ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Diagnostic Utility Of Immunohistochemical Analysis Of Tumours Of Sino-Nasal Region And Nasopharynx.

Annu Khokhar[1], Manjiri Karandikar[2]*, Anuja Patil[3], Reena Bhardwaj[4], NS Mani[5], and RC Nimbargi[6].

[1]Resident in Pathology, BVDUMC Pune, Maharashtra, India.
[2]Professor of Pathology, BVDUMC Pune, Maharashtra, India.
[3]Assistant Professor, Pathology, BVDUMC Pune, Maharashtra, India.
[4]Professor of Pathology, BVDUMC Pune, Maharashtra, India.
[5]Professor of Pathology, BVDUMC Pune, Maharashtra, India.
Professor of Pathology, BVDUMC Pune, Maharashtra, India.

ABSTRACT

Sino-nasal region and nasopharynx are composed of a complex functional mixture of epithelia, sero-mucinous glands, melanocytic metaplasia and specialised olfactory mucosa. Hence, neoplasms in these regions present bewildering complexities of histogenetic types which will be presented in this series. Objective- To study the role of immunohistochemistry (IHC) in the diagnosis of sino-nasal and nasopharyngeal neoplasms. 15 uncommon neoplasms from the sinonasal region and nasopharynx out of 45 neoplasms were studied immunohistochemically. The lone benign lesion was a meningioma infiltrating the base of skull. The malignant neoplasms comprised of 3 lymphomas, 6 carcinomas and 5 round cell/ poorly differentiated neoplasms. IHC was critical in arriving at the final histopathological diagnosis in 14 of these 15 cases. The analysis of the above will be presented. IHC is a critical investigation for definitive diagnosis of poorly differentiated neoplasms in the sino-nasal and nasopharyngeal regions.

Keywords: Immunohistochemistry, Sinonasal, nasopharyngeal

https://doi.org/10.33887/rjpbcs/2023.14.3.22

Corresponding author

ISSN: 0975-8585

INTRODUCTION

The nasal cavity, paranasal sinuses, and nasopharynx make up the intricate upper respiratory tract. This area is home to a variety of tissues, including epithelial, glandular, lymphoid, cartilaginous and bone tissue. It is also susceptible to infections, tumour-like conditions, and true tumours. The purpose of our study was to examine histopathological spectrum of nasal, paranasal, and nasopharyngeal masses.

Aim And Objective

To study the role of immunohistochemistry (IHC) in the diagnosis of sino-nasal and nasopharyngeal neoplasms.

MATERIAL AND METHODS

A total of 45 neoplasms were studied over a study period of 2 years in a tertiary hospital, Pune. Slides were prepared from paraffin embedded blocks and stained with H and E using standard protocols. IHC were done wherever required. Clinical details and relevant information were obtained. All the data were collected and studied for frequencies and percentages were calculated.

RESULTS

A total 22 benign neoplasms were identified of which Inverted papilloma was the most common benign tumour, 10 cases, (45.45%). Five cases (22.72 %) each of Juvenile nasopharyngeal angiofibroma and Hemangioma , and one case each of Meningioma (4.54%) and Melanotic neuroectodermal tumor of infancy.

A total of 23 malignant neoplasms with wide variety were found of which Non-Hodgkin Lymphoma (NHL) was the commonest. The distribution of malignant neoplasms is demonstrated in Table 1and distribution of Non-Hodgkin Lymphoma in Table 2.

Of these total 45 neoplasms, IHC was significant for diagnosis in 14 cases.

Case 1

Histopathological Diagnosis: D/D: 1. PNST 2. Meningioma 3. Solitary fibrous tumor
Positive IHC markers: EMA, S100p, BCl2
Negative IHC markers: CD 34, Synaptophysin, CK, Desmin, SMA, p63, PR- Negative
Final Diagnosis: Fibrous Meningioma,WHO CNS grade 1 (Figure 1)

Case 2

Histopathological Diagnosis: Hodgkin Lymphoma, Classical type
Positive IHC markers: CD 15
Negative IHC markers: CD30
Final Diagnosis: Hodgkin Lymphoma, Classical type (Figure 3)

Case 3

Histopathological Diagnosis: Large cell NHL s/o Anaplastic large cell lymphoma
Positive IHC markers: : LCA, ALK, CD30
Negative IHC markers: CK, CD79a
Final Diagnosis: Large cell NHL s/o Anaplastic large cell lymphoma (Figure 5)

Case 4

Histopathological Diagnosis: D/D: 1.High grade large cell lymphoma 2. High grade Sinonasal undifferentiated carcinoma
Positive IHC markers: BCl-6, LCA, S-100p, CD 10, CD20, CD 79a, Ki67-90 %
Negative IHC markers: BCl-2, CK, CD5, CD3

Final Diagnosis: B cell NHL, sporadic Burkitt lymphoma (Figure 4)

Case 5

Histopathological Diagnosis: Melanocytic neuroectodermal tumor of infancy
Round tumor cells
Positive IHC markers: Synaptophysin, MiC-2 (CD99),
Negative IHC markers :Vimentin, S-100p, HMB-45 and chromogranin
Epithelioid cells
Positive IHC markers: Vimentin, HMB-45 and MiC-2
Negative IHC markers : CK, Synaptophysin, Chromogranin and S-100p
Final Diagnosis: Melanocytic neuroectodermal tumor of infancy (Figure 2)

Case 6

Histopathological Diagnosis: Malignant melanoma
Positive IHC markers: Pan CK, S-100p , Melan A, Vimentin, Ki 67 -65%
Negative IHC markers: CD117
Final Diagnosis: Malignant melanoma (Figure 7)

Case 7

Histopathological Diagnosis: D/D: 1. Neuroendocrine carcinoma 2. Vascular neoplasm 3. Adenomatous polyp
Positive IHC markers: CK, Synaptophysin, Desmin
Negative IHC markers: LCA, CD31
Final Diagnosis: Neuroendocrine carcinoma (Figure 11)

Case 8

Histopathological Diagnosis: Undifferentiated nasopharyngeal carcinoma
Negative IHC markers: CK7, CK20, Inhibin, LCA, Synaptophysin
Final Diagnosis: Undifferentiated nasopharyngeal carcinoma

Case 9

Histopathological Diagnosis: D/D 1. Sinonasal adenocarcinoma 2. Undifferentiated nasopharyngeal carcinoma
Negative IHC markers: CK7, CK20, Inhibin, LCA, Synaptophysin
Final Diagnosis: Undifferentiated sinonasal carcinoma (Figure 9)

Case 10

Histopathological Diagnosis: Poorly differentiated carcinoma
Positive IHC markers: CK, p63
Negative IHC markers: LCA
Final Diagnosis: Poorly differentiated carcinoma (Figure 6)

Case 11

Histopathological Diagnosis: D/D 1. Alveolar rhabdomyosarcoma 2. Esthesio neuroblastoma
Positive IHC markers: Desmin, S-100p, Ki67-25%
Negative IHC markers: LCA, Chromogranin A, Synaptophysin
Final Diagnosis: Alveolar rhabdomyosarcoma (Figure 10)

Case 12

Histopathological Diagnosis: Olfactory neuroblastoma (Grade 2-3)
Positive IHC markers: S-100p, Desmin, Synaptophysin

Negative IHC markers: Chromogranin A, LCA
Final Diagnosis: Olfactory neuroblastoma (Grade 2-3) (Figure 8)

Some unusual tumours / rare tumours found in this study

Meningioma

Meningiomas are rarely found in the nasal cavity. A 45 year old female had history of on and off epistaxis since 6 months. CT-PNS revealed a heterogeneously enhancing mass involving ethmoid sinuses bilaterally with bony erosions. Neoplastic midline mass in bilateral ethmoidal sinuses and nasal cavities with intracranial extension. Extracranial meningiomas can be found in head and neck region. But this case had intracranial extension through the olfactory groove. IHC was performed to rule out other spindle cell tumours like PNST and Solitary fibrous tumour and final diagnosis given as Meningioma.

Hodgkin Lymphoma

A 16 year old female, known case of Classic Hodgkin Lymphoma of the cervical lymph nodes had presented with nasopharyngeal mass. Pateint had history of receiving 3 cycles of chemotherapy. PET scan revealed lymphomatous involvement of parapharyngeal tissue, nasopharyngeal soft tissue. It is unusual to get involvement of the Waldeyer ring by Hodgkin Lymphoma. Still the patient had developed Hodgkin lymphoma lesion in the nasopharynx even after chemotherapy was given.

Primitive neuroectodermal tumor

A 6 month old male child had presented with a nasal mass over the tip of nose since birth. The mass was gradually increasing in size and measured 3x2.5 cm on examination. FNAC suggested a small round cell tumour. Embryonal rhabdomyosarcoma is the common small round cell tumour in the nasal cavity but this proved to be PNET.

Malignant melanoma

A case of Malignant melanoma, originating in the lacrimal sac had involved and extended into the inferior nasal orbital sinomaxillary bone and caused its destruction. The patient had symptoms of nasal obstruction and bleeding and hence was included in this study.

Neuroendocrine carcinoma

These are rare tumors of the nasal region . In our study, a 45 year old, female had presented with right sided nasal obstruction and hyposmia since 6 months and right sided nasal bleed since 2 months. Clinical suspicion of malignancy was present. Specimen were sent from bilateral nasal cavities.

Melanocytic neuroectodermal tumor of infancy

A 3-month old male infant had a progressive swelling in the left maxillary alveolus noted 1 month after his birth. It had been growing progressively. A large, round, sessile, firm, non-tender, painless, pale-pinkish mass extending from the left maxillary alveolus to the midline of the alveolar ridge and further extending to the right posterior portion of the maxillary alveolus. This mass was occupying the maxillary alveolar ridge, GBS with extension out of the mouth. It had areas of black pigmentation with no ulceration. The child was unable to approximate the alveolar ridges. Liquid Chromatography Tandem Mass Spectrometry was done to evaluate VMA (Vanillylmandelic acid) levels in the urine of the infant and was determined as 10 mg/24 hours (Normal: 2-7mg/24 hrs), hence further supporting the diagnosis.

ISSN: 0975-8585

Table 1: Distribution of malignant neoplasm

Diagnosis	Number of cases	Percentage (%)
Hodgkin Lymphoma	1	4.34
Non-Hodgkin Lymphoma	7	30.43
Moderately differentiated squamous cell carcinoma	3	13.04
Undifferentiated nasopharyngeal carcinoma	3	13.04
Poorly differentiated carcinoma	2	8.69
Neuroendocrine carcinoma	2	8.69
Undifferentiated sinonasal carcinoma	1	4.34
Olfactory neuroblastoma	1	4.34
Malignant melanoma	1	4.34
Alveolar Rhabdomyosarcoma	1	4.34
Primitive neuroectodermal tumor	1	4.34
Total	23	100

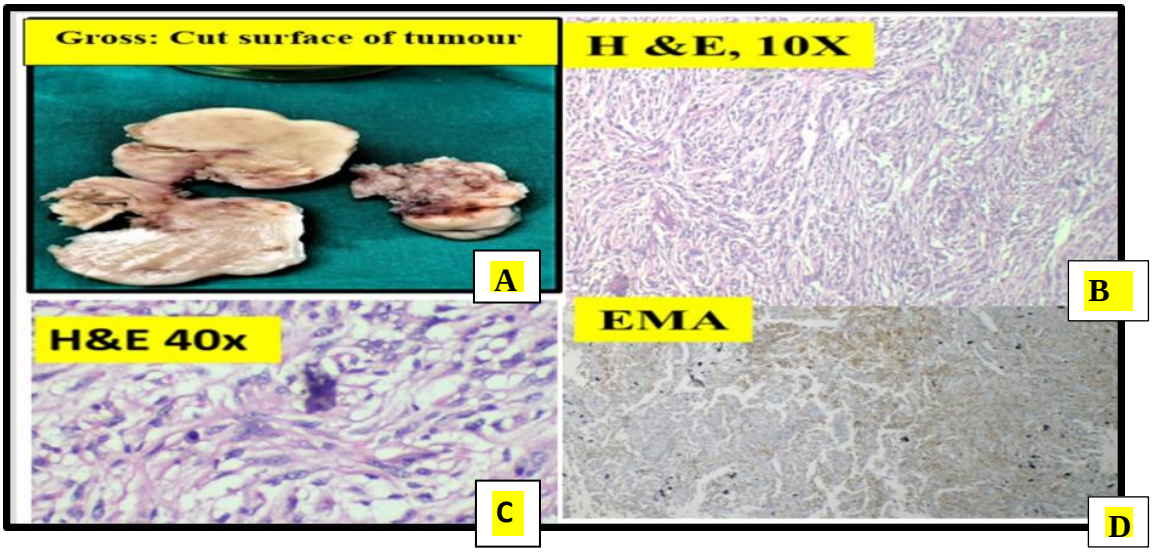

Figure 1 A) The tumour is well circumscribed and cut surface is whitish and firm B) Low magnification reveals whorls of of meningothelial cells. C) High magnification shows spindled cells with unfirom round nuclei. D) EMA is positive in tumour cells favouring a diagnosis of Fibrous Meningioma, WHO CNS Grade 1.

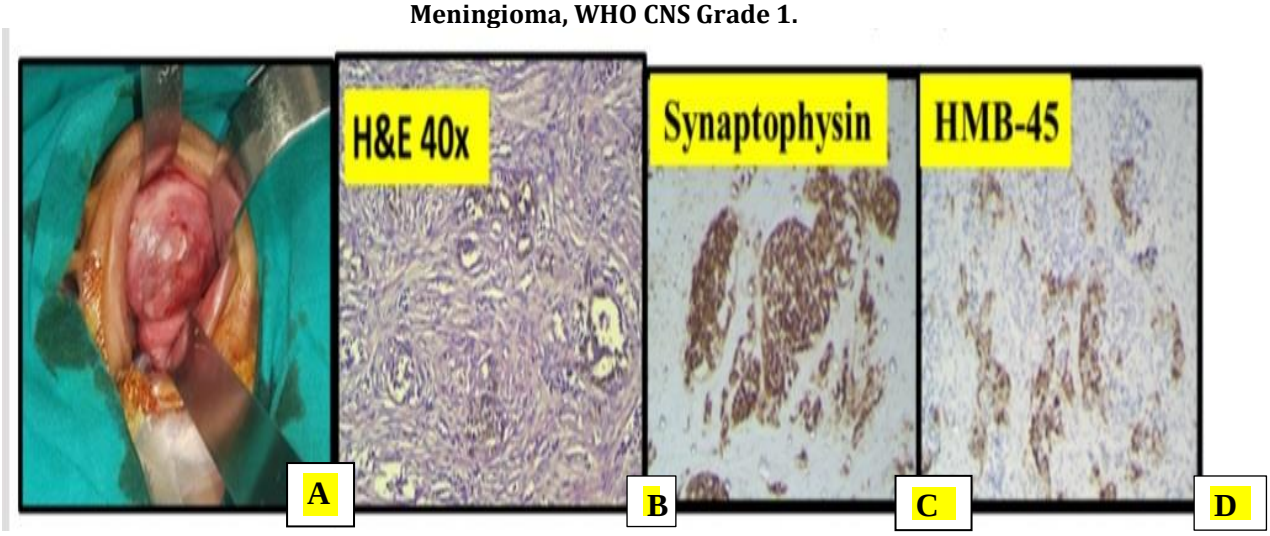

Figure 2 A) Intra-operative well circumscribed pink tumour in maxillary sinus. B)H&E shows biphasic population of small round cells and large epithelioid cells with melanin. C)Round cells reactibe for Synaptophysin D)Epithelioid cells reactive for HMB-45 favoring a diagnosis of Melanotic neuroectodermal tumour of infancy.

ISSN: 0975-8585

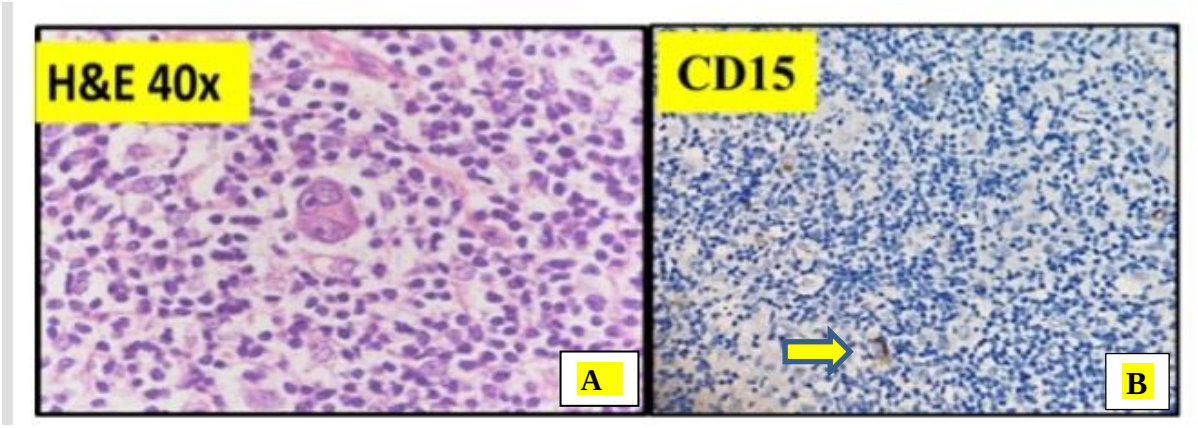

Figure 3 A) H&E shows scattered Reed-Sternberg cell (RS) in a background of inflammatory milieu. B) RS cells (arrow) show positivity for CD15 suggesting a diagnosis of Hodgkin lymphoma, Classical type.

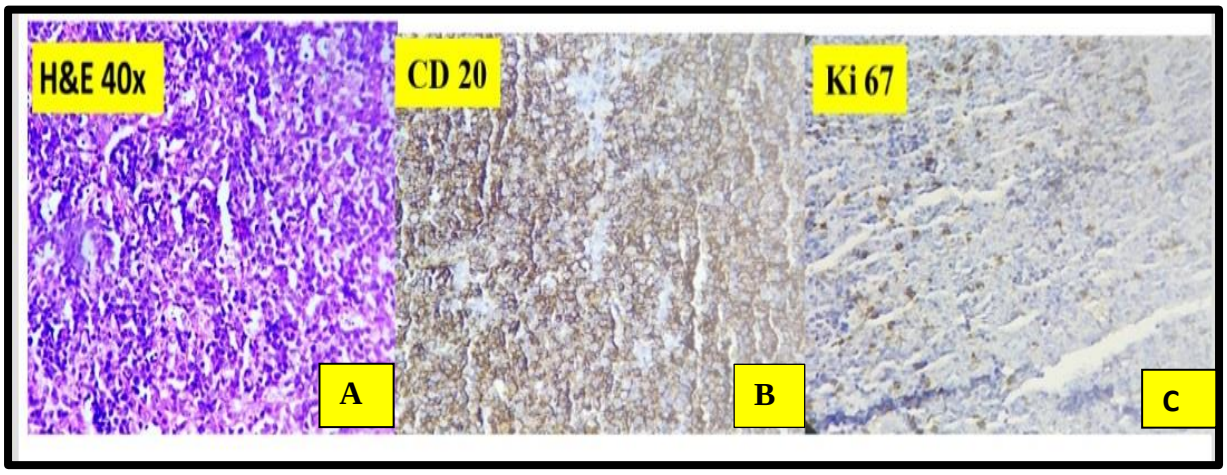

Figure 4 A)H&E shows sheets of monomorphic atypical cells with interspersed tingible body macrophages giving a starry sky appearance. B)CD 20 is positive C) Ki67 is almost 100% suggestinga diagnosis of Burkitt lyphoma.

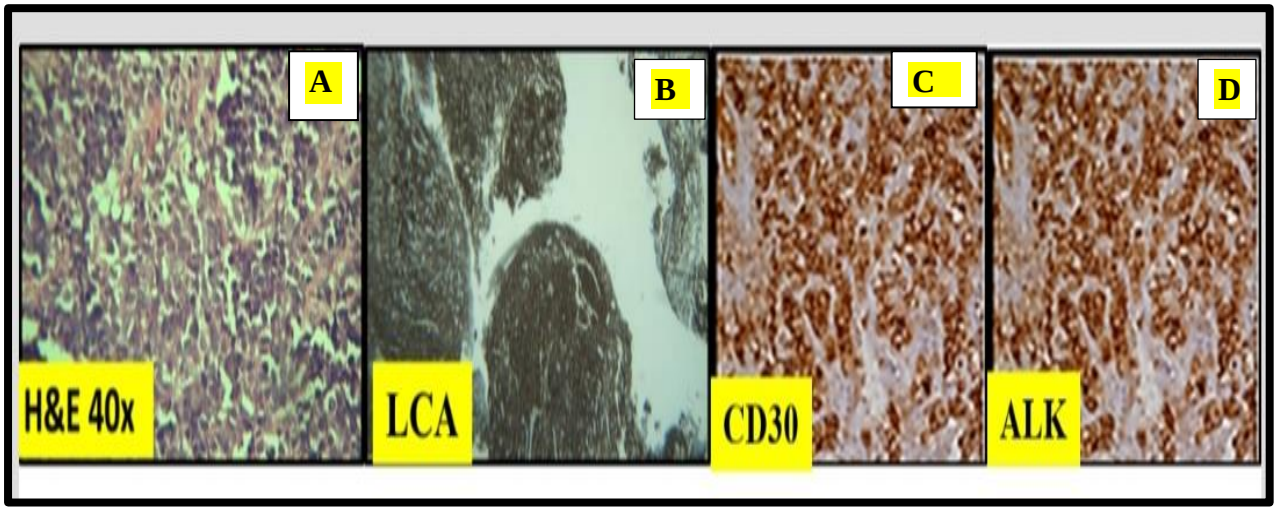

Figure 5 A) H&E shows large anaplastic cells with pleomorphism, hyperchromasia and mitosis. B)LCA is strong positive C)&D)CD30 and ALK are strongly positive suggesting a diagnosis of Anaplastic large cell lymphoma. .

ISSN: 0975-8585

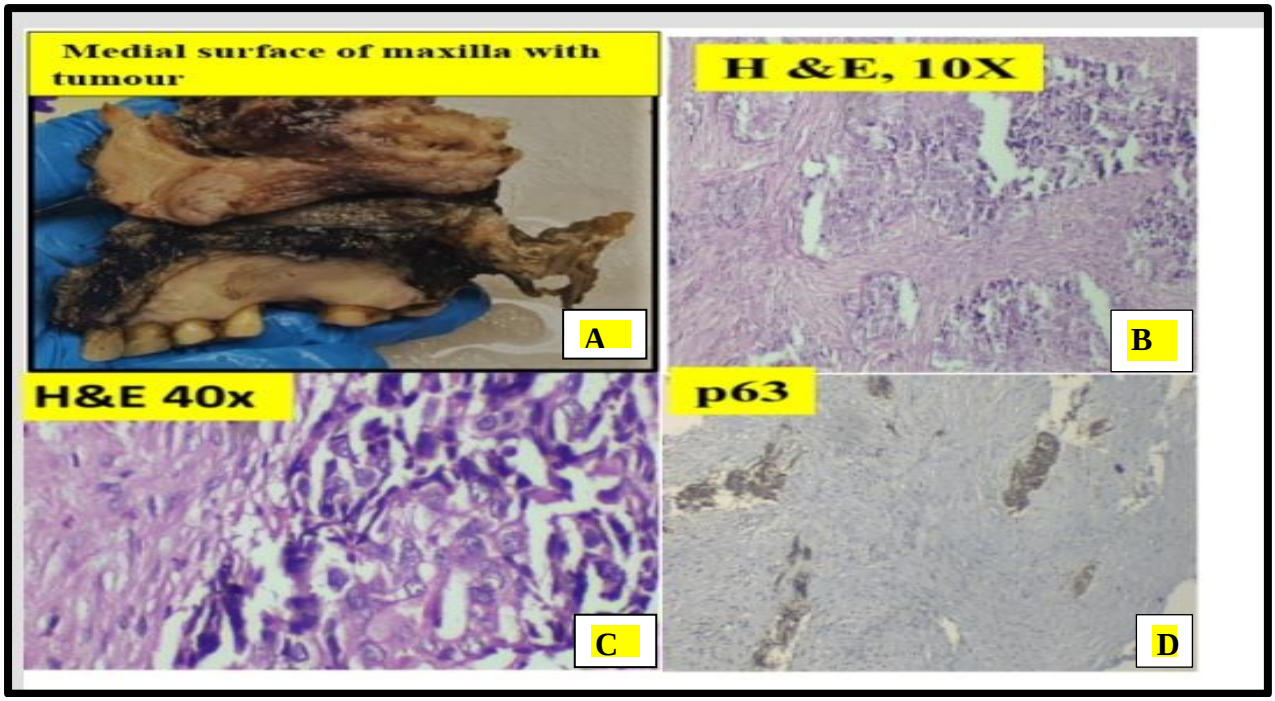

Figure 6 A) Gross shows large necrotic tumour encroshing the paranasal sinuses. B)Low magnifications atypical cells with marked atypia. c) High magnification shows large hyperchromatic pleomorphic cells with minimal keratinisation. D) p63 shows positivity in tumour cells favoring a diagnosis of Poorly differentiated carcinoma.

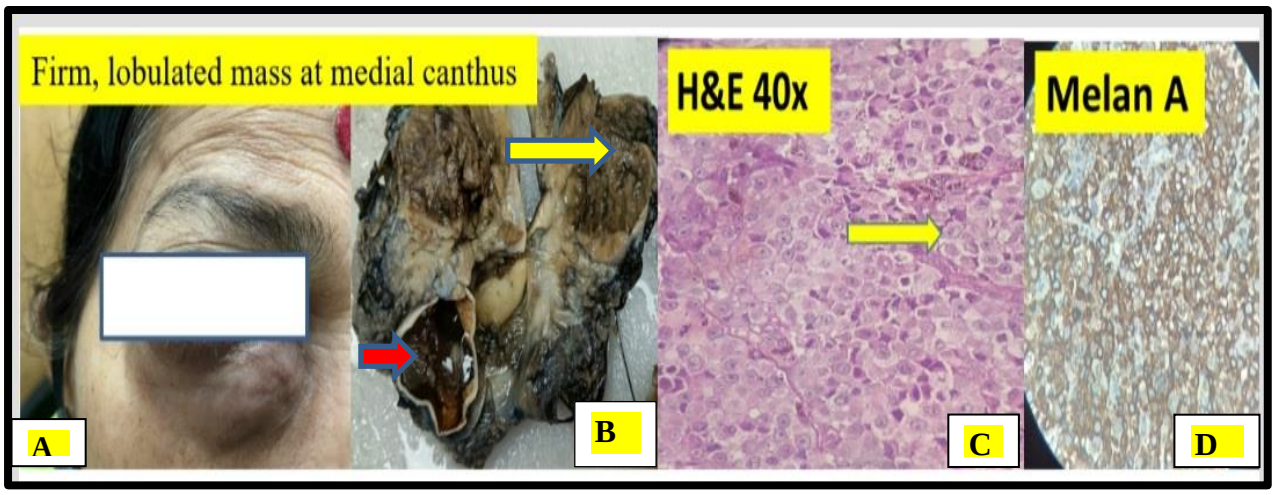

Figure 7 A) Patient with blackish mass at the medial canthus. B) Cut surface shows infiltrating tumour (yellow arrow) and remnant of cystic eye (red arrow). C) H&E shows large cells with prominent eosinophilic nuclei and granular melanin pigment(yellow arrow). D) Melan A shows positivity. Overall features favour Malignant Melanoma.

ISSN: 0975-8585

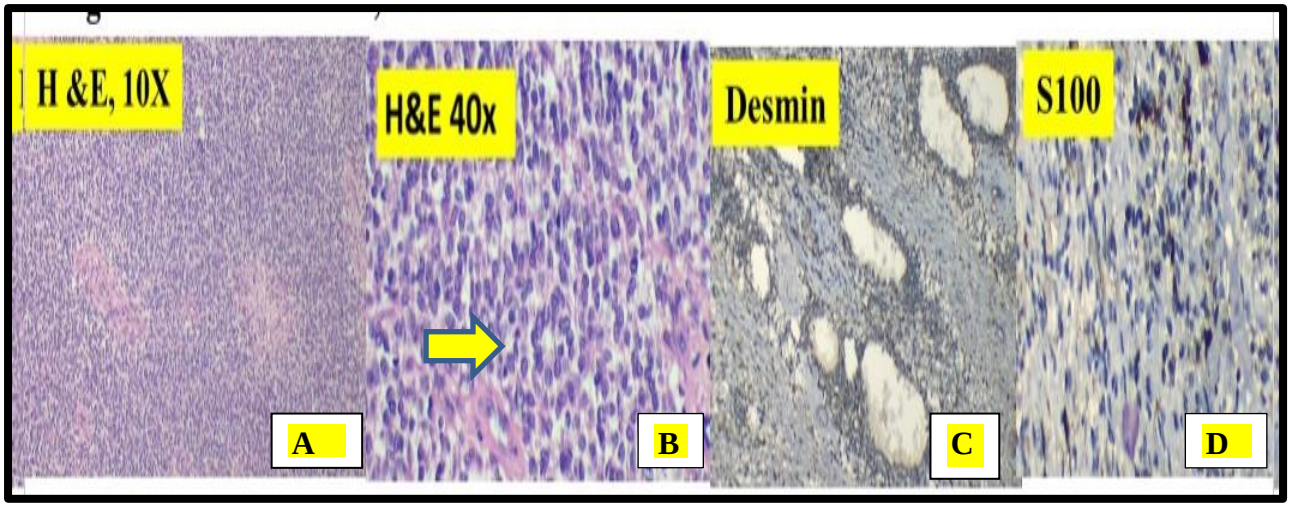

Figure 8 A) Low power shows nests and lobules of monotonous tumour cells. B) High power shows tumour cells have round nuclei, indistinct nucleoli and scant cytoplasm. Homer Wright pseudo-rosette noted (yellow arrow). C)&D) Tumour cells show positivity for Desmin and S100p favouring diagnosis of Olfactory Neuroblastoma.

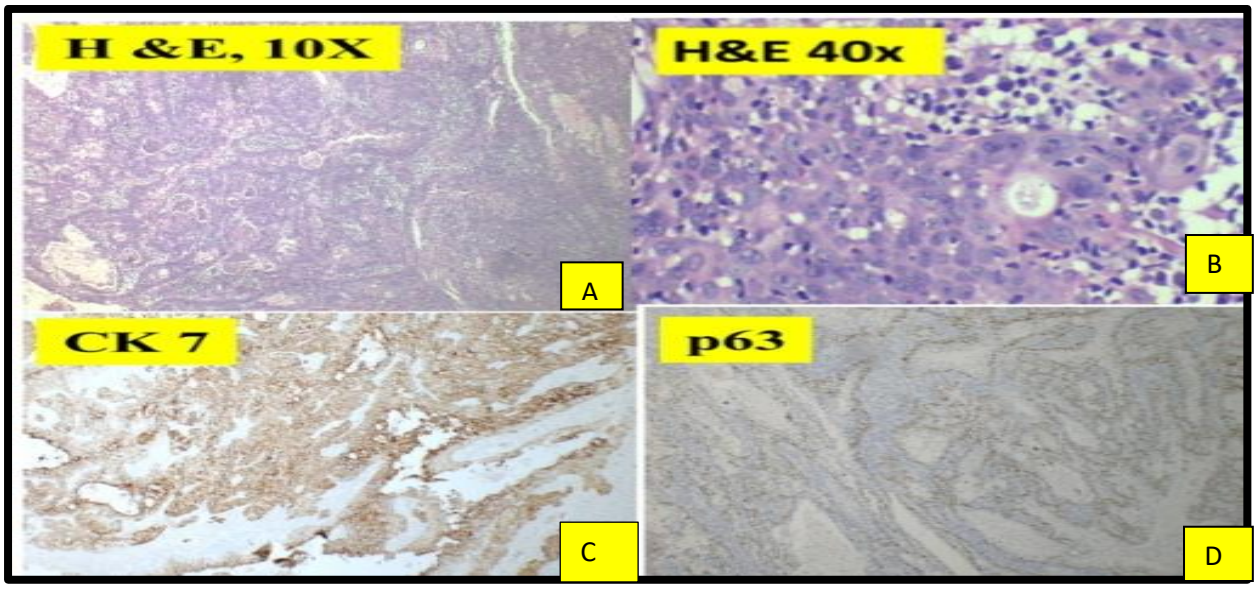

Figure 9 A) power reveals nests and lobules of atypical cells . B) High power shows medium to large sized cells with hyperchromatic to vesicular nuclei, prominent nucleoli, poorly defined cell membrane with brisk mitosis. C) &D) Tumour cells show positivity for CK7 and p63 favoring the diagnosis of Sinonasal undifferentiated carcinoma.

ISSN: 0975-8585

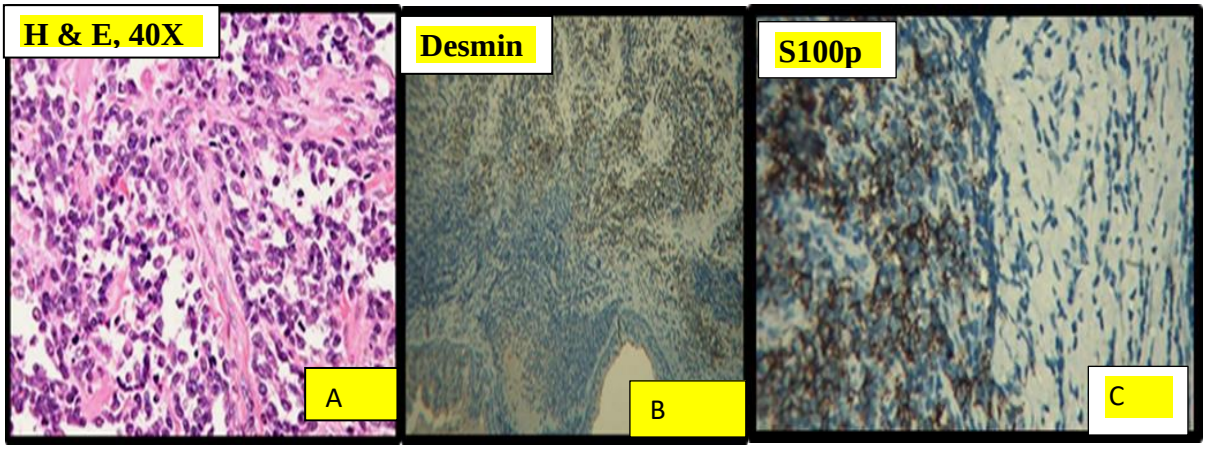

Figure 10 A) High power shows nests, cords, trabeculae of primitive round cell separated by thick fibrovascular septa. B) & C) Tumour cells are positive for Desmin and S100p thus favouring a diagnosis of Alveolar Rhabdomyosarcoma.

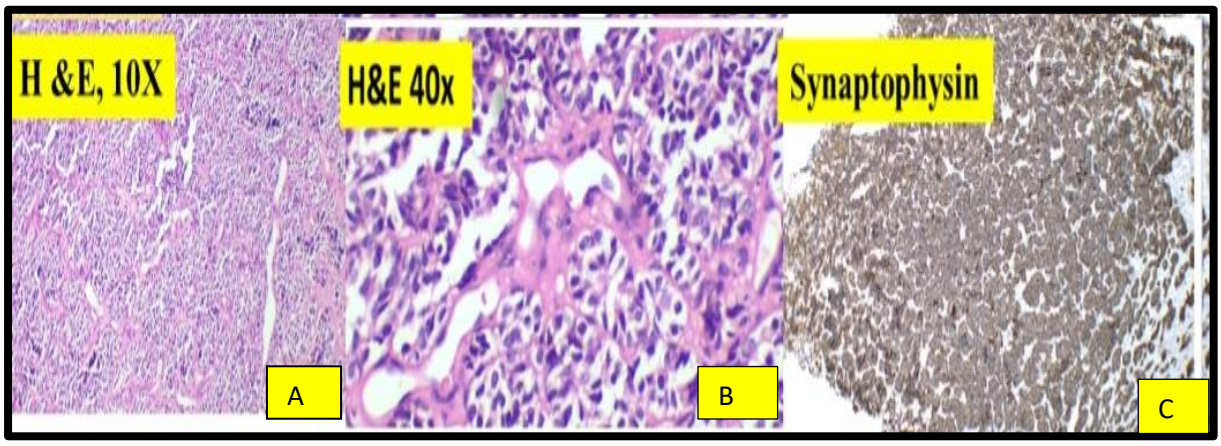

Figure 11 A) Low power shows organoid arrangement of tumour cells. B) High magnification shows small cells with nuclear hyperchromasia and mild to moderate eosinophilic cytoplasm. C) Tumour cells show positivity for Synaptophysin, this favouring a diagnosis for Neuroendocrne carcinoma.

DISCUSSION

The head and neck region is a frequent site of tumoral invasion in lymphoma. Cervical lymph-node involvement is found in 39–72% of cases . Extranodal involvement mainly concerns Waldeyer ring. Sinonasal involvement is rarer in Caucasian populations, at 0.2–5% of cases , unlike in Asian and South American populations, where it holds second place after digestive tract locations .In Caucasian populations, diffuse large B-cell lymphoma is the prevalent type, while in Asia and South America nasal NK/T lymphoma predominates [1].

Burkitt lymphoma was first described as a mandibular malignancy of children in 1958 . This high-grade lymphoma can be subdivided into endemic, sporadic and immunodeficiency-associated forms with incidence of 50-100/million, 2-3/million and 6/1,000 acquired immune deficiency syndrome cases respectively. The sporadic form usually involves the abdomen or bone marrow and seldom (<25%) involves the head and neck . Burkitt lymphoma in the head and neck usually presents as lymphadenopathy, whereas primary involvement of the nasal cavity and paranasal sinuses is uncommon.Histologically, "starry-sky" pattern is a microscopic hallmark. Immunophenotypically, Burkitt lymphoma expresses B-cell lineage markers, including CD19, CD20, CD22, CD74, and CD79a, and coexpressing CD10, Bcl-6, CD43, and p53, but not CD5, CD23, Bcl-2, CD138 or TdT. Ki-67 index is almost 100%. [4]

Anaplastic lymphoma kinase (ALK)-positive diffuse large B-cell lymphoma (DLBCL) is a rare subtype of non-Hodgkin's lymphoma (NHL) with distinct morphologic and immunohistochemical features. It was first reported in 1997 by Delsol, and no more than 100 cases have been reported up to now. This disease exhibits a more aggressive clinical course and worse prognosis than typical diffuse large B-cell lymphoma Histologically, the tumor cells were characterized by plasmablastic morphology and tested positive for ALK in a cytoplasmic granular staining pattern. The neoplastic cells were positive for CD38, CD4, MUM1, CD138 and Vimentin. However, they failed to express CD56, CD30, as well as mature B cells markers, such as CD79a, CD20 and T cells markers such as CD2, CD3, CD5, CD7 and CD8. [5]

Hodgkin lymphoma (HL) of the nasopharynx is rare, the frequency of occurrence <1 % with slightly over 100 cases reported in worldwide literature, 35 of them primarily isolated to nasopharynx without nodal involvement at presentation.[2] Adepitan A. Owosho, Casey E. Gooden, and Alden G. McBee reported a case where the lymphoid cells were negative for AE1/AE3, S100, and HMB-45 performed to evaluate for carcinoma and melanoma. The small lymphocytes were positive for CD45, CD20 (staining B lymphocytes), CD3 (staining background T lymphocytes forming rosettes around large atypical cells), and PAX5 (staining B lymphocytes). The large atypical cells were negative for CD45, CD20, and CD3. However, the cells were weakly positive for PAX5, and strongly positive for CD15, and CD30 in a typical membrane and paranuclear dot-like staining pattern.[2]

In conclusion HL of the nasopharynx is rare, but should be included as a possible differential diagnosis when a patient presents with a nasopharyngeal mass, and proper investigative and immunohistochemical stains should be performed to rule out other lymphoid neoplasms.[2]

In our study, we observed 7 cases of NHL and 1 case of HL.

Sinonasal undifferentiated carcinoma (SNUCs) are a rare tumor, with fewer than 200 reported cases. The majority of SNUCs react with simple keratins (CK7, CK8, CK19) and have focal positivity for epithelial membrane antigen, neuron-specific enolase, and p53; synaptophysin and chromogranin may show patchy rare immunoreactivity. [3]

Neuroendocrine carcinomas (NEC) are rare with a wide spectrum of histological differentiation and are classified into well-differentiated (typical carcinoid), moderately differentiated (atypical carcinoid), and poorly differentiated (small and non-small cell types), with the latter one being extremely rare and carrying a poor prognosis due to its aggressive nature. Shaqul Qamar Wani, Ishtiyaq A ,Talib Khan, and Mohammad M Lone presented a case where Biopsy revealed small cell neuroendocrine carcinoma (SCNEC) strongly positive for cytokeratin (CK) and epithelial membrane antigen (EMA), moderately positive for CD-56 and neuron-specific enolase (NSE) and negative for p-63, CK-5/6, synaptophysin, chromogranin A, desmin, and p-40.[6]

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare tumor which occurs during infancy, often within the first year of life. MNTI was first reported in 1918 and since then there have been approximately 500 diagnoses. MNTI typically affects the face or the skull, with rapid, distended growth, and a high recurrence rate. Around 93% of MNTIs occur on the head and neck; most commonly in the maxilla (68-80%), skull (10.8%), jaw bone (6%), and head (4.3%). In 1961, Borello and Gorlin found that vanillymandelic acid (VMA) levels in MNTI patients' urine were significantly higher, but dropped back within normal limits following surgery. This is a common occurrence in many neurogenic tumors, and as such MNTI was considered a neurogenic tumor and was acknowledged by the World Health Organization (WHO). Shaojie Wang, MDS , Changlong Song, MDS Xinjie Yang, MD, PhD, Yaowu Yang, DDS, MD, and Jianhua Wei, DDS, MD observed a case in which histopathology revealed a mixture of epithelioid cells and lymphocyte-like cells which formed a clumped cord-like structure, and some epithelial cells were pigmented. Immunohistochemical examination revealed Vimentin/NSE/HMB45/Syn(+), CK/EMA (large cell+), GFAP/S-100(+), Desmin (scattered+), Ki-67 (3%+). [7]

Malignant Melanoma of nasal cavity is an extremely rare tumour and is more aggressive than its cutaneous counterpart. Primary malignant melanoma of nasal cavity arise from melanocytes located in the mucous membrane. Only 0.5% of malignant melanoma arises in nasal cavity. Richa Bhartiya and K M Prasad reported a case of malignant melanoma of the nasal cavity in a 51-year-old male which was later

confirmed by histopathology examination along with immunohistochemistry by using S100p and HMB 45.[8]

Olfactory neuroblastoma (ONB) is a neuroectodermal malignant tumor derived from the olfactory epithelium of the nasal cavity and sinuses. Xiaoling Cheng, Qingliang Li, Xudong Weiand Jianghao Wu reportedaA 63-year-old male patient had nasal congestion and runny nose with no obvious cause 5 years ago. He underwent a nasal polypectomy. Immunohistochemical staining results: Syn (+); CgA (weak +); NSE (+); CD99 (weak +); CKP (-); Vimentin (-); p40 (-); p63 (-); P- 100 (Supporting cells +); CK5/6 (-); CD56 (+); HMB45 (-); EMA (-); CD57 (+); P53 (wild type, 20%); SOX-10 (-); GFAP (-); Ki-67 (index: 20%) . (Nasal cavity) Morphology combined with immunohistochemical staining, the final diagnosis was olfactory neuroblastoma with necrosis. [9]

The incidence of rhabdomyosarcoma is approximately six cases per 1,000,000 population per year.Rhabdomyosarcoma is the most common form of soft tissue sarcoma and is the third most common extracranial solid tumor in childhood. On the basis of histology, two main rhabdomyosarcoma subgroups can be distinguished: ARMS and embryonal rhabdomyosarcoma Hui-Min Hu, Wei-Ling Zhang,Dong-Sheng Huang, Sha Luo, Azeem Sarang,and Xiao-Hong Chen reported a 29-month-old boy with a 10-month history presented with a gradually increasing mass in the left nasal wing. After biopsy of the left nasal alar tumor, Hematoxylin-Eosin staining showed small round blue cells which were positive for immunohistochemical stain of Desmin and Myogenin. Hence, pathological diagnosis of ARMS was made. [10]

Primitive neuroectodermal tumor is a malignant small round cell tumor of presumed neural crest origin, usually affecting the bony structures of the nasal cavity. Jae Pil Hwang reported a case of a 17-year-old boy with right eyeball deviation and right nasal obstruction. The histology showed proliferation of noncohesive cellular proliferation of atypical round cells with eccentric pleomorphic nuclei and large amount of dense eosinophilic or glassy cytoplasm. In addition, immunohistochemistry disclosed positive for Vimentin and CD99 only, which suggested PNET. [11]

Meningiomas are benign tumors that account for 13%–26% of all primary intracranial tumors . Extracranial meningiomas are very rare, and are reported to account for 1%–2% of all meningiomas . Depending on the anatomical location of these lesions, extracranial meningiomas are clinically classified as primary or secondary . Most extracranial meningiomas are secondary extensions from the intracranial lesion. Hidenori Yokoi, Satoru Kodama, Keisuke Maruyama, Masachika Fujiwara,Yoshiaki Shiokawa, and Koichiro Saito reported a case of a 54-year-old man with a left-sided sphenoid ridge meningioma; the tumor was exerting pressure on the brain parenchyma and extended further from the temporal lobe into the sphenoid sinus. Hematoxylin-eosin staining at the initial craniotomy had uniform type circular nucleus and spindle cells with abundant cytoplasm exhibited substantial hyperplasia. This was diagnosed as transitional (mixed) meningioma, World Health Organization CNS grade I Anti-Ki-67 antibody staining was 1% or less. [12]

CONCLUSION

Sino-nasal and nasopharyngeal tumours comprise of a wide varierty of neoplasms with bewildering overlapping complex histopathological features. Hence, IHC is a must for supporting the diagnosis and to rule out differentials for the best assessment of the tumour and appropriate management.

Limitation

- Limited number of IHC markers available.
- Small sample size with single cases as these tumours are very rare to occur.

ACKNOWLEDGEMENT

I extend my gratitude to the faculty of Department of Pathology for their constant support and guidance through this journey. I also acknowledge the encouragement provided by my family, colleagues and technical staff in the department.

REFERENCES

[1] Lombard M, Michel G, Rives P, Moreau A, Espitalier F, Malard O. Extranodal non-Hodgkin lymphoma of the sinonasal cavities: a 22-case report. European annals of otorhinolaryngology, head and neck diseases. 2015 Nov 1;132(5):271-4.

[2] Owosho AA, Gooden CE, McBee AG. Hodgkin lymphoma of the nasopharynx: case report with review of the literature. Head and neck pathology. 2015 Sep;9:369-75.

[3] Su SY, Bell D, Hanna EY. Esthesioneuroblastoma, neuroendocrine carcinoma, and sinonasal undifferentiated carcinoma: differentiation in diagnosis and treatment. International Archives of Otorhinolaryngology. 2014 Apr;18:149-56.

[4] Lee DH, Yu MS, Lee BJ. Primary Burkitt's Lymphoma in the Nasal Cavity and Paranasal Sinuses. *Clin Exp Otorhinolaryngol*. 2013;6(3):184-186. doi:10.3342/ceo.2013.6.3.184

[5] Chen J, Feng X, Dong M. Anaplastic lymphoma kinase-positive diffuse large B-cell lymphoma presenting in nasal cavity: a case report and review of literature. *Int J Clin Exp Pathol*. 2015;8(2):2123-2130. Published 2015 Feb 1.

[6] Wani SQ, Dar IA, Khan T, Lone MM. Primary Sino-nasal Neuroendocrine Carcinoma: A Rare Tumor. *Cureus*. 2019;11(2):e4144. Published 2019 Feb 27. doi:10.7759/cureus.4144

[7] Wang S, Song C, Yang X, Yang Y, Wei J. Melanotic neuroectodermal tumor of infancy: Case report and literature review. Ear, Nose & Throat Journal. 2022 Jul 6:01455613221112353.

[8] Bhartiya R, Prasad KM. Malignant Melanoma of Nasal Cavity- A Case Report. *J Clin Diagn Res*. 2015;9(12):ED21-ED22. doi:10.7860/JCDR/2015/17009.6995

[9] Cheng X, Li Q, Wei X, Wu J. A case of olfactory neuroblastoma and literature review. Asian journal of surgery. 2022 Feb;45(2):832-3.

[10] Hu HM, Zhang WL, Huang DS, Luo S, Sarang A, Chen XH. Perfect prognosis of a boy with alveolar rhabdomyosarcoma of the nasal wing treated with brachytherapy and chemotherapy. *Chin Med J (Engl)*. 2020;134(3):370-372. Published 2020 Nov 3. doi:10.1097/CM9.0000000000001188

[11] Hwang JP. Primitive Neuroectodermal Tumor of Nasal Cavity on ^{18}F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography. *Indian J Nucl Med*. 2017;32(4):363-364. doi:10.4103/ijnm.IJNM_62_17

[12] Yokoi H, Kodama S, Maruyama K, Fujiwara M, Shiokawa Y, Saito K. Endoscopic endonasal resection via a transsphenoidal and transpterygoid approach for sphenoid ridge meningioma extending into the sphenoid sinus: A case report and literature review. *Int J Surg Case Rep*. 2019;60:115-119. doi:10.1016/j.ijscr.2019.06.003