

Research Article

Hodgkin's disease in adults: the royal medical services experience

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ABSTRACT

Background: The aim of this study to examine our experience in the presentation and management and to determine the factors that potentially influenced the outcome in 96 patients with Hodgkin's lymphoma.

Methods: A retrospective study done at oncology unit in royal medical services hospitals, a total 96 patient whom diagnosed with Hodgkin's lymphoma between 2005 and 2013, data include age, sex of patients, presenting and duration of symptoms, staging of disease, and prognosis of disease.

Results: 66 males and 30 females, the most common enlarged lymph node was at cervical region. The most common histopathology subtype was nodular sclerosis. Most of our patients were staged as stage 4. Systemic symptoms developed in 50 (52%) patients. The most common site of extralymphatic involvement was lung. Complete remission was noted in all 29 patients whom presented with early stages of disease and less in advanced stages. Failure of remission post treatment was noticed more in mixed cellularity and lymphocyte rich subtypes. On regular follow up of patients 8 patients whom were in complete remission developed relapse of disease; mean time of relapse was 9 months post remission.

Conclusion: Hodgkin's lymphoma has high rates of cure. Epidemiological, clinical, histological and therapeutic results in our series are similar to those Western series. Long term evaluation is necessary to assess relapse and late toxicity treatment.

Keywords: Hodgkin's lymphoma, Prognosis, Epidemiology

INTRODUCTION

Hodgkin's Lymphoma (HL) was firstly described by Thomas Hodgkin in 1832.¹ It is un common malignancy with incidence 2 in 100.000 population per year which is 1/10 of incidence of non-Hodgkin's lymphoma.² It incidence is higher in developed countries, and is more frequent in male than females with peak incidence in young patients, and in elderly above age of sixty.³ HL is sub classified according to histology and immunophenotype into classical Hodgkin which accounts for 95% of HL which is further sub classified into four types, (nodular sclerosis, mixed cellularity, lymphocyte-

rich, and lymphocyte-depleted). The second type is nodular lymphocyte-predominant HL (NLPHL),⁴ which typically presents with limited nodal disease of the neck without constitutional symptoms.⁵ The malignant cells in classical type is Reed-Sternberg cells, and in NLPHL they are lymphocyte-predominant cells.⁶ These cells are large cells with a distinct morphology and immunophenotype which differ from normal cell in humans.⁷ HL usually have a very good prognosis especially in early stage of disease which reached 100% remission rate.⁸ Most of patients with HL present with enlarged lymph nodes typically in cervical region, but in few patients it discovered incidentally with enlarged

mediastinal lymph nodes in routine chest X-ray.⁹ In about 20% of patients develop systemic symptoms, as fever, weight loss, and night sweats.¹⁰ Staging of disease depend on extent of enlarged lymph nodes and infiltration of organs.¹¹ Disease extent at presentation predicts outcome with early stage carrying better prognosis.¹² The objective of this study was to examine our experience in the presentation and management of Hodgkin's lymphoma also we intended to determine the factors that potentially influenced the outcome in 96 patients with HL.

METHODS

A retrospective study done at oncology unit in Al-Husain hospital at services. in Amman, Jordan, which is a referral hospital to cancer patient throughout Jordan, a total 96 patient whom diagnosed with HL between 2005 and 2013, diagnosis of HL done by excision biopsy in all patients whether from palpable lymph nodes, laparoscopic biopsy or even thoracoscopy. Data of these patients were collected from medical files of patients. These data include age, sex of patients, presenting and duration of symptoms, symptoms of superior vena cava obstruction, site of enlarged lymph nodes. Staging of disease started with complete history and focus on systemic symptoms of disease, and complete physical examination of any lymph nodes enlargement and hepatosplenomegaly, investigations included blood count and differential, kidney and liver function, lactate dehydrogenase. Radiology examinations include CT and PET scans, and bone marrow study to evaluate involvement of marrow by disease, staging of disease according to Ann Arbor staging system with Cotswold's modifications. Histopathology report documented and included histopathology subtype of lymphoma, Complete Remission (CR) was defined as disappearance of all enlarged and hypermetabolically active lymph nodes on PET/CT scan which done after two cycles of chemotherapy and after last cycle. Failure of treatment and refractory disease also depend on result of PET/CT scan which define with less complete remission after chemotherapy. Therapeutic guidelines were given to patients with HL were according to NCCN guidelines. Radiotherapy given to enlarged and active lymph nodes in early stages of disease after 3-6 cycles of chemotherapy while in advanced stages of disease chemotherapy given, without radiotherapy. All statistical analyses were performed using SPSS ver.19 (Statistical Package for Social Sciences for Windows; SPSS Inc., Chicago, IL, USA). A P value of <0.05 was considered statistically significant.

RESULTS

Between 2005 and 2013, 96 patients (66 males and 30 females) with HL at a ratio 2.2/1, mean age of patients 31 years, (35 years in male and 27 years in females). The most common symptoms were enlarged lymph nodes in 88 patients, anemic symptoms in 2 patients, unexplained fever in 2 patients, and incidental finding of widened

mediastinum in 2 patients, facial and neck swelling (Symptoms of superior vena cava obstruction) in 1 patients and dyspnea due to pleural effusion in 1 patient. Mean duration of symptoms in all patients were 4 weeks. The most common enlarged lymph node was cervical region in 84 patients, axillary, mediastinal lymph nodes, inguinal and Para aortic in the remainder. Diagnosis of disease done by excisional biopsy of lymph nodes in all patients, from neck lymph nodes in 86 (90%) of patients, inguinal lymph nodes in 6 patients, laparoscopic biopsy from intra-abdominal and thoracoscopy and biopsy from enlarged mediastinal lymph nodes in 1 patients respectively. The most common histopathology subtype was nodular sclerosis in 68 (71%) of patients then mixed cellularity in 13 (13.5%) patients, lymphocyte rich and lymphocyte depleted were documented in 5 (5%) and 3 (3%) patients respectively. Nodular lymphocyte predominant (NLPHL) in 7 (7%) patients, and showed in Table 1. The age of patients were different among histopathology subtypes, the mean age of lymphocyte rich was 58 years, NLPHL 43 years, mixed cellularity 33 years nodular sclerosis 31 years. HL were differ between male and females, nodular sclerosis in all female patients were no other histopathology were seen. Most of our patients were staged as stage 4, which was seen in 46 (47%) of patients, stage 3 in 22 (23%) patients, stage 1 and stage 2 were documented in 9 (9%) and 20 (21%) respectively. All seven patients with NLPHL sub type presented with stage 1 A and stage 2 A, while most of patient in other histopathology presented with advanced stages. 37 and 12 patients in nodular sclerosis presented with stage 3 and stage 4 respectively. Systemic symptoms developed in 50 (52%) patients, most commonly was fever, its more seen in stage 4. 68% of patients with stage 4 had B symptoms, while no one patient in stage 1 developed B symptoms. The most common sites of extralymphatic involvement were lung in 21 patients, bone in 20 patients bone marrow in 10 patients liver and pleura in 4 and 1 patient respectively, in most of patients there more than one of extra lymphatic organ involvement, splenic involvement documented in 30 patients. Prognosis post first line chemotherapy demonstrates in Table 2. Complete remission were noted in all 29 patients whom presented with early stages of disease (stage 1 and stage 2) while in stage 3.19 (86%) patients developed complete remission post chemotherapy, in stage 4.35 (77%) patients in complete remission after chemotherapy. Over all remission after chemotherapy in all patients were 83 (86%) of patients .failure of achieve complete remission post first line treatment was seen more in male 15% of patients, while in female 10% developed failure of remission post first line treatment, mean age of patients whom developed failure of treatment 36 years in contrast to 27 years the mean age of patients whom developed complete remission, failure of remission post treatment was noticed more in mixed cellularity and lymphocyte rich subtypes. 5 patients from 13 in mixed cellularity subtype developed failure of treatment and 3 patients from 5 in lymphocyte rich subtype developed failure of treatment, while in

nodular sclerosis 5 patients from 68 developed failure of treatment. Of the 13 patients whom failed remission post first line of chemotherapy 5 patients developed complete remission post second line treatment, while in 8 patients developed failure of treatment and resistant disease post second line.

On regular follow up of patients 8 patients whom was in complete remission developed relapse of disease, mean time of relapse was 9 months post remission.

Table 1: Histopathology and staging of disease in all patients.

	Count
Stage	
1	9
2	20
3	22
4	45
B symptoms	4
A	42
B	50
Pathology	
Lymphocyte rich	5
Mixed cellularity	13
Lymphocyte depleted	3
NLPHL	7
Nodular sclerosis	68

Table 2: Prognosis post first line treatment in all patients.

	Remission post first line treatment	
	Complete remission	Failure of remission
	Count	Count
Sex		
Male	56	10
Female	27	3
Mean age	32	35
Stage		
1	9	0
2	20	0
3	19	3
4	35	10
B symptoms	4	0
A	42	0
B	37	13
Pathology	8	0
Lymphocyte rich	2	3
Mixed cellularity	8	5
Lymphocyte depleted	2	1
NLPHL	7	0
Nodular sclerosis	63	5

DISCUSSION

HL account for approximately 0.6% of all malignancy in adults and 1/10 of incidence of non-Hodgkin's lymphoma.¹³ It has a bimodal age distribution curve. But in developed countries it has one peak age.¹⁴ In our study there is one peak age incidence which was at age of 21 years which is similar to developed countries, in USA the peak age approximately 20 years.¹⁵ In our study there was a male predominance at ratio of 2.2/1 which is relatively lower than many other regions. The overall male/female ratio calculated from the African registries' data was 2.4:1,¹⁶ while in Asia 3.5:1,¹⁷ but higher than Europe and America which ratio male:female 2:1.¹⁸ HL typically presents as painless lymphadenopathy, which is commonly the cervical lymph nodes.¹⁹ More than 50% of patients have a mediastinal mass, which can be asymptomatic or can present as dyspnoea, or superior vena cava obstruction.²⁰ Most of our patients presented with enlarged cervical lymph nodes, in one patient superior vena cava obstruction were the presenting symptom of disease. Superior vena cava obstruction caused by major vessel compression in the superior mediastinum. It occur in 10% of patients with mediastinal tumors, it's often caused by non-Hodgkin's lymphoma, and rarely seen in HL.²¹ Pleural effusion commonly seen in HL, it caused by pleural infiltration of disease.²² It may the presenting sign of HL.²³ In one patient in our study it was the presenting sign, and in further four patients pleura infiltration with lymphoma caused effusion. The WHO classification of HL is classical and nodular lymphocyte predominant HL.²⁴ Classical HL are 4 histopathology types; nodular sclerosing, mixed cellularity, lymphocyte rich and lymphocyte depleted with higher proportion of nodular sclerosis in young adults,²⁵ which was same finding in our study. The mean age was 31 years while in lymphocyte rich it was 58 years. With nodular sclerosis being the commonest sub type with rarity of other histopathology types, there was no other pathology other nodular sclerosis in female patients. Patients with NLPHL more often present with early stage disease compared to classical type and commonly present with asymptomatic, chronic lymphadenopathy.²⁶ All patients with NLPHL in our study presented with early stage of disease, absence of systemic symptoms and with no spleen involvement, which similar findings in pub listed studies.²⁷ Many studies indicate that lungs are the most common extra lymphatic site involvement in HL patients and associated with poor prognosis and failure of remission with conventional chemotherapy.²⁸ In our study lung then bone were the most common sites. Systemic symptoms generally correlate with advanced stage and bulky disease and portend a worse prognosis.²⁹ It is seen in one third of patients with HL; in our study 50% of patients had systemic symptoms. The most common was fever; this higher percentage of patients with systemic symptoms could be due to more patients presented with higher stages of disease. PET scan has high sensitivity and specificity to assess remission of disease after

chemotherapy.³⁰ According to cancer treatment guidelines PET after 2-3 cycles and after last cycle of chemotherapy.³¹ In our study 86% of all patients had a complete remission of disease, with more patients in early stages developed remission compared to patients whom presented with higher stage. All patients whom presented with early stages of disease went to complete remission irrespective to age, gender or histopathology subtype, similar to many previous studies that concluded that patients with early stage (stage I-II) HL have a high likelihood of achieving long-term complete remission.³² Less ratio of complete remission was noted in advanced stages of disease, and thus higher percentage of refractory disease in advanced stages, especially in stage 4 disease, which complete remission in 77% of patients in contrast to 86% in stage 3 developed complete remission. Non-remission post first line chemotherapy was noted more in male patients, in elderly patients, and in mixed cellularity and lymphocyte rich sub types, second line treatment was given an after failure of first line or at disease relapse. Complete remission with second line treatment was noticed in only 40% of patients likely similar to literature. During follow up period of our study 8 patients from 88 patients (9%) whom achieved complete remission whether after first or second line treatment developed relapse of disease, relapse rate of about 10% is same to many previous studies.³³ Most of patients relapse occur within the first year post remission, so it's wise close follow up especially within first years. Because our study is retrospective and lack of data about long term follow up of patients, so we couldn't account mortality rate and real relapse rate of disease because of short term follow up of patients, partly due to lost follow up of some patients, and re referral of patients after remission to other hospitals for follow up.

CONCLUSION

Hodgkin's lymphoma is a group of biologically heterogeneous neoplasms brought together by morphologic and phenotypic similarities. It has high rates of cure in developed countries, and over 90% of adults with HL in early stages of disease will be cured, while for advanced stages the percentage of therapeutic success is above 70. Epidemiological, clinical, histological and therapeutic results in our series are similar to those Western series. Long term evaluation is necessary to assess relapse and late toxicity treatment we recommend treating patients in a specialized hospitals with demanding management.

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