

Hodgkin's Disease Frequency and Patterns in Yemeni Patients

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Abstract

Objective: To find out the frequency of Hodgkin's disease among lymphomas and to defined the frequency and patterns of Hodgkin' disease in relation to age, sex and site effected in Yemeni patients. **Methods:** A retrospective study of 366 cases of Hodgkin's disease was carried out in the department of pathology, Faculty of Medicine and Health Science, Sana'a University during the period from 1st January 2004 to the 30th December 2007. The diagnosis were made primarily on hematoxylin and eosin stained sections and categorized according to Rye classification. **Results:** The frequency of Hodgkin's disease among lymphomas was 31.4%. The commonest histological type was mixed cellularity 71.9%. The lymphocytes predominance was the second 14.8%, followed by nodular sclerosis 9.6% and lymphocyte depletion 1.6%. Eight cases 2.2% were unclassifiable. Hodgkin's disease was seen in all age groups with a range of age between 3-75years and peak incidence during second and third decades. The female and male ratio was 1: 1.7 with a distinct male predominance in all histological types. Nodal Hodgkin's disease account for 95.4% with high frequency in cervical lymph nodes 77.2%.

Conclusion: The study shown high frequency of mixed cellularity with high percentage of Hodgkin's disease in the childhood and young adult male with predominance effect of cervical lymph nodes in all histological types.

Introduction:

Hodgkin's disease has been traditionally used for a type of malignant lymphoma in which Reed -Sternberg cells are present in a background of reactive inflammatory cells of various types accompanied by fibrosis of variable degree¹. The first detailed account of Hodgkin's disease originating primarily in the organs of lymphoreticular system was given in 1832 by Thomas Hodgkin that was later to bear his name². Because of its inflammatory histological appearance and the variable distribution of Reed-Sternberg cells, Hodgkin's disease usually lacks the histologic monotony that is characteristic of most of non-Hodgkin's lymphomas and others neoplasms³. The finding of Reed-Sternberg cells and their morphologic variant (collectively termed Reed-Sternberg cells) in the appropriate histological setting

is a corner stone for the diagnosis of Hodgkin's disease⁴.

Methodology:

A descriptive record based study of 366 cases of Hodgkin's disease was carried out in the department of pathology, Faculty of Medicine and Health Science, Sana'a University during the period from 1st January 2004 to the 30th December 2007. The diagnosis were made primarily on private laboratories of three well-known pathologist in Sana'a who received the histopathologic biopsies from Sana'a and and the other Yemeni provinces. The biopsies of the tissue effected were fixed in 10% formalin solution before being processed by manual and automatic tissue processor. After embedding in paraffin blocks several thin sections of 2 to 3 micrometer thickness from each block were cut. The sections were stained with

hematoxylin and eosin stain for routine histological diagnosis. During histological analysis the sample was evaluated regarding the type of tissue, total or partial effacement of architecture, presence of Reed-Sternberg cells and mononuclear variants Hodgkin's cells, nodular arrangement, presence of inflammatory cells, and degree of fibrosis and reticulin fibers and finally categorized according to Rye classification. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine and Health Sciences of Sana'a University. Statistical analysis was done using a calculator to compute percentages, mean and median.

Results:

A total number of lymphomas through the period of study were 1167 cases, amongst these 801 (68.6%) were non-Hodgkin's lymphomas and 366 (31.4%) Hodgkin's disease. The commonest histological type of Hodgkin's disease was mixed cellularity 71.9%. The lymphocytes predominance was the second 14.8%, followed by nodular sclerosis 9.6% and lymphocyte depletion 1.6%. Eight cases 2.2% diagnosis of Hodgkin's disease were made but none of them fulfilled the histologic criteria of Rye classification; hence they were labeled nonclassifiable" Table 1.

Both the presence of mononuclear variants (Hodgkin's cell) and Reed-Sternberg cells and a characteristic cytological environment are required for a pathological diagnosis of Hodgkin's disease⁵. The nature of Hodgkin's disease has been the subject of intense debate for more than 115 years². The occurrence of massive lymphadenopathy, the relative frequency of spread to the liver, bone marrow and other lymphatic tissue and inevitably fatal course of the disease suggested to many scholars that it was a form of malignant neoplasm². Others, however were impressed with its frequently febrile course with occasional waxing and waning in size of enlarged lymph nodes and with the frequent coexistence of tuberculosis or other infectious diseases

at autopsy and therefore considered it to be some form of granulomatous inflammation². Definitive evidence that Hodgkin's disease is indeed a malignant neoplasm finally emerged during the last decades as a consequence of cytogenetic and culture studies which have demonstrated that the giant cells of Hodgkin's disease satisfy two of the most fundamental attributes of neoplasm; viz, aneuploidy and clonal derivation⁶. The origin of Reed-Sternberg cells has been the subject of a number of conflicting reports^{7,8} and have not yet been clarified⁶. The disease occurs in all age groups⁹. Its highest incidence in young adults with evidence of great preponderance in males¹⁰. Although overall it is an uncommon form of cancer, its importance stems from the fact that it is one of the most common form of malignancy in young adults¹¹. The aim of this study is to find out the frequency of Hodgkin's disease among lymphomas and to define the frequency and histologic patterns of Hodgkin's disease in relation to age, sex and site effected of Yemeni patients compared to other studies undertaken in the region.

The age distribution in 318 cases of Hodgkin's disease (in 48 cases ages were not mentioned). Maximum number of cases 93 (29.2%) was encountered in age group of second decade, followed by age group of third decade 85 (26.7%) and the minimum i.e 21 (6.9%) was encountered in the age group of fourth decade Table 2. The age range 3-75 years was broad as shown in Table 1 and forming unimodal distribution pattern with median and mean age of 20 years. The sex distribution is shown in Table 3 231 (63.1%) cases were male and 135 (36.9%) were female. The female to male ratio is 1:1.7 with a distinct male predominance in all histological types. The site distribution of Hodgkin's disease is shown in Table 4. Nodal site accounts for 348 (95.4%) cases and 17 (4.6%) were extranodal. Among nodal sites the highest number was encountered in cervical lymph nodes 262 (77.2%).

Discussion:

Hodgkin's disease comprises about 40% of all malignant lymphomas in the United States and Western Europe, but a much lower percentage in Japan and other oriental countries¹. Although overall it is an uncommon form of cancer, its importance stems from the fact that it is one of the most common form of malignancy in young adults with an average age at diagnosis of 32 years¹¹. According to the present study the frequency of Hodgkin's disease among lymphomas was 31.4% and non-Hodgkin's lymphomas constituted 68.6%. The frequency of Hodgkin's disease among lymphomas is identical to the international reports from USA¹² Pakistan¹³, Ethiopia¹⁴ and Sudan¹⁵ and slightly differ from other findings noted in United Arab Emirate¹⁶ and in Pakistan¹⁷. The possible reasons for this variation are the criteria of studies, number of the cases and the overlap in the diagnosis of Hodgkin's disease and non-Hodgkin's lymphomas mainly the lymphocyte predominance and lymphocyte depletion, in those some pathologists consider them as non-Hodgkin's lymphomas and vice versa. Rye histopathologic classification of Hodgkin's disease has gained widespread recognition throughout the world, and had provided a good correlation between histologic type and the prognosis which is generally followed¹³

Table 1 - Age range in various types of Hodgkin's disease

Type	No	%	Age range (Yrs)	Mean (Yrs)	Median
Mixed cellularity	263	71.9	3-75	20	22
Lymphocyte predominance	54	14.8	3-64	18.8	18.5
Nodular sclerosis	35	9.6	5-45	21.6	20
Lymphocyte depletion	06	1.6	15-65	36.5	32.5
Nonclassifiable	08	2.2	4-65	20.6	10
Total	366	100	3-75	20	20

Table-2 Age distribon of 318 cases of Hodgkin's disease

Age groups (years)	No	%
0-10	63	19.8
11-20	93	29.2
21-30	85	26.7
31-40	25	7.8
41-50	21	6.9
≥ 51	31	9.7

Table 3 Sex distribution of 366 cases of Hodgkin's disease

Sex	No	%
Male	231	63.1
Female	135	36.9

Female to male ratio 1:1.7

Table 4 Site distribution of Hodgkin's disease.

Nodal	No	%	Extranodal	No	%
CLN	262	75	Spleen	5	1.4
ALN	28	8	Liver	4	1.1
ILN	14	4	Soft tissue	4	1.1
VALN	13	3.7	Tonsil and Nasopharynx	3	0.8
MLN	6	1.7	Bone marrow	1	0.3
LN*	25	7			
Total	348	95.4 **		17	4.6+

CLN- Cervical lymph nodes. ALN- Axillary lymph nodes. ILN- Inguinal lymph nodes. VALN- Visceral abdominal lymph nodes. MLN- Mediastinal lymph nodes. LN*- Lymph nodes of nonrecording site. 95.4%** percentage of nodal Hodgkin's disease. 4.6%+ Present study was therefore planned according to Rye classification. The commonest histologic type in this study was mixed cellularity (71.2%) in contrast to the studies carried out in USA and western world^{18,19,20} those found mixed cellularity to be less than 35%. But there is agreement with some studies carried out in

middle east countries^{13,15,17,21}. Lymphocyte predominance 14.8% was the second most frequent histologic type in this study which was similar to many previous literatures^{18,22}. However, much higher figures up to 35% of this variant have been reported by some investigators^{14,15}. The third histologic type was nodular sclerosis 9.5% which was much lower than those reported by many international workers in USA¹², Western countries^{20,23} Middle East countries^{16,24} and Hong Kong²⁵. But similar figures have been encountered too in frequent studies carried out in the Middle East countries^{13,14}. The fourth subcategory of Hodgkin's disease in this study was lymphocyte depletion 1.6 % which appear lower than many reports^{13,17} and shows slight similarity to some experience¹⁴. The paucity of lymphocyte depletion in this study may be due to the atypical histological appearance of some cases of this entity where they were considered by some pathologist as sarcoma or anaplastic lymphoma^{14,26}. Eight (2.2%) cases could not be placed in a specific class of Hodgkin's disease due to marked overlap and diversity of histologic features. This is in conformity with findings of some observers^{22,25,27}. Medeiros and Greiner had shown 9.1 % of Hodgkin's disease cases unclassified and designated as miscellaneous. The decrease in the number of nonclassifiable is due to improvement of classification. Nevertheless, a subset of cases of Hodgkin's disease remained difficult to subclassify²⁷. In general it may be said that while comparing the frequency of histologic types in the present study with others local and international, a clear divergence was observed. Such a divergence could be explained in terms of diagnostic approach and/or techniques applied, number of patients studied as well as culture, economical, racial, geographical and immunological differences. However, Epstein-Barr virus capsid antigens in serum from many patients with Hodgkin's disease^{16,28} so this raised the

possibility of a chronic stimulatory process of the lymphatic system in Hodgkin's disease and may be added as another explanation for these variations¹⁵. In developing countries patients usually consult very late and the histological diagnosis is also delayed, so that the possibility of transformation from one histological type of Hodgkin's disease to another, the more so untreated cases should be considered as noted by Poppema and Lennert¹⁹. It may be added that progression usually occurs toward a histologically more malignant form of Hodgkin's disease while the reverse seldom possible²⁹. In present study age range was 3-75 years. Thus the cases of Hodgkin's disease were seen in all age groups, similar to that reported by many investigators^{10,20,25}. MacMahon A¹⁰, Abu ElHassan et al¹⁵ and Cobly TV et al²⁰ noted that the age incidence of Hodgkin's disease forms a bimodal peak, one at 25-29 years and the other at 70-75 years. However there was no evidence of bimodality in present study as unimodal distribution pattern was seen with a median age of 20 years and a mean of 20 years similar to that observed by Muzaffar M et al¹³, Saleh A and colleagues¹⁷. The peak incidence of the Hodgkin's disease in present series was noted below 20 years group 49%. It was identical to that noted by many workers^{17,31} and differ from that reported by others^{9,13}. Geographical differences, patient population, and other factors such as race, socioeconomic conditions, nutrition and immunologic status may be contributing to the early occurrence of Hodgkin's disease³⁰. In most previous international studies a male preponderance was found in Hodgkin's disease. In present series 231(63.1 %) out of 366 patients were male, the male to female ratio was 1.7:1 which appear identical to the previous findings of some literatures^{17,24,25} and slightly lower than that founds by others^{17,19}. A distinct male predominance in all histologic types was seen in our study similar to that reported by Saleh A et al¹⁷ and Naiem & Waisman²².

The nodal site for Hodgkin's disease in this study was 348 (95.4%) which was appear similar to that found in the results of some workers³¹. A first site involved in this study was cervical lymph nodes 75% and this finding was identical to the observations of Smithers et al³¹.

Conclusion:

We have shown in this study the frequency of Hodgkin's disease among lymphomas and the different histopathologic patterns of Hodgkin's disease in our local patients which correlate with some studies and shows discrepancies with others. The study showed high frequency of mixed cellularity with high percentage of Hodgkin's disease in the childhood and young adult male with predominance effect of cervical lymph nodes in all histological types.

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