. The study of nasal and paranasal sinus neoplastic lesions needs to be done in a larger group of patients and in varied clinical setting to extrapolate for incidence and prevalence data. The small sample size of the study forms a major drawback to give any irrefutable data in this context.

CONCLUSION(S)

The lesions of the nasal and paranasal sinus region have overlapping clinical features and also can cause difficulty in diagnosis. The concurrent use of histopathology and IHC helps in arriving at the accurate diagnosis and also aids in treatment and leads to better survival among affected patients. This study shows the importance of IHC in diagnosing even rare lesions and lesions with ambiguous clinical and morphological picture.

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