Section: Pathology

Case Series

UNUSUAL PRESENTATIONS OF RARE HEMATOLYMPHOID MALIGNANCIES IN NASAL CAVITY- AN ENIGMA

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Abstract

Background: Neoplasms of plasma cell precursors and lymphoid cell origin are rare in the sinonasal region. These tumours may present with non-specific clinical features and causes difficulty in reaching clinical as well as tissue diagnosis. The plasmablastic neoplasms include plasmablastic lymphoma, plasmablastic myeloma. Rare lymphoid neoplasms include mantle cell lymphoma, follicular lymphoma, and other variants of non-Hodgkin's type lymphomas. The authors are reporting three cases of plasmablastic and lymphoid cell tumour that we came across in the nasal cavity. **Material & Methods:** Here we are reporting three cases of haematolymphoid tumours of sinonasal region. The first case was a 61-year-old male presented with visible nasal mass from nasal cavity. Endoscopic resection of the same was performed and tissue examination revealed a tumour of plasmablastic cell origin with immunocytochemistry showed positivity for CD138, LCA, MUM-1 and Lambda light chain restriction. Next case is of a 58-year-old male patient evaluated for chronic weight loss, showed a mass lesion in the nasopharyngeal region. The patient underwent trans nasal endoscopic biopsy and histopathology revealed small to medium sized lymphocytes and on IHC the tumour showed positivity for CD20, CD5, BCL2 and Cyclin D1. A diagnosis of Mantle cell lymphoma was made. The third case, a 50-year-old male evaluated for epiphora, diagnosed with a capillary haemangioma on pre op radiological evaluation. Following endoscopic debulking and dacryocystorhinostomy, the tumour was found to have lymphoid cells arranged in follicular pattern. The immunohistochemistry studies confirmed the diagnosis of Follicular type of extra nodal lymphoma. **Conclusion:** Plasmablastic cell origin tumours are very rare in sinonasal region, incidence of these neoplasms is almost equal to that of different variants of extra nodal site lymphomas of this region. Tissue diagnosis and immunohistochemical studies often help in reaching the correct diagnosis and thereby helping in further adjuvant therapies appropriate for the condition.

INTRODUCTION

Plasmablastic neoplasms and Non-Hodgkins Lymphomas (NHL) though rare in nasal cavity pose diagnostic dilemma to pathologists. This case series is intended to shed some light on Plasmablastic myeloma, a rare presentation in the nasal cavity and also discuss some rare cases of NHL- Mantle cell Lymphoma and Follicular Lymphoma in the nasal cavity. Plasmablastic neoplasms comprise a heterogenous group of haematolymphoid neoplasms which include Plasmablastic lymphoma (PBL), and Plasmablastic plasma cell myeloma and their distinction is a diagnostic challenge.[1] Mantle cell lymphoma is a rare, aggressive subtype of NHL with a poor prognosis and high recurrence rates.[2] Herein we report three cases one each of Plasmablastic myeloma, Follicular lymphoma, and Mantle cell lymphoma in the nasal cavity.

MATERIALS AND METHODS

The authors are reporting 3 different cases of lymphoid cell origin neoplasms in the nasal cavity. Written informed consent was obtained from all the patients for inclusion of the clinical data and relevant histopathological and cytopathological images. The study is performed in accordance with the ethical standards laid out in the Declaration of Helsinki (2013 amendment).

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CASE 1

61yr old male presented with a 2-month history of progressively enlarging right nasal mass. Patient had history of on & off epistaxis and severe head ache. HIV status of patient was negative. The physical examination showed a nasal mass which extended to the nasopharynx on CT scan. The clinical differential diagnoses included an inverted papilloma and pyogenic granuloma. The endoscopic assisted resected specimen was assessed by histopathological examination which showed diffuse infiltration by medium sized cells with plasmablastic morphology [Figure 1]. The differential diagnosis favoured were plasmacytoid lymphoma and plasmablastic myeloma. Tissue was taken up for immunohistochemistry and the cells were positive for CD138, LCA, MUM-1, Lamda light chain and negative for CD20, SOX10, S-100, PAX-5, CD56 & Kappa light chain. Ki67 showed 70-75% positivity. EBER Chromogenic In Situ Hybridization was positive. Following this detailed workup, a diagnosis of Plasmablastic neoplasm with Epstein-Barr virus positivity was rendered. Bone marrow aspiration material and trephine biopsy showed normal haematopoiesis with no evidence of neoplastic infiltrate.

CASE 2

58yr old male presented with nasal obstruction, fever, and weight loss to the ENT OPD. The endoscopic examination showed obstruction of choanae by a nasopharyngeal mass with associated friable necrotic material. There was no cervical lymphadenopathy. Computed tomography (CT) of paranasal sinus showed a homogenous solid mass with mild enhancement involving both nasopharyngeal walls and extending to the oropharynx. A trans nasal endoscopic biopsy of the mass was performed, and histopathological examination showed sinonasal mucosa with subepithelial infiltrate of predominantly small to medium sized round lymphoid cells with high nucleocytoplasmic ratio with irregular nuclear membrane, inconspicuous nucleoli, clumped chromatin, and scant cytoplasm [Figure 3-5]. There was no morphological evidence of transformation to aggressive lymphoma (blastoid/pleomorphic variant). Immunohistochemistry studies were performed, and atypical lymphoid cells were positive for CD20, CD5, BCL2 and Cyclin D1. The Negative markers were CD10 & CD3.Ki67 showed 38-40% positivity. [Figure 6-9] Finally after the workup, a diagnosis of Mantle cell lymphoma (B cell Non-Hodgkin Lymphoma)-classic variant was rendered.

CASE 3

50yr old male underwent endoscopic dacryocystorhinostomy for nasal block and epiphora and the clinical and radiological diagnosis given was cavernous hemangioma. On microscopy it showed sinonasal type mucosa with patchy dense infiltrates of lymphoid cells. These cells were arranged predominantly in follicular pattern with some areas showing diffuse pattern. The cells were small to medium admixed with few large cells with vesicular nuclei and prominent nucleoli. Also seen was a focus of cavernous hemangioma. Immunohistochemistry studies were carried out and findings were as follows.

CD20: Many lymphoid cells positive.

CD3: Few lymphoid cells positive.

Ki-67: High in follicles (about 50-55%) and in foci in interfollicular region.

Bcl-2: Large cells and B cells appear negative.

CD10, MUM1 and Bcl-6: Positive in large lymphoid cells.

Tdt, CK and Cyclin D1: Negative.

A diagnosis of Atypical lymphoid proliferation with large B lymphoid cells arranged mainly in follicular pattern with CD 10, MUM-1 & BCL-6 positivity was made. Molecular genetic testing for IRF4 rearrangement was suggested to rule out follicular lymphoma and to differentiate from reactive lymphoid proliferation.

Further workup carried out by FISH analysis on the tissue showed positivity for IRF4/DUSP22 gene rearrangement on chromosome,[6] band p25.3 which was consistent with the diagnosis of Follicular Lymphoma.

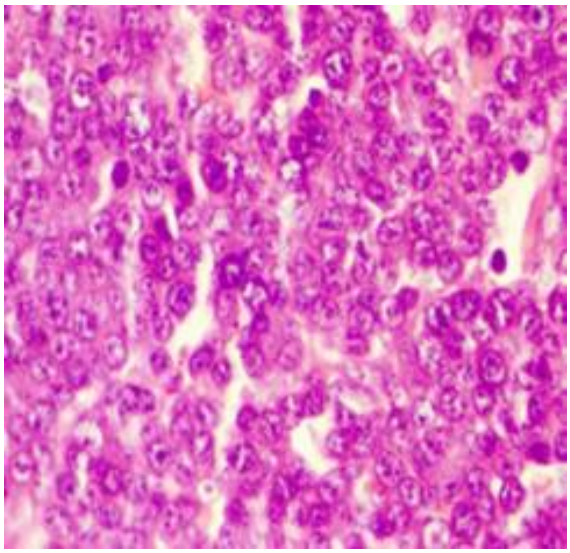

Figure 1: Medium sized tumor cells with plasmablastic morphology.

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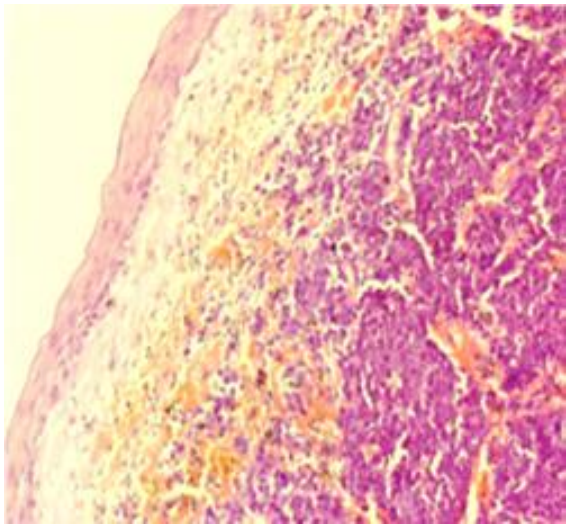

Figure 2: Diffuse infiltration by Plasmablastic tumor cells.

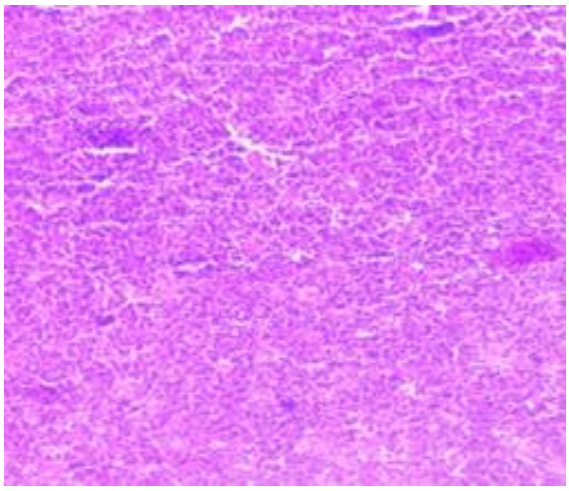

Figure 3: Diffuse architectural effacement by monomorphic atypical lymphoid cells

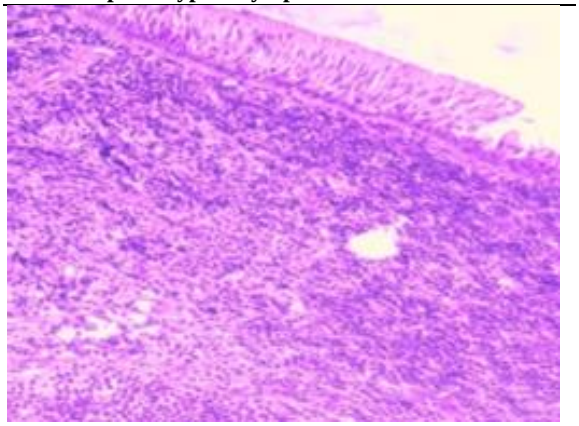

Figure 4: shows sinonasal mucosa with subepithelial infiltrate of lymphoid cells with hyalinized vessels.

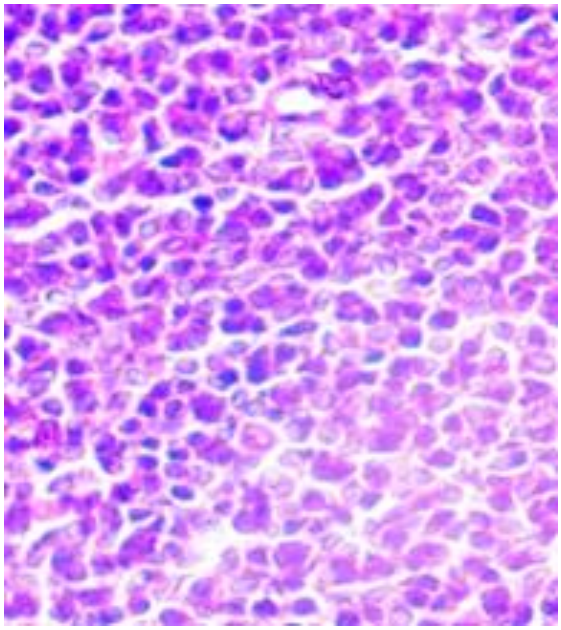

Figure 5: Small to medium sized round atypical lymphoid cells with high N:C ratio, irregular nuclear membrane, inconspicuous nucleoli, clumped chromatin with minimal cytoplasm

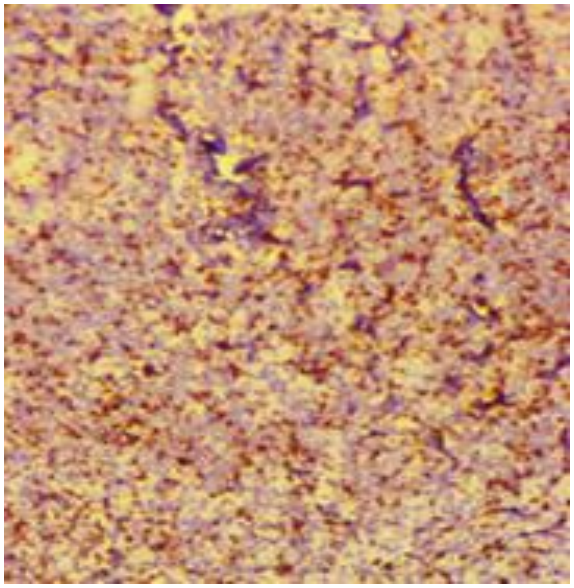

Figure 6: Ki67 showed 38-40% positivity

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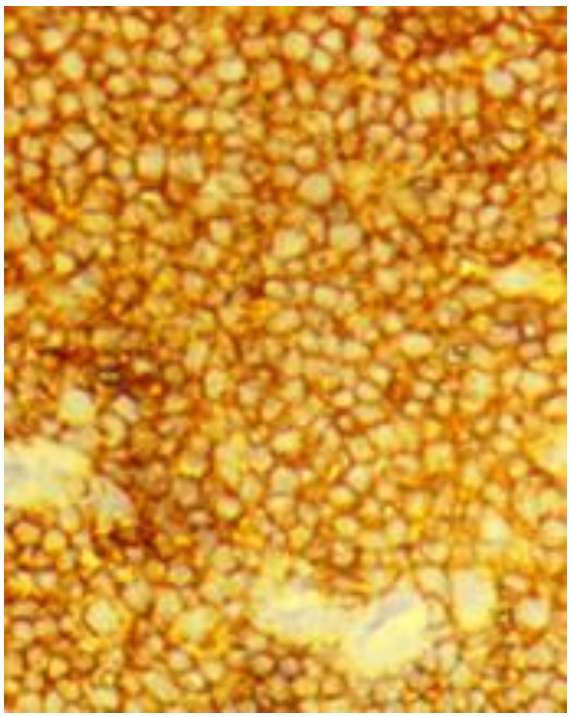

Figure 7: CD5 positivity noted.

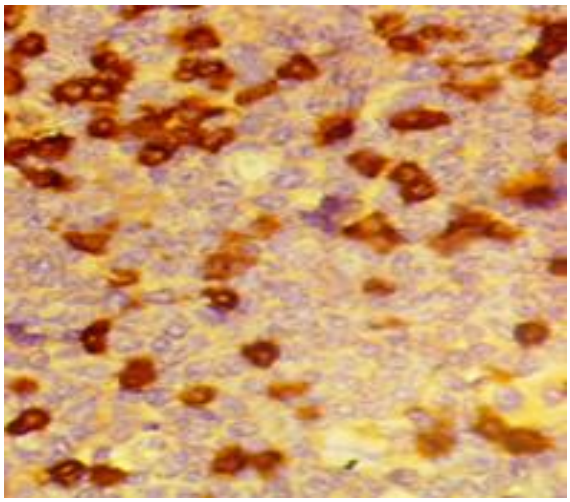

Figure 8: CD3-Negativity

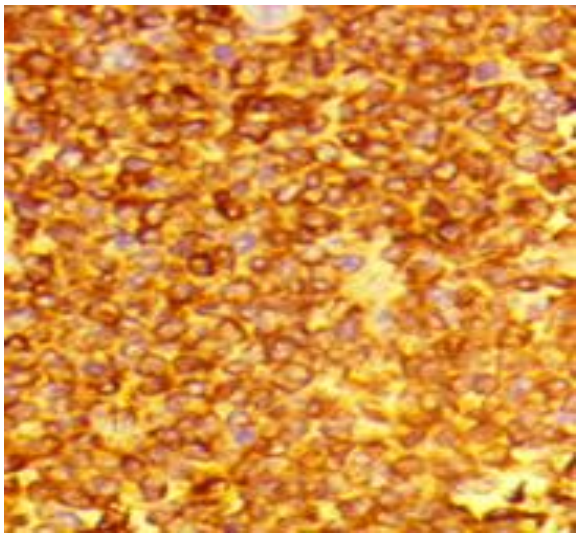

Figure 9: BCL2-Positivity.

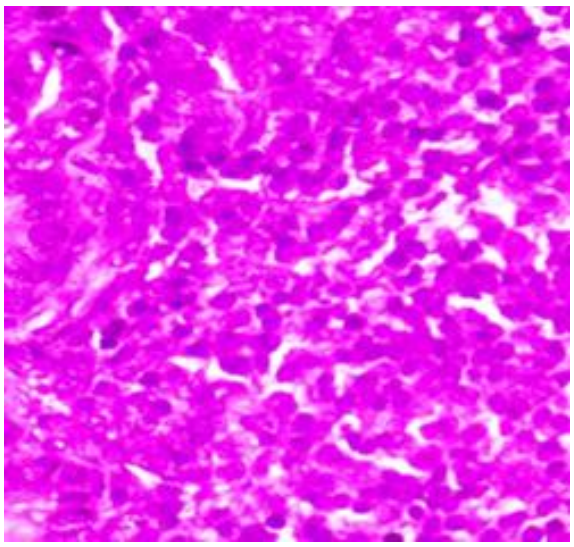

Figure 10: Atypical lymphoid cells arranged in follicular &diffuse pattern composed of small to medium sized cells with vesicular nuclei & prominent nucleoli

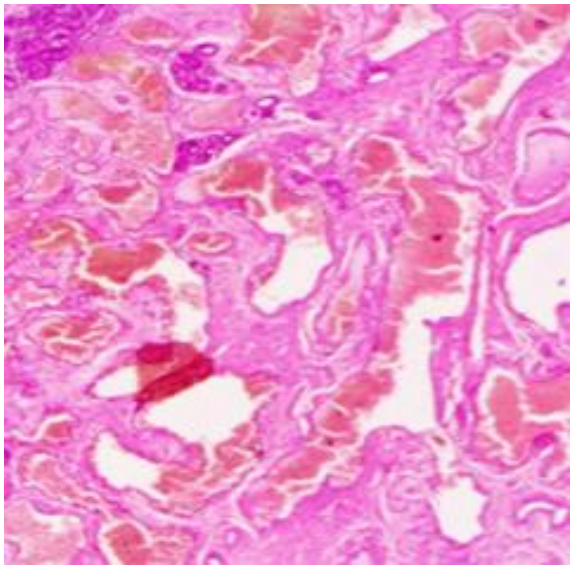

Figure 11: Cavernous Haemangioma- Anastomosing cords of large, dilated blood vessels lined by flattened endothelium and vessels engorged with blood.

DISCUSSION

Plasma cell dyscrasias are a group of disorders characterized by monoclonal plasma cell expansion.[4] Depending on their site of development and clinical features, plasma cell neoplasms have been divided into: a)Solitary extramedullary plasmacytoma b)Solitary bone plasmacytoma c)Multiple Myeloma d) Multifocal form of multiple myeloma e) Plasmablastic sarcoma.4Plasmablastic neoplasms comprise a heterogenous group of haematolymphoid tumours that includes several types of Non-Hodgkin Lymphoma and Plasmablastic plasma cell myeloma.1 Non Hodgkins B cell lymphomas with plasmablastic morphology include Plasmablastic lymphoma (PBL), ALK+ large B-cell Lymphoma, Primary effusion lymphoma (PEL) and

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HHV8+ diffuse large B-cell lymphoma.[1] The Plasmablastic Lymphoma has a close resemblance to plasmablastic myeloma which leads to frequent misdiagnosis. Plasma cell disorders occur at higher incidence in HIV infected patients and the aetiology of HIV related plasma cell neoplasm appears to be chronic antigenic stimulation.[3] The prevalence of plasmablastic morphology in newly diagnosed myeloma cases is approximately 10%.[4]

Extramedullary plasmacytoma (EMP) is a localized collection of monoclonal plasma cells, arising within soft tissues in an extra skeletal site. They can either be Primary (true) plasmacytoma (without evidence of systemic disease) or extramedullary manifestation during the course of multiple myeloma.[4] Scridde reported the first case of EMP in 1905.[4] The most commonly affected site is the nasal cavity/paranasal sinuses (43.8%) followed by nasopharynx (18.3%), the oropharynx(17.8%) and larynx(11.1%).[4] In the present case, it was primary extramedullary plasmacytoma. Plasmablastic myeloma represents a small morphological subtype of multiple myeloma and is associated with a poor prognosis.[4] Histopathologically, the tumor is characterized by a diffuse infiltration by medium sized tumour cells of plasmablastic morphology with fine reticular nuclear chromatin, large nucleus, with very little perinuclear halo.[4] Amyloid deposition maybe seen in 15%-38% of extramedullary plasmacytoma.[5] The treatment of extramedullary plasmacytoma is still controversial. Some advocate radiotherapy while others prefer surgical excision. Most clinicians recommend a combined approach (surgery and radiotherapy) for the management.

The incidence of sinonasal lymphomas is higher in Asian countries than in the West; these malignancies account for 2.6%–6.7% of all lymphomas in Asia, and they are the second most common extra nodal lymphoma, after gastrointestinal lymphoma.[7] Mantle cell lymphoma is a NHL accounting for approximately 6% of all NH.[7] The MCL is extremely rare in nasal cavity and paranasal sinus.[8] This condition is due to a translocation(11;14) in CD5+ B-cells in the mantle zone, which causes over expression of cyclin D1 disrupting the central cell cycle pathway balance resulting in MCL.[7,8] The clinical presentation of leukaemia and lymphomas can vary drastically depending on the type of leukaemia or lymphoma and generally patients can experience B symptoms, bleeding and or bruising, infection, lymphadenopathy and/or hepatosplenomegaly. The clinical signs could be a diffuse erythematous swelling inside the nasal cavity covered with exudates and crust or in some advanced cases there maybe extensive ulceration and necrosis.[9] The patients usually present at later stages of the disease with extensive lymph nodes, liver, spleen and bone marrow involvement.[8] Rarely MCL may involve the orbit, eyelid, conjunctiva, lacrimal gland, lacrimal sac, iris and floor of mouth.[9] Like NHL, staging of this illness is done using the Ann Arbor system based on presence and location of disease based on imaging.[8-11] The differential diagnosis for MCL includes carcinoma, malignant melanoma, olfactory neuroblastoma and rhabdomyosarcoma.[10]

According to the most current WHO classification of hematopoietic and lymphoid tumours, there are 3 subtypes of MCL: classical MCL, leukemic non-nodal MCL, and in situ mantle cell neoplasia. The present study was classical MCL. Within the classical MCL, there are 4 variants: blastoid, pleomorphic, small cell and marginal zone like.[11] Among the MCL variants, the blastoid and pleomorphic variants have a poorer prognosis, whereas the marginal zone-like and small cell variants tend to have a better prognosis.[11]

Microscopically the tumor tissue was arranged as nodular or diffuse pattern composed of monotonous, small to intermediate sized lymphocytes with dispersed chromatin, inconspicuous nucleoli with abnormal nuclear contours.[10,11] The immunophenotype of these cells are positive for pan-B cell markers (CD19, CD20, CD79a, PAX5), BCL-2, Cyclin D1, and aberrant expression of CD5(a T-cell marker).It is negative for CD10,CD23 and BCL-6.Differential diagnoses to consider are other “small B-cell lymphomas such as CLL/SLL,HCL,FL and MZL. The best way to distinguish is by immunophenotyping, either by flow cytometry or immunohistochemistry.[11]

In a study by Chalastras et al on Non-Hodgkins lymphoma of the nasal cavity and paranasal sinuses, Follicular lymphoma was found to be 8.33% of all the sinonasal lymphomas.[12] On a genetic level t(14;18) translocation has been recognized as a genetic hallmark of FL, but additional genetic aberrations are required for the development of FL14 . Cytogenetic analyses of FL samples have revealed that they contain 4 to 6 additional genomic alterations on average and 6q-, trisomy 7, trisomy 12, der (18) and +X are frequently observed. Follicular lymphoma is associated with constitutive expression of BCL 2. Recently additional recurrent gene aberrations such as TNFRSF14, EPHA7, EZH2, CREBBP, EP300, MLL2 and MEF2B have been identified in FL at large.[14]

Morphologically, FL is defined as a proliferation of malignant germinal centre B cells(GCBs) that are admixed with non-malignant cells such as T cells, follicular dendritic cells (FDCs) and macrophages and whose normal counterparts, i.e. centrocytes and centroblasts, represent the predominant cell types of the germinal centre reaction12 .The most distinctive feature of follicular lymphoma is a nodular growth pattern.[11] FL usually shows numerous neoplastic follicles with a monotonous appearance composed of small lymphoma cells with irregular ,twisted nuclei(called centrocytes) admixed with large lymphoma cells that have vesicular nuclei and prominent nucleoli(centroblasts).[13] The tumor cells are larger than normal lymphocytes.[11] The mantle zones of the follicles are effaced and the follicles lack the tingible body macrophages seen in normal

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reactive follicles.[13] Follicular lymphomas are composed of uniform, densely packed follicles, which may coalesce, simulating diffuse areas, with compression of interfollicular stroma and vessels, that can be highlighted by reticulin stain. The follicular population is uniformly atypical. Small cells have cleaved, indented, angulated nuclei, large cells maybe cleaved or non-cleaved. Mitotic figures are less frequent in FL than follicular LH; however, grade 3 FL may have high mitotic rate.[14] FL grading is performed by estimating the average number of centroblasts per HPF in 10 neoplastic follicles(grade 1,0-5 centroblasts per HPF; grade 2, 6-15 centroblasts per HPF; grade 3, >15 centroblasts per HPF).[14]

By IHC, FL cells express pan B-cell markers (CD19,CD20,CD22,CD79,PAX5) and monotypic surface Ig, most commonly IgM with or without Ig D. Germinal centre markers, including CD10, BCL6, HGAL, LMO2, STMN1, GCET, MEF2B etc are variably expressed by FL cells. BCL2 is positive in 85%-90% of FL grades 1 and 2.BCL2 and CD10 show decreased intensity and frequency of staining as the grade of FL increases. FL cases are negative for T cell markers CD2,CD3,CD4,CD5,CD7,CD8 and are usually negative for CD43 and cyclin D1. Ki-67 marker assess the proliferation rate of follicular lymphomas and the Ki-67 proliferation index correlates with FL grade.[15]

Conventional cytogenetic analysis can detect t(14;18)(q32;q21) IGH-BCL-2 in up to 90% of FL cases. Fluorescent in-situ hybridization (FISH) is more sensitive than PCR- based approaches in detecting IGH-BCL2 due to variation in breakpoint regions.[15]

CONCLUSION

Extra nodal lymphomas like Mantle cell lymphoma and Follicular lymphoma and Plasmablastic neoplasms are a group of rare neoplastic presentation encountered in the nasal cavity and is often a concern to the oncopathologist. This article intends to shed some light on these three cases which are uncommon, unusual presentations in the nasal cavity and requires special mention.

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