

## Original Research Article

## Study of Hodgkin Lymphoma with Special Reference to NLPHL in A Tertiary Care Hospital in Eastern India

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**Abstract:** Hodgkin lymphoma is one of the most common lymphomas in the developed world. There is a great importance of histological sub classification of Hodgkin lymphoma so far prognostic importance is concerned. Moreover, PTGC may proceed to the development NLPHL and at present an overlap between NLPHL and TCRLBCL cannot be excluded. So a detailed clinical and morphological study is essential in Hodgkin lymphoma to assess proper diagnosis and prognosis. As there is scarcity of study in this field in Eastern India, our study was performed. Forty known cases of Hodgkin lymphoma was studied with detailed clinical history, examination findings, routine histopathological examination with IHC correlation (CD20, CD3, CD30, CD15). Special emphasis is given on T cell (CD3) infiltration in NLPHL. Out of 40 cases, 3 were NLPHL, 25 were NSCHL, 9 were MCCHL, 2 were LRCHL and 1 was LDCHL. Two cases of NLPHL showed 8 to 10% of T cell (CD3 positive) infiltration in the background. One case of NLPHL showed 50 to 60% T cell positivity in the background suggesting close follow up to rule out progression to TCRLBCL. Our study was done to assess these important prognostic parameters in Hodgkin lymphoma. However study involving more number of cases will be more informative.

**Keywords:** Hodgkin lymphoma, CD 20, CD3, CD30, CD15, NLPHL, Tcell.

### INTRODUCTION

Hodgkin lymphoma is one of the most common lymphomas in the developed world, with an incidence of approximately three per 100000 person-years [1]. Hodgkin lymphoma comprises about 11% of all lymphomas in Western countries and a unique bimodal age- incidence shape [2]. In Taiwan, the crude and age adjusted rates of Hodgkin Lymphoma were 0.19-0.62 and 0.21-0.60 per 100000 per year respectively from year 1979 to 2002 [3].

Hodgkin lymphomas are comprised of two disease entities –Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) and Classical Hodgkin lymphoma (CHL). Classical Hodgkin Lymphoma has four subtypes – NSCHL, MCCHL, LRCHL, and LDCHL. NLPHL develops slowly with frequent relapses. It usually remains responsive to therapy, thus rarely fatal. The prognosis of patients is very good with 10 yrs survival in early stage. Advance stages have an

unfavourable prognosis. NSCHL has a better prognosis overall than that of other types of CHL. Before the introduction of modern therapy MCCHL had a worse prognosis than nodular sclerosis and a better prognosis than lymphocyte depleted CHL. With current regimens, these differences are largely vanished, although not entirely. With modern risk adjusted treatment survival is slightly better in LRCHL than other subtypes of CHL and similar to that of NLPHL except that relapses are more common in NLPHL than in LRCHL. Prior to modern therapy, the course of LDCHL was aggressive [4].

Traditionally NLPHL and nodular sclerosis have been the most favourable prognosis, mixed cellularity has been intermediate and the lymphocyte depletion form has had worst prognosis [5].

So we see that there is a great importance of histological sub classification of Hodgkin lymphoma so

far prognostic importance is concerned. Moreover, Progressive transformation of germinal centre (PTGC) is the morphologic expression of a distinct type of follicular hyperplasia. It can occur as an isolated self reactive process, particularly in young men [6]. PTGC may proceed to the development NLPHL. The main differential diagnosis of PTGC is with NLPHL which should be suspected if with T cell rosettes are prominent. Occasionally, there is reactive follicular hyperplasia with progressive transformation of germinal centres (PTGC) adjacent to the lesion or it may proceed or follow a diagnosis of NLPHL [7]. At present an overlap between NLPHL and TCRLBCL cannot be excluded. Most of the LP cells in NLPHL are ringed by CD3 + T cells, Most of the LP cells is associated with a propensity to develop a diffuse pattern resembling T-cell histiocyte -rich large B-cell lymphoma (THRLBCL-like) . This is seen more frequently in patients with recurrence [8].

As there is scarcity of study in this field in Eastern India, our study was performed with the following objectives-

- 1) Detailed clinical and histological study of different types of Hodgkin lymphoma with IHC correlation.
- 2) Detailed study of NLPHL with special importance to T cell infiltration in the background.

#### MATERIAL AND METHODS

The study was conducted for retrospective three years and prospective one and a half years with collected biopsy specimens of lymph node diagnosed as Hodgkin lymphoma. Total forty cases were studied. Paraffin blocks were collected from histopathology store. Relevant clinical history & other findings were obtained from histopathology records. In clinical history, special emphasis was given on lymph node swelling associated with fever, weight loss, night sweat etc and on clinical examination we looked for groups of lymph node involvement, hepatosplenomegaly and general assessment. Routine histopathological examination was done from the stored slides by H/E stain, reticulin stain and PAS stain. Immunohistochemistry was done as per the provisional diagnosis made from histopathological examination. Monoclonal antibody against CD20 was performed for demonstration of B cells (also popcorn variety of Reed Sternberg cell); CD3 was done for T cells. CD30 and

CD15 were done for demonstration of classical Reed Sternberg cell. Final diagnosis was done in each case and the results were analysed. T cell population (CD3 positive) were evaluated, especially in NLPHL to differentiate between progressive transformation of germinal centre (PTGC) and T cell rich large B cell lymphoma (TCRLBCL).

#### RESULT AND DISCUSSION

The study was conducted with collected biopsy specimens of lymph node. Total 40 cases of Hodgkin lymphoma were studied. Table -1 show out of forty cases 25 were of nodular sclerosis, 9 were mixed cellularity (Fig. 1), 2 were lymphocyte rich, 1 case of lymphocyte depleted and 03 cases of nodular lymphocyte predominant Hodgkin lymphoma. Most of the cases were 20-40yrs age group of which 52% were NSCHL followed by MCCHL. Only 01 case of LDCHL and 01 case of NSCHL was found in older age group. 20% patients of NSCHL were found in 40-60yrs age group. All the cases of LRCHL occurred in 40 – 60yrs age group.

Table 2. Shows predominant variants of RS cells in different types of Hodgkin lymphoma. In NSCHL mostly found RS cell was lacunar type, whereas NLPHL, MCCHL, LRCHL, LDCHL and also NSCHL all showed classical RS cell and mononuclear RS cell. One case of LDCHL showed classical RS cell, pleomorphic RS cell & mummified RS cell. All the cases of NLPHL showed popcorn cell. Different types of Hodgkin lymphoma were diagnosed by following protocols. Firstly, nodular architecture was noted, followed by background cellularity and identification of RS cell and its variants. Nodularity was best demonstrated by reticulin stain. If only nodularity present along with presence of popcorn cells and background cellularity consisted of small lymphocytes, then provisional diagnosis of NLPHL was made. This was confirmed by IHC study where the popcorn cells of NLPHL were CD20 positive. When nodularity with fibrosis (best demonstrated by reticulin stain) was present and background cellularity consisted with eosinophils, lymphocytes and RS cells of lacunar type, classical or mononuclear type found then provisional diagnosis of NSCHL was made. This was confirmed by IHC study. RS cells of NSCHL were positive for CD30 and CD15 but negative for both CD20 and CD3 [9].

NLPHL was also differentiated from Follicular lymphoma and NSCHL. In NLPHL nodule was bigger and popcorn cell was present within nodule where as in

follicular lymphoma nodule was smaller, may be perinodular involvement and monomorphic cell population present. In NSCHL sclerosis surrounding the nodule and lacunar type of RS cell was present whereas in NLPHL no sclerosis was present surrounding the nodule with presence of popcorn cell .When no nodularity was present, possibility of MCCHL, LRCHL, LDCHL was suspected. MCCHL showed background of lymphocytes, eosinophils, plasma cells, histiocytes along with classical type RS (which were positive for CD30 and CD15 but negative for CD20) [Table-3, Fig.-1]. Background cellularity of LRCHL showed presence of lymphocytes. Here classical RS cell and mononuclear RS cell were present (CD30 and CD15 positive) (Table-2). LDCHL showed pleomorphic and mummified RS cell along with scanty background cellularity of lymphocytes. (RS cell was CD30 and CD15 positive) (Table-2).

MCCHL was differentiated from Reactive hyperplasia of Lymph node. In the later, lymph nodal architecture was maintained, mantle zone was present and atypical cell was absent, whereas in MCCHL lymph nodal architecture was lost, mantle zone was absent and atypical cells were present [10].

Dilip K Das *et al* showed that most of the cases of NHL and HL can be diagnosed based on cyto/histomorphology, immunohistochemistry, cytogenetic and molecular studies [11].

Out of three NLPHL cases, two showed 8 to 10% background cells were CD3 positive. 50 to 60% of background cells were CD3 positive in one case indicating increased population of T cells. In LDCHL 12 to 15% of background cells were CD3 positive whereas only 5 to 10% of background cells were

positive in MCCHL. 90% popcorn cells in NLPHL showed CD 20 membrane positivity. In CHL background B lymphocytes were CD 20 positive but classical Reed Sternberg (RS) cells and lacunar cells were CD20 negative. Classical RS cells, mononuclear RS cells, pleomormhic and mummified RS cells were CD15 and CD30 positive in classical HL but all popcorn cells in NLPHL were CD 15 and CD 30 negative (Table 3).

Study of Nathwani *et al.* showed increase in activated lymphocytes leads to better prognosis like PTGC but diffuse infiltrate of CD20 positive B cell & small lymphocytes consisting of CD3 positive T cell leads to aggressive clinical course like TCRLBCL [12]. In our study, one case of NLPHL showed 50 to 60% of background cellularity was consisted of CD3 positive T cells (indicating possibility of poor prognosis). Other two cases of NLPHL showed less number of CD3 positive background T cell.

According to WHO, there is an overlap between NLPHL and TCRLBCL. Occasionally there is reactive follicular hyperplasia with PTGC adjacent to the lesion. PTGC may proceed or follow a diagnosis of NLPHL. In our study we could not found any reactive follicular hyperplasia.

Gorde- Grosjean S et al showed that NLPHL differs clearly from classical Hodgkin lymphoma (CHL) by clinical presentation and more favourable outcome [13].

So it is very important to classify Hodgkin Lymphoma systematically with special emphasis on NLPHL so that proper prognosis can be assessed accurately.

**Table-1: Showing age distribution of all the cases-**

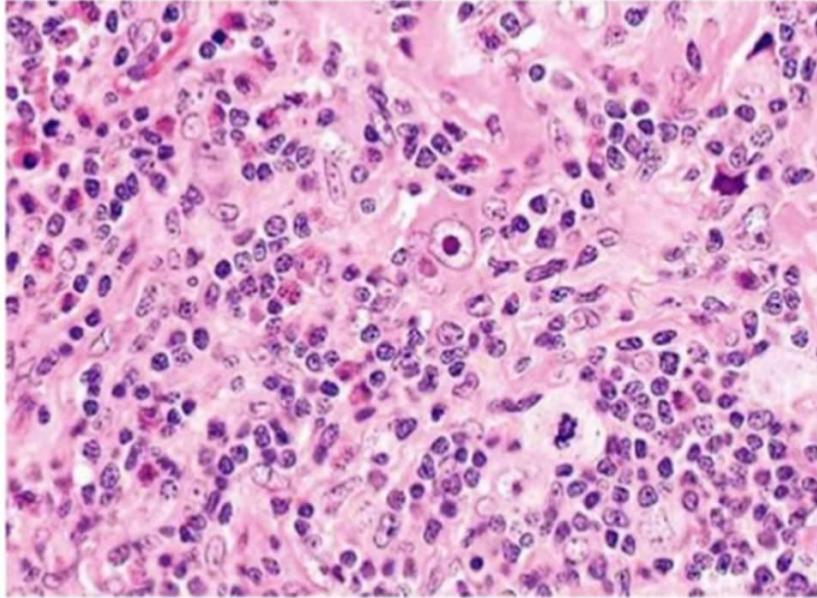
Diagnosis Age groups	NLPHL (n=3)	NSCHL (n=25)	MCCHL (n=9)	LRCHL (n=2)	LDCHL (n=1)
0-20 yrs		6 (24%)	4(44%)		
20-40 yrs	1(33%)	13(52%)	4(44%)		
40- 60 yrs	2(67%)	5 (20%)	1(12%)	2(100%)	
Above 60 yrs		1 (04%)			1(100%)

**Table-2. Showing variants of RS cell in all the cases**

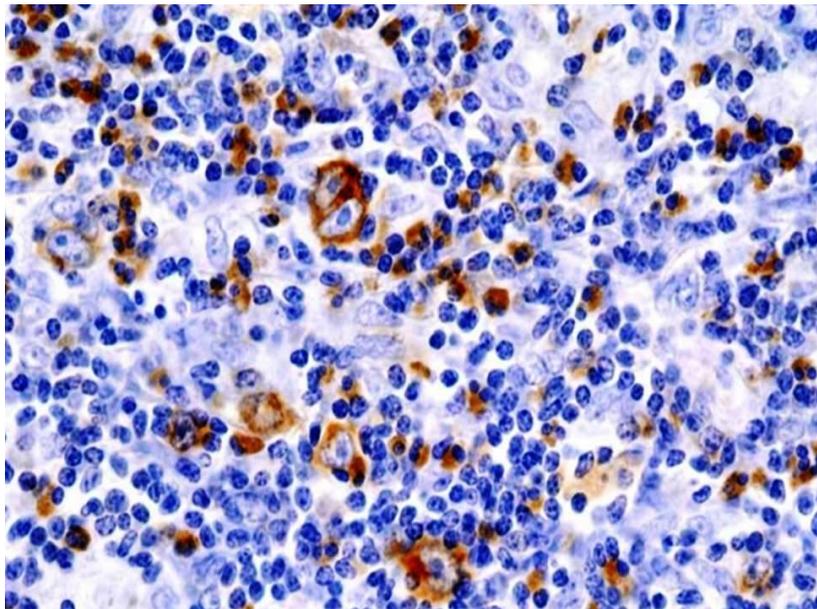
Diagnosis Variants of RS Cells	NLPHL (n=3)	NSCHL (n=25)	MCCHL (n=9)	LRCHL (n=2)	LDCHL (n=1)
Classical RS cell	01(33%)	10(40%)	08(88%)	02(100%)	01(100%)
Lacunar RS cell	-	25(100%)	-	-	-
Mononuclear RS cell	01(33%)	03(12%)	04(44%)	02(100%)	-
Pleomorphic RS cell	-	-	01(11%)	-	01(100%)
Mummified RS cell	-	-	-	-	01(100%)
Popcorn cell	03(33%)	-	-	-	-

**Table-3. Showing IHC results found in all the cases**

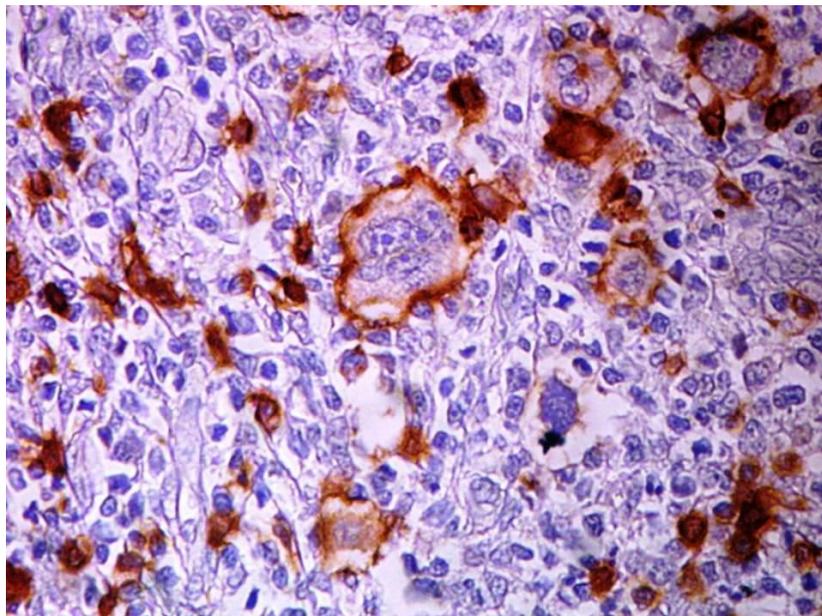
Diagnosis IHC	NLPHL (n=3)	NSCHL (n=25)	MCCHL (n=9)	LRCHL (n=2)	LDCHL (n=1)
CD3	2 cases - 8 to 10% of background cells positive. 1 case - 50 to 60% of background cells positive.	10 to 15% of background cells were positive.	5 to 10% of background cells were positive.	8 to 12% of background cells were positive.	12 to 15% of background cells were positive.
CD20	90% of popcorn cells were membrane positive	Background B lymphocytes were positive but classical Reed Sternberg (RS) cells and lacunar cells were negative.	50% of background B lymphocytes were positive but classical RS cells, lacunar cells and mononuclear R.S cells were negative.	70% of background B lymphocytes were positive but classical RS cells, lacunar cells and mononuclear RS cells were negative.	30% of background B lymphocytes were positive but classical RS cells, mononuclear RS cells, pleomormhic and mummified RS cells all were negative.
CD30	All popcorn cells were negative	Classical RS cells, lacunar cells and mononuclear RS cells all were positive.	Classical RS cells, lacunar cells and mononuclear RS cells all were positive.	Classical RS cells, lacunar cells and mononuclear RS cells all were positive.	Classical RS cells, mononuclear RS cells, pleomormhic and mummified R.S cells all are positive
CD15	All popcorn cells were negative	Classical RS cells, lacunar cells and mononuclear RS cells all were positive.	Classical RS cells, lacunar cells and mononuclear RS cells all were positive.	Classical RS cells, lacunar cells and mononuclear RS cells all were positive	Classical RS cells, mononuclear RS cells, pleomormhic and mummified RS cells all were positive.



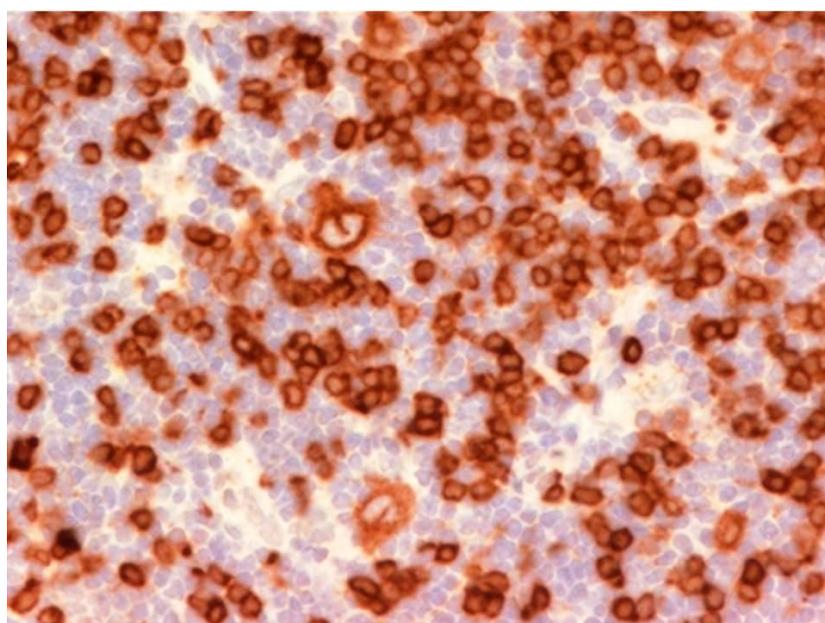
**Fig-1 - Microphotograph showing Classical Hodgkin lymphoma with mixed cellularity (HE, 400x).**



**Fig-2 - Microphotograph showing CD 30 positive Reed Sternberg cell (CD30, 400x).**



**Fig. 3 - Microphotograph showing CD 20 positive Popcorn cell (CD20, 400x).**



**Fig. 4 - Microphotograph showing CD 3 positive NLPHL (CD3, 400x).**

#### **CONCLUSION**

Proper sub classification of Hodgkin lymphoma is extremely important to assess appropriate prognosis. Increased population of T lymphocytes in NLPHL may lead to progression to T cell rich large B cell lymphoma. Progressive transformation of germinal centre (PTGC) may also evolves to NLPHL. Our study was done to asses these important prognostic

parameters in Hodgkin lymphoma. However study involving more number of cases will be more informative.

#### **Abbreviations**

CHL =Classical Hodgkin Lymphoma  
H/E = Haematoxylin and Eosin  
IHC = Immunohistochemistry

LDCHL = Lymphocyte depleted classical Hodgkin lymphoma

LRCHL = Lymphocyte rich Hodgkin lymphoma

MCCHL = Mixed cellularity classical Hodgkin lymphoma

NLPHL = Nodular lymphocyte predominant Hodgkin lymphoma

NSCHL = Nodular lymphocyte predominant classical Hodgkin Lymphoma

PTGC = Progressive transformation of germinal centre

RS cells = Reed Sternberg cells

TCRLBCL= T cell rich large B cell lymphoma

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