RESEARCH ARTICLE

Clinico-Hematological Findings for Classical Hodgkin's Lymphoma: an Institutional Experience

Sadia Sultan[1], Syed Mohammed Irfan[1], Saira Parveen[1], Saif Ali[2]

Abstract

Background: Classical Hodgkin's lymphoma (cHL) is a B-cell lymphoid neoplasm characterized by a distinctive biological behavior with potentially curable disease characteristics. It is an uncommon hematological malignancy which primarily affects younger individuals. The rationale of this study was to determine its clinico-hematological profile along with stage stratification in Pakistani patients. Materials and Methods: In this descriptive study, adult patients with Hodgkin's lymphoma were enrolled from January 2010 to December 2014. Results: Sixty two histopathologically confirmed cases of cHL were identified. There were 42 males and 20 females, with a male to female ratio of 2: 1. The mean age was 29.7±13.8 years with the median age of 30 years. B symptoms were present in 72.5% of patients. Histopathologically, the mixed cellularity type constituted 62.9% of cases, followed by nodular sclerosis in 25.8%, lymphocyte predominant in 9.6% and lymphocyte depleted in 1.6%. Stages I and II were present in 43.5% of patients at disease presentation, with 56.4% in stages III and IV. Conclusions: Our analysis shows that clinico-pathological features of Hodgkin's lymphoma in Pakistan are comparable to published data. Mixed cellularity is the commonest histological variant and advanced stage at presentation are common findings in our patients.

Keywords: Hodgkin's lymphoma - staging - histopathology - Pakistan

Asian Pac J Cancer Prev, **17 (8)**, 4009-4011

Introduction

Hodgkin's lymphoma is a relatively rare malignancy which was first depicted by Thomas Hodgkin in 1832 (Hodgkin., 1832). It is an uncommon disease with an overall incidence of 2.4-2.8/100,000 population with the peak occurrence reported between 15-29 years of age (Sader-Ghorra et al., 2014).

Classical Hodgkin lymphoma includes a group of lymphoid neoplasms with a complex etiology and varied epidemiology (Roshandel et al., 2011). It shows a bimodal age distribution demonstrated in developed nations with first peak in the 20's and a subsequent peak over the age of 50 years. Whilst in the developing countries, the adult peak is not seen and instead a higher incidence is seen among children less than 15 years (MacFarlane et al., 1995). There are plausible explanations that correlate socioeconomic factors and disease incidence (Gutensohn et al., 1981). Although the etiology of HL is unclear, epidemiologic data suggest that viral factors especially Epstein Barr virus infection and human immunodeficiency virus may play a causal role (Tang et al., 2013; Li et al., 2012).

The disease has been reclassified using the WHO classification system into four pathological subtypes includes nodular sclerosis, mixed cellularity, lymphocyte rich and lymphocyte depleted (Swerdlow et al., 2008). The most frequent subtype in western countries is nodular sclerosis but in Asia it is mixed cellularity (Yung et al., 2003; Fatima et al., 2011).

Ann Arbor staging classification for Hodgkin's lymphoma had been widely accepted and applicable due to its ease and good reproducibility. It was initially developed for Hodgkin's, but has several uses in NHL as well. The staging is very crucial not only to determine disease spread but also it will dictate treatment modalities.

The epidemiological features of HL are still poorly defined locally. There is no registry maintained in Pakistan to track a record of regional HL. The present study is designed to investigate the clinicopathologic pattern, its subtypes and disease staging assessment to compare the results with those documented in the literatures.

Materials and Methods

This descriptive cross sectional study, conducted at Liaquat National Hospital & Medical College, extended from January 2010 to December 2014. During the study period, 62 patients diagnosed to have cHL were enrolled in this analysis.

All cases were diagnosed based on morphology

*[1]Department of Hematology & Blood bank, Liaquat National Hospital and Medical College, [2]Liaquat National Medical College, Karachi , Pakistan *For correspondence: sadiasultan96@yahoo.com*

and IHC profile as per WHO classification of lymphoid neoplasms. Immunohistochemical (IHC) stains using antibodies against CD 20, CD 3, CD 10, CD 5, CD 23, CD 79a, CD 30 and CD 15 were done in each case.

Patients diagnosed as classical HL (CD 15 & 30 positivity) who were ≥15 years of age were included in the study. All post-chemotherapy and radiotherapy cases were not included in the study.

Complete blood counts were determined by Automated Cell Dyne counter. Bone marrow aspirate and trephine samples were taken from posterior superior iliac spine after written consent. Patients disease were staged according to Ann Arbor staging by computed tomography (CT scan) as:

Stage I indicates disease located in a single region, Stage II indicates that disease is located in two separate regions, but confined to one side of the diaphragm, Stage III indicates that disease has spread to both sides of the diaphragm, Stage IV indicates diffuse involvement of extralymphatic organs.

Statistics analysis

Data was entered and analyzed using the Statistical Package for the Social Sciences version 22.0. The results were expressed as mean (±SD) for quantitative variables and are presented as frequency & percentages for qualitative parameters.

Results

Age and Gender

There were 42 (67.7%) males and 20 females (32.2%) with male to female ratio of 2:1. Patient's age ranged between 15 and 76 years with the mean age was 29.7±13.8 years and the median age of 30 years. Preponderance of patients (74.1%) was under 30 years of age.

Clinical Findings

B symptoms were present in 45 (72.5%) patients, out of whom fever was commonest, seen in 64.5%; drenching night sweats in 55% patients, while 37% patients had history of weight loss. Lymphodenopathy was present in 53 (85.4%) cases. The most common lymph node palpable was cervical and axillary nodes. The splenomegaly and hepatomegaly were noted in 25.8% and 17.7% patients respectively.

Histopathological Classification

Histopathologically, mixed cellularity type constituted 62.9% (n=39) of cases, followed by nodular sclerosis in 16 (25.8%) patients , lymphocyte predominant in 6 (9.6%) patients and lymphocyte depleted was in only single (1.6%) patient.

Laboratory Features

Mean hemoglobin was 9.4±1.9g/dl (6.8-15.8g/dl). The mean total leukocyte count of 10.9±20.6x10^9/l (1.5-22.9x10^9/l); mean absolute neutrophils count of 3.8±3.0 x10^9/l and the mean platelets count were 241.6±150.1x10^9/l (16-651x10^9/l). Anemia (Hb<10gm/dl) was noted in 24.1% patients.

Ann Arbor stages

Stage stratification according to Ann Arbor system revealed 10 (16.1%) patients were in stage 1; 17(27.4%) patients in stage II, while 18 (29.0%) patients in stage III at presentation, whereas 17 (27.4%) patients presented in very advanced stage IV with bone marrow infiltrations. Overall an early stage (stage I and II) was present in 43.5% of patients at disease presentation, while 56.4% patients presented in advanced stages (stage III and IV).

Discussion

Hodgkin's lymphoma is a comparatively uncommon neoplasm, mostly affecting younger adults. It characterizes one of the most curable disease among all lymphomas with curability in >80% of patients (Koren et al., 2015). Overall survival rates for HL have significantly improved over the past several decades (Grover et al., 2015).

Around 9000 new patients are affected yearly with HL (Ansell., 2015). Hodgkin's lymphoma in developed and developing countries display diversity in the incidence, age, gender distribution and morphology subtypes distribution. This study analyzed the clinical and histopathological characteristics among Pakistani patients.

Unlike western studies definite bimodal age peak, is absent in our study. In Pakistani population disease is identified in younger age, as majority (74.1%) of our patients were <30 years. Previous regional reports published on cHL by Siddiqui and Fatima et al were also determined young age at presentation (Siddiqui et al., 2006; Fatima et al., 2011). This is in concurrence to earlier studies from India and Egypt where average age were 30 and 31 years at presentation respectively (Ganesan et al., 2011; Gad et al., 2014).

The present study revealed a male preponderance with mixed cellularity (MCHL) being the commonest (62.9%) subtype. Previously, published studies from Pakistan also revealed MCHL as a major subtype accountable in 57% and 69.1% respectively (Fatima et al., 2011; Nagi et al., 2008). Likewise, studies from India and Srilanka also reported the predominance of MCHL entity in their patient's series (Maddi et al., 2015; Waravita et al., 2015). It is noteworthy that in studies from Asia, the number of MCHL patients comprised the major bulk of the disease, suggesting a similar disease epidemiology in this region.

Nodular sclerosis (NSHL), the predominant histological variant in the Western Europe and United States is less frequent in developing countries like us (Khan et al., 1993; Matteo et al., 2003). Therefore, it indicates that Pakistan, being a developing country shows more or similar epidemiological features as other developing countries. Conversely these features are in contrast to that of developed country.

Staging of the cHL is of prime importance for the decisions of therapeutics modalities in the management of these patients. Bone trephine biopsy and computed tomography scanning are two main investigations, which is being carried out in all patients for staging workup.

Bone marrow infiltration indicating stage IV disease in cHL has been reported from various ethnic groups ranging from 2% to as high as 38% (Lone et al., 2011). Previous

studies reported from Pakistan revealed relatively higher prevalence of disease infiltration compared with western studies. Our findings are comparable with those of Butt (27.5%) and Hamid (30%) who reported high percentages of stage IV disease from different regions of country (Butt et al., 2002; Hamid et al., 2010).

Recently, Maddi from India reported that majority patients presented in advanced stage (Stage III and IV) disease (64.7%) (Maddi et al., 2015). However, another recent study from Australia, disclosed that 68% patients presented in early stages (stage I &II) while remaining 32% presented in advanced stage (stage III & IV) (Jalali et al., 2016). Distinctly in economically developed countries where majority of patients present with early stage (stage I and II), 56.4% of patients at our center presented with advanced stage. A higher percentage of advanced disease presentation may be explained by the delay in seeking medical attention which is attributed to financial constraints and lack of diagnostic and referral facilities.

Lastly limitations of our study are related to its retrospective nature and comparatively small sample size. These findings are from a single tertiary care centre and consequently, there may be a referral bias and results may not be validated at large. Multicenter studies on large sample size are definitely required to determine disease characteristics in our population.

The present study reflects the advanced stage of classical Hodgkin's lymphomas at disease manifestation in our setting. Another important observation of this study includes young age at diagnosis and predominance of mixed cellularity variant in our population.

References

Ansell SM (2015). Hodgkin lymphoma: diagnosis and treatment. *Mayo Clin Proc*, **90**, 1574-83.

Butt F, Akhtar R, Rahmani T, et al (2002). Bone marrow involvement in lymphoma: Incidence and co-relation with age and sex. *Biomedica*, **18** , 53-7.

Fatima S, Ahmed R, Ahmed A (2011). Hodgkin lymphoma in Pakistan: an analysis of subtypes and their correlation with Epstein Barr virus. *Asian Pac J Cancer Prev*, **12**, 1385-8.

Ganesan P, Kumar L, Raina V (2011). Hodgkin's lymphoma-long-term outcome: an experience from a tertiary care cancer center in North India. *Ann Hematol*, **90**, 1153-60.

Gad Allah H, El-Azzazi MO, Elafifi AM, et al (2014). Treatment outcome in Egyptian lymphoma patients, 2-year results, single-center experience. *Egypt J Haematol*, **39**, 209-16.

Grover NS, Park SI (2015). Novel targeted agents in hodgkin and non-Hodgkin lymphoma therapy. *Pharmaceuticals*, **8**, 607-36.

Gutensohn N, Cole P (1981). Childhood social environment and Hodgkin's disease. *N EngL J Med*, **304**, 135-40.

Hamid A, Hamid Am, Jabbar N, et al (2010). Significance of bone marrow biopsy in staging of Hodgkin's lymphoma. *Ann King Edward Med University*, **16**, 12-16.

Hodgkin (1832). On some morbid appearances of the absorbent glands and spleen. *Med Chir Trans*, **17**, 68-114.

Jalali A, Ha FJ, Chong G, et al (2016). Hodgkin lymphoma: an Australian experience of ABVD chemotherapy in the modern era. *Ann Hematol*, [Epub ahead of print]

Khan G, Norton AJ, Slavin G, (1993). Epstein Barr virus in Hodgkin's disease: Relation to age and subtype. *Cancer*, **71**, 3124-9.

Koren J, Trneny M (2015). Hodgkin´s lymphoma - the treatment approaches development and current trends. *Klin Onkol*, **28**, 387-94.

Li X, Yang SE, Guo YQ, et al (2012). Clinical significance of quantitative analysis of plasma epstein- barr virus DNA in patients of Xinjiang Uygur nationality with Hodgkin's Lymphoma. *Asian Pac J Cancer Prev*, **13**, 6379-84.

Lone A, Naeem S (2011). Frequency and pattern of bone marrow infiltration in Hodgkin's Lymphoma. *Biomedica*, **27**, 132-5.

MacFarlane GL, Evstifeeva T, Boyle P, et al (1995). International patterns in the occurrence of Hodgkin's disease in children and young adult males. *Int J Cancer*, **61**, 165-9.

Matteo ED, Baron AV, Chabay P, et al (2003). Comparison of Epstein Barr virus presence in Hodgkin's lymphoma in pediatric versus adult Argentine patients. *Arch Pathol Lab Med*, **127**, 1325-9.

Maddi RN, Linga VG, Iyer KK, et al (2015). Clinical profile and outcome of adult Hodgkin lymphoma: Experience from a tertiary care institution. *Indian J Med Paediatr Oncol*, **36**, 255-60.

Nagi AH, Al-Menawy LA, Samiullah, et al (2008). A comparison of histological appearances of Hodgkin's disease in Pakistani and Saudi patients. *J Ayub Med Coll Abbottabad*, **20**, 66-9.

Roshandel G, Semnani S, Aarabi M, et al (2011). Lymphomas in Golestan province of Iran: results of a population-based cancer registry. *Asian Pac J Cancer Prev*, **12**, 219-22.

Sader-Ghorra C, Rassy M, Naderi S, et al (2014).Type distribution of lymphomas in Lebanon: five-year single institution experience. *Asian Pac J Cancer Prev*, **15**, 5825-8.

Siddiqui N, Ayub B, Badar F, et al (2006). Hodgkin's lymphoma in Pakistan: a clinico-epidemiological study of 658 cases at a cancer center in Lahore. *Asian Pac J Cancer Prev*, **7**, 651-5.

Swerdlow SH, Campo E, Harris NL, et al (2008). WHO classification of tumors: pathology and genetics of tumors of haematopoietic and lymphoid Tissues. Lyon: IARC Press. pp. 321-34.

Tang Y, Sun LG, Liu CS, et al (2013). Clinical analysis of stages of HBV infection in 100 cases of lymphoma. *Asian Pac J Cancer Prev*, **14**, 959-62.

Waravita TS, Wijetunge TS, Ratnatunga NV (2015). Pattern of lymphoma subtypes in a cohort of Sri Lankan patients. *Ceylon Med J*, **60**, 13-7.

Yung L, Linch D (2003). Hodgkin's lymphoma. *Lancet*, **361**, 943-51.