Lymphocyte Predominance Hodgkin Lymphoma Clincopathological and Immunohistochemical Interpretations Using CD15 and CD20

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SUMMARY:

BACKGROUND:

Hodgkin disease is a lymphoid tumor that accounts for less than (1%) of all DeNovo neoplasms occurring every year worldwide.

OBJECTIVE:

The aims of the study was to assess the expression of immunohistochemical markers namely (CD_{20},CD_{15}) in malignant cells of Hodgkin's disease.

METHODS:

Over the period extending from (January 2006-March 2008), specimens form 31 cases of lymphocyte predominance Hodgkin lymphoma (Rye's classification) as formalin fixed, paraffin embedded tissue blocks from excisional lymph node biopsies. For each case, five representative sections were prepared. One stained with hematoxyline and eosine (HxE), and four other sections (on positively charged slides) prepared for IHC procedures using CD_{15}, and CD_{20}. For the evaluation of markers expression, a semiquantitative evaluation system was used to register the staining intensity and the numbers of positive cells.

RESULTS:

The most common site of lymph node biopsy was the cervical lymph node in (61.2%) of cases. Immunohistochemically, CD_{20} was expressed in (12.9%) of cases, while CD_{15} was expressed in (77.4%) of cases.

CONCLUSION:

This study has shown that HD with a nodular growth pattern and a lymphocyte-rich background encompasses 2 entities with distinct morphologic, phenotypical features. Therefore, the precise classification of such case requires a combination of conventional histology and immunohistology with distinct panel of antibodies.

KEYWORDS: hodgkin disease, immunohistochemical markers

INTRODUCTION:

Hodgkin's disease (HD) was first described by a British physician in 1932 and has attracted the attention of physicians and researchers for more than a century to a degree out of proportion to its relative incidence (1%) out of all body malignancies).

Interestingly the nature of Hodgkin's disease is still controversial whether a true neoplasm, an inflammatory, infectious disease, an unusual immunologic reaction, or a combination of these. The compelling feature about HD is the amazing therapeutic success story of the disease being a largely curable one.[1]

Hodgkin disease was divided according to Rye's classification in 1966 into 4 classes:

1. Lymphocyte predominant (nodular or diffused).
2. Nodular sclerosis.
3. Mixed cellularity.
4. Lymphocyte depleted.

This classification was adopted from (1966-till 1999) when a revised European-American classification of lymphoma (REAL) was proposed and adopted by the World Health Organization (WHO). This REAL/WHO system reclassification Hodgkin's lymphoma into:[2]

(a) Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL).

(b) Classical Hodgkin's disease (CHD) (which included the Rye's 4 subclasses).

The NLPHL is characterized by nodules, and malignant cells the Lymphocytic and Histocytic cells (LxH) or pop corn cells, while the classical category is characterized by the malignant Reed-Sternberg cells (RS) and characteristic reactive inflammatory background.

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The NLPHL was considered as a subtype of lymphocyte predominant Hodgkin lymphoma, but now it is a special entity.

Immunophenotyping (one of the ancillary studies) of the lymphoid disorders has evolved into a highly complex field, and fortunately immunohistochemical studies on paraffin embedded tissue sections are of great use in the diagnosis of Hodgkin disease with a high sensitivity and specificity for Hodgkin cells. Add to it, an internationally agreed upon nomenclature (the CD system, which stands for cluster designation) has evolved, and over 250 CD antigens were discovered. The 2 subclasses of HD have different expression of CD markers leading to different immuohistochemical interpretations that was a corner stone in the last classification of HD[(3)].

PATIENTS AND METHODS:

This retrospective and prospective study involved the collection of specimens from (31) cases diagnosed as lymphocyte predominance Hodgkin's lymphoma (according to Rye's classification) form the Department of pathology of Al-Kadhemyia Teaching Hospital, the Department of Pathology of Baghdad Teaching Hospital, central Health Laboratory, and several laboratories for the period between (January 2006-March 2008).

These specimens were formalin fixed, paraffin embedded tissues blocks from excisional lymph node biopsies, and were diagnosed as lymphocyte predominance Hodgkin's lymphoma according to Rye's classification system. The information about these cases were recovered from the histopathological reports regarding the site of the biopsy, age, sex, and histological type.

For each case, five representative sections were prepared. One stained with hematoxyline and eosine (H x E), and four other sections (on positivity charged slides) prepared for IHC procedures using CD_{15} and CD_{20}.

RESULTS:

Over the period extending from (January 2006-March 2008), specimens from 31 cases of lymphocyte predominance Hodgkin lymphoma (Rye's classification) as paraffin embedded tissue blocks were collected for this study.

The mean age of the patients was (19-42) years, with a range of (5-63) years. The highest percentage of patients was in the age group interval (1-19 years) comprising 55% of the total cases, while the lowest percentage was in the age group interval (>60 years), comprising 3% of the total cases, as shown in table (1).

Of those patients, males constituted the majority of cases accounting for (81%) of the total cases, and females constituted (19%) of them, with this male predominance the male to female ratio was (4.2:1) as shown in table (2).

These specimens were subjected to immunohistochemical procedures using CD markers. The first one was CD_{20} which was expressed in the giant malignant cells and found to be positive in (12.91%) of cases and negative in (87.09%) of cases, with the highest positivity in the age group interval (20-30) years as shown in table (3).

The second marker used in the study was CD_{15}. It was expressed in the malignant cells (RS and Hodgkin cells) in the cell membrane, and sometimes diffuse cytopolasmic and paranuclear and regarded positive in (77.41%) of cases and negative in (22.59%) of the total cases, being highly expressed in the age group interval (1-19 years) accounting for (45.16%) of cases as shown in table (4).

Depending on the immunohistochemical picture the 31 cases of lymphocyte predominance Hodgkin disease were reclassified following the Revised-European-American lymphoma (REAL) classification criteria and this give rise to two distinct groups:

1. Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) group which involved 4 cases (13%) of the total cases. This groups showed the immunohistochemical pattern of staining of the malignant cells (CD_{20} +ve, CD_{15} –ve).
2. Lymphocyte rich classical Hodgkin disease (LR-CHD) group involving 27 cases (13%) of the total cases showing the immunohistocheimcal pattern of staining of the maliant cells (CD_{20}-ve, CD_{15}+/-ve shown in table (5).
3. The site of initial biopsy was analyzed in this study showing that the cervical lymph node is the most common site of biopsy according for (61.29%) as shown in table (6).

Table 1: Age distribution of the collected cases

Age groups	Frequency of cases	Percentages
1 to 19	17	55%
20 to 39	9	29%
40 to 59	4	13%
Over 60	1	3%
Total	31	100%

Table 2: Sex distribution of the collected cases

Sex	Frequency	Percentages
Male	25	81%
Female	6	19%
Total	31	100%

Table 3: CD_{20} expression regarding age group of the patients

Age groups	CD20 Expression				Total
	positive		Negative		
	No. of cases	%	No. of cases	%	
1 to 19	1	3.23%	16	51.61%	17
20 to 39	2	6.45%	7	22.50%	9
40 to 59	1	3.23%	3	9.67%	4
Over 60	0	0%	1	3.23%	1
Total	4	12.91%	27	87.01%	31

Table 4: CD_{15} expression regarding age groups of the patients

Age groups	CD_{15} Expression				Total
	Positive		Negative		
	No. of cases	%	No. of cases	%	
1 to 19	14	45.16%	3	9.68%	17
20 to 39	6	19.36%	3	9.68%	9
40 to 59	3	9.68%	1	3.23%	4
Over 60	1	3.23%	0	0%	1
Total	24	77.41%	7	22.59%	31

Table 5: Subtypes of lymphatic patients after using anti CD20 and CD15 Hodgkin's disease

Subtypes	No. of cases	Percentages
NLPHL	4	13%
LR-CHD	27	87%
Total	31	100%

Table 6: Distribution of cases according to the site of biopsy

Site of LN biopsy	Frequency of cases	Percentage
Cervical	19	61.29%
Submandibular	4	12.9%
Supraclavicular	6	19.35%
Axillary	2	6.45%
Total	31	100%

DISCUSSION :

Hodgkin disease is a lymphoid tumor that accounts for less than (1%) of all De Novo neoplasms occurring every year worldwide.

Despite its well known histological and clinical feature, HD has recently been the object of intense research activity, leading to a better understanding of its phenotype, molecular characteristics, histogenesis and possible Mechanisms of lymphogenesis.[4]

In our country according to the Iraqi cancer registry(ICR) the HD comes in the tenth rank among the common malignancies in male in the years 1999, and 2000 and it accounts for (3.4%) and (3.3%) of cancels in male respectively[5].In United States of America about 7500 new cases and about 1500 deaths occur annually.[6]

In economically developed countries of the west, HD has a characteristic biomodal distribution with peaks in the (15-40 years) and another peak in the seventh decade of life. In this study, HD was predominantly seen in children and young adults (the peak in the first two decades of life). Studies

from Oman, KSA, Iran and Kuwait so suggest a (regional peak occurrence in childhood with highest frequency occurring within the first 2 decades of life.[7,8,9]

The overall incidence of Hogdkin's disease in Asian women is lower than that of men but the overall pattern is similar[10]. This is obvious in this study since the peak of cases was in the first 2 decades of life, males consisted the majority of cases. Accounting for (81%) of the total cases, and females consisted (19%) of them, with this male predominance the male to female ratio was (4.2:1). In comparison to (3.57:1) among children in North Jordan(11), and (3.5) in the similar Turkish study.(12)

Regarding the most common site of initial biopsy, the cervical L.Ns are the commonest site (60%-80%) followed by the supraclavicular L.Ns. In the present study the cervical nodes represented (61.29%) of initial biopsy site and this can be explained by their easy accessibility to surgery, their large number, distribution in the neck, and common early involvement by the disease. This finding coincides with many previous Iraqi and western studies.(13,14,15)

In our study we tried to reclassify the 31 collected cases according to REAl/WHO criteria. The initial attempt was to classify the cases depending on the morphological features in slides stained with H x E alone to detect any case of NLPHL looking for the L x H cells in a nodular background. One case was diagnosed as NLPHL with classical L x H cells. A nodular background was prominent in 25 cases, and diffuse pattern in 6 cases. From these 25 cases, 11 cases showed atypical giant cells that didn't express clear morphological features to enable us putting them into either L x H or HRS cell groups, necessating the use of immunohistochemical analysis. The nodular background became more prominent on CD_{20} staining.

The expression of CD_{15} in this study was positive in (77%) of cases which is a little bit higher than the pattern in the published studies, and that of European task force on lymphoma (ETFL)(16) project which was (81%), while the expression pattern of CD_{20} was positive in all the cases of NLPHL that is so close to the published pattern which is (>95%) and matching the (ETFL) pattern.

CONCLUSION:

1. This study has shown that HD with a nodular growth pattern and a lymphocyte-rich background encompasses 2 entities with distinct morphologic, phenotypical features. Therefore, the precise classification of such cases requires a combination of conventional histology and immunohistology using a distinct panel of antibodies.
2. This study showed a unimodel age distribution of collected cases and the majority of cases in the first 2 decades of life with a mean age of life that matches the regional countries and younger by a decade from the European pattern.

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