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TO DECEMBER PRIMARY EXTRANODAL LYMPHOMAS: AN EXPERIENCE AT A TERTIARY CARE CENTER IN NORTH KARNATAKA.

Pathology

Dr. Varsha U. Reddy

ABSTRACT

Aim: The present study highlights various sites of extranodal lymphomas in a tertiary care hospital in North Karnataka region. **Materials and Methods:** A retrospective and prospective analysis of 17 cases of extra nodal lymphomas. **Results:** The age of patients of extranodal lymphomas ranged from 26-78 years. Female preponderance observed was carried out with immunohistochemistry wherever necessary, female to male ratio of 1:0.8. Of the 17 cases, 3 cases were seen in GIT and thyroid each, 2 cases in testis and 1 case in CNS, parotid, tonsil, breast lung spleen, skin, soft tissue and ovary each. **Conclusion:** 1. The occurrence of extranodal lymphomas in various sites must be kept in mind and diagnosis can be done by correlating clinical presentation with histopathological features. 2. Histopathological evaluation is one of the most valuable means of diagnosis of extra nodal lymphomas.

KEYWORDS

INTRODUCTION :

Primary extranodal lymphomas were recognized first in the mid-20th century.[1] The term extranodal lymphoma is used when there is infiltration of malignant lymphomatous cells in the organs other than lymph node. Any organ in the body can be affected.[2]

The site at which lymphoma cells proliferate is a reflection of an interaction between growth-promoting microenvironmental features (presence of corresponding ligands and growth factors) and tumour cell characteristics (e.g. homing and adhesion molecules, growth factor receptors, etc.).[3,4]

Lymphomas are broadly classified as Hodgkin's lymphoma (HL) or non-Hodgkin's lymphoma (NHL). HL rarely shows extranodal disease as opposed to NHL [13]One third of NHL are extra nodal [12] and 15% of all HL are extra nodal. [11]

In the present study we are emphasing on the various sites of the extra nodal lymphomas.

MATERIALS AND METHODS :

The present study was conducted in a tertiary care teaching hospital in north Karnataka region of India. A retrospective study of 17 cases was carried out. The study was conducted from Janurary 2019 to December 2021. The parameters analysed were name, age, sex, site , histopathological features and immunohistochemistry.

RESULTS

Out of 17 cases of extra nodal lymphomas , 9 were female , 8 were male, Female to male ratio was1:0.8 denoting female preponderance in the present study.

Table no 1: Age & Sex distribution.

Age	No. of cases	Male	Female	Percentage
21-30	2	1	1	11.76%
31-40	2	0	2	11.76%
41-50	2	0	2	11.76%
51-60	1	0	1	5.88%
61-70	7	5	2	41.17%
71-80	3	2	1	17.64%
Total	17	8	9	100%

Age group ranged from 26-78 years, oldest age was 78 years, youngest age 26 years, mean age was 52 years. Maximum number of cases were see in the age group of 71-80 years. Female to male ratio was 1:0.8.

Table 2 : Histological variants of lymphomas in various sites of extra nodal lymphomas.

Site	Histopathological Variants	Number of cases
CNS	DLBCL	1
Parotid	DLBCL	1
Thyroid	B cell lymphoma	3
Tonsil	DLBCL	1
Breast	DLBCL	1
Lung	DLBCL	1
Spleen	Follicular lymphoma	1
Intestine	DLBCL	3
Skin	Mycosis fungoides	1
Soft tissue (Gluteal)	DLBCL	1
Testis	DLBCL	2
Ovary	DLBCL	1

Of the 17 cases, 3 cases each were seen in GIT and thyroid each, 2 cases in testis and 1 case each in CNS, parotid, tonsil, breast, lung, spleen, skin, soft tissue and ovary each.

Most of the extra nodal lymphoma was DLBCL on histopathology.

Table 3 Predominant Clinical features of extra nodal lymphomas.

Site	Clinical features
CNS	headache and vomiting
Parotid	Pre auricular mass
Thyroid	swelling infront hypothyroid features
Tonsil	recurrent episodes sore throat , pain during swallowing and loss of appetite
Breast	palpable rubbery mass in the breast, which is not fixed to the chest wall or to overlying skin
Lung	cough weight loss
Spleen	bleeding gums macules on face and neck with mild splenomegaly
Intestine	Abdominal pain
Skin	papules nodules on chest trunk limbs with intense itching
Soft tissue	Mass in gluteal region
Testis	testicular swelling
Ovary	ascites

In the present study IHC was done in three cases. The case of CNS lymphoma showed immune positivity for CD 3, CD20, BCL2 and CD10. KI 67 was 85% in this case. Primary extra nodal lymphoma of tonsil was CD 20 positive and cytokeratin negative. CD 20 and CD 19 were positive in the case of lymphoma of thyroid.

DISCUSSION

Disease presenting with only extranodal involvement without any palpable lymphadenopathy or not visible on imaging tests is classified as primary extranodal NHL[7] .Primary extranodal lymphomas with different pathologic subtypes manifest at various anatomical sites. Rare extra nodal sites include cardiac, meningeal, esophageal, pancreatic,gall bladder, adrenal, genitourinary and soft tissue lymphomas[5]

Several infectious agents cause non-Hodgkin's lymphoma. These include human immunodeficiency virus (HIV), Epstein–Barr virus (EBV), human herpes virus 8 (HHV-8), hepatitis C virus (HCV), and

Helicobacter pylori. In addition to these a role of hepatitis B virus (HBV), Borrelia burgdorferi, Campylobacter jejuni, and various Chlamydia species is also suspected. [5]

JAK/STAT Pathway

In extranodal NK/T-cell lymphoma, STAT3 of the JAK/STAT cascade is the most frequently mutated gene. Other genes involved are JAK1, JAK3, SOCS1and Tp53

Tumor Microenvironment

Chemokines play an important role in the proliferation of tumour cells with the recruitment of inflammatory cells. Tumour cells secrete the monocyte-attractant chemokines that is IP-10 (interferon gamma-induced protein 10), CCL2 (C-C motif chemokine ligand 2), and CCL22 (C-C motif chemokine ligand 22). Monocytes, in turn, promote proliferation, LMP-1 expression, and IP-10 production of tumor cells via membrane-bound IL-15/IL-15 receptor alpha complex. This positive feedback loop between tumor cells and monocytes contributes to the progression of lymphoma.[6]

The major sites of involvement can vary in different studies but in general there is agreement that the gastrointestinal tract, Waldeyer's ring, and skin make up for the majority, approximately 65%, with the remainder being central nervous system (CNS), lung, testis, salivary glands, and bone[8,9]

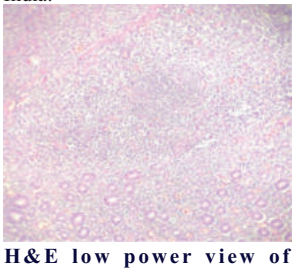
The incidence of extranodal non-Hodgkin's lymphoma (NHL) is high in HIV-positive patients and hence these patients should be advised HIV testing [10]

Table 4 : Comparative analysis of site and histological type .

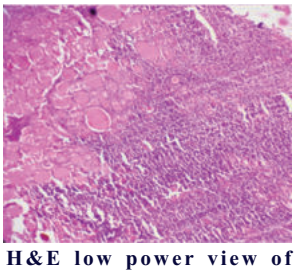
Study	No. of cases	Mean age (years)	Commonest site	Commonest histological type of lymphoma
Das et al (2013)	61	-	GIT	DLBCL
Pai et al 15 (2017)	41	48.2	GIT	DLBCL
Narang et al (2021)	56	61.3	GIT	DLBCL
Present study (2022)	17	52	GIT and Thyroid	DLBCL

CONCLUSION

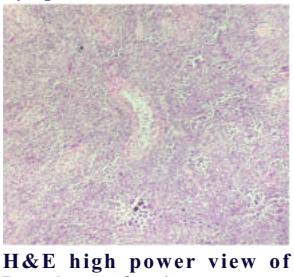
Extra nodal lymphomas comprise of a significant proportion of all lymphoma patients worldwide. The occurrence of extranodal lymphomas in various sites must be kept in mind and can be done by correlating clinical presentation with histopathological features. Histopathological evaluation is one of the most valuable means of diagnosis of extra nodal lymphomas. This study reveals the spectrum of extra nodal sites of the disease in the population of North Karnataka, India.



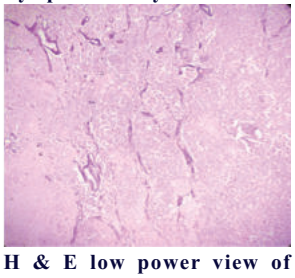
H&E low power view of Lymphoma of intestine



H&E low power view of Lymphoma of thyroid



H&E high power view of Lymphoma of testis



H & E low power view of Lymphoma of lung

REFERENCES .

1 Gall EA, Mallory TB. Malignant lymphoma. A clinicopathologic survey of 618 cases. Am J Pathol 1942;18: 381–429.
2 Das J, Ray S. Extranodal involvement in lymphoma – A Pictorial Essay and Retrospective Analysis of 281 PET/CT studies. Asia Oceania J Nucl Med Biol. 2014; 2(1):42-56.
3 d'Amore F, Christensen BE, Brincker H, et al. Clinicopathological features and prognostic factors in extranodal non-Hodgkin lymphomas. Danish LYFO Study Group. Eur J Cancer 1991; 27(10): 1201–8
4 Krol AD, le Cessie S, Snijder S, et al. Primary extranodal non-Hodgkin's lymphoma (NHL): the impact of alternative definitions tested in the ComprehensiveCancer Centre West population-based NHL registry. Ann Oncol 2003; 14(1): 131–9.
5 Cavalli f, Stein H, Zucca E, Extra Nodal Lymphomas Pathology and Management. Informa Healthcare. United Kingdom. 1st edition,2008.
6 Thida AM, Gohari P. Extranodal NK-Cell Lymphoma. [Updated 2022 Jul 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan
7. Salem H. AlShemmari, Reem M. Ameen & Kamlesh P. Sajnani (2008) Extranodal lymphoma: a comparative study, Hematology, 13:3, 163-169
8 Krol ADG, le Cessie S, Snijder S, et al. Primary extranodal non-Hodgkin's lymphoma (NHL): the impact of alternative definitions tested in the Comprehensive Cancer Centre West populationbased NHL registry. Ann Oncol 2003; 14: 131–9.
9. Lopez-Guillermo A, Colomo L, Jimenez M, et al. Diffuse large B-cell lymphoma: clinical and biological characterization and outcome according to thenodal or extranodal primary origin. J Clin Oncol 2005; 23: 2797–804.
10 Rastogi M, Revannasiddaiah S, Seam RK, Gupta MK, Gupta M. Extranodal lymphoma masquerading as carcinoma of the breast in an HIV-positive male patient. BMJ Case Rep. 2012 Dec 23;2012
11 Gupta RK, Gospodarowicz MK, Lister TA. Clinical evaluation and staging of Hodgkin's disease. In: Mauch PM, Armitage JO, Diehl V, et al, eds. Hodgkin's Disease. Philadelphia: Lippincott Williams & Wilkins, 1999.
12 Gurney KA, Cartwright RA. Increasing incidence and descriptive epidemiology of extranodal non-Hodgkin lymphoma in parts of England and Wales. The Hematology Journal : the Official Journal of the European Haematology Association. 2002; 3(2):95104
13 Shah GH, Panwar SK, Chaturvedi PP, Kane SN. Isolated primary extranodal lymphoma of the oral cavity: A series of 15 cases and review of literature from a tertiary care cancer centre in India. Indian J Med Paediatr Oncol. 2011 Apr;32(2):76-81.
14 Narang V, Steffi, Singh A, Sood N, Garg B, Kaur H, Jain K, Grover S. Primary Extranodal Non Hodgkin Lymphomas: A First tertiary care experience from Punjab, North India. South Asia J Cancer 2021;(4):230-232.
15 Pai A, Kannan T, Balambika RG, Vasini V. A study of clinical profile of primary extranodal lymphomas in a tertiary care institute in South India. Indian J Med Paediatr Oncol 2017;38(3):251–255