CLINICO-PATHOLOGICAL PRESENTATION AND THERAPEUTIC OPTIONS FOR HAIRY CELL LEUKEMIA

Abid Jameel[1], Sadaf Chiragh[2], Saira Iqbal[3], Muntajeeb Farooq[4]

ABSTRACT

Objective: *To look at clinical and hematological presentation as well as treatment outcome of patients with diagnosis of Hairy Cell Leukemia (HCL) in our population.*

Methodology: *All patients diagnosed with HCL by morphological and immunohistochemical methods presenting to Medical Oncology Ward at Hayatabad Medical Complex, Peshawar since August 2008 were included in the study.*

Results: *Out of 7 patients diagnosed with HCL, 6 were male and 1 was female (M:F ratio 6:1). Median age at diagnosis was 44 years. Fever, pallor, palpitations and fatigue were the commonest presenting complaints. Spleenomegaly was noted in all patients (100%). Pancytopenia was noted in all patients at presentation. Five patients were treated with Interferon while 2 were treated with Cladribine. At 18 months of follow-up, one out five patients treated with IFN had relapse while both the patients treated with Cladribine were in complete remission.*

Conclusion: *Our study showed that HCL patients present at a younger age in our region but further studies with larger sample size are required to confirm this. All patients showed a complete response to Interferon and Cladribine with all patients alive at 18 months of follow-up.*

Key Words: *Hairy cell leukemia (HCL), clinical presentation, treatment, interferon, cladribine, Pakistan*

This Short Communication may be cited as: Jameel A, Chiragh S, Iqbal S, Farooq M. Clinico-Pathological Presentation and Therapeutic Options for Hairy Cell Leukemia(HCL). J Postgrad Med Inst 2012; 26(3): 336-9.

INTRODUCTION

Hairy cell leukemia (HCL) is a relatively rare B-cell chronic lymphoproliferative disorder with distinct morphological features. HCL was first described by Bouroncle in 1958 who termed it as "Leukemic Reticuloendotheliosis"[1]. HCL comprises of 2% of all leukemias with an overall incidence rate of 0.32/100000 population[2]. HCL can often be confused with other diseases causing pancytopenia such as aplastic anemia, B-cell prolymphocytic leukemia, myelofibrosis and myelodysplastic syndromes[3]. Diagnosis of HCL can be confirmed with the help of bone marrow aspiration and immunophenotyping. The characteristic morphological feature of HCL is cytoplasmic hair like projections on the involved cells[3]. Typical immunophenotypic markers that distinguish HCL from other conditions include CD 20, CD 103, CD 11c and CD 25 while cells are usually negative for CD 10, CD 5 and CD 23[4]. Tartarate Resistant Acid Phosphatase (TRAP) may also be positive. A variant of HCL (HCL-V) has been identified which is distinguished from classic HCL as HCL-V is mostly CD 25 or CD 103 negative, patients have a high white blood cell count and the disease runs an aggressive course showing poor response to treatment[4].

Clinical presentation of HCL includes middle age at diagnosis, fatigue, cytopenias and spleenomegaly that may result in pain in the abdomen. Patients with HCL may initially present with infectious complications due to pancytopenia however one third to one half of HCL patients may be asymptomatic[5].

Fortunately, HCL is a disease with a multitude of treatment options. However, purine nucleoside analogs, pentostatin and cladribine, are currently considered the treatment of choice. Despite being a rare disease, the outcome of HCL

[1-4]Department of Medical Oncology, Hayatabad Medical Complex, Peshawar - Pakistan

Address for Correspondence:
Dr. Abid Jameel
Associate Professor,
Department of Medical Oncology,
Hayatabad Medical Complex, Peshawar - Pakistan
E-mail: ajameel99@yahoo.com

Date Received: December 8, 2011
Date Revised: April 10, 2012
Date Accepted: April 18, 2012

has transformed completely in the past two decades with the introduction of new treatment modalities, i.e. purine nucleoside analogs. From a median survival of 4 years in 1960s & 70s, patients with HCL can now expect a normal life expectancy with an overall survival of 97% at 9 years with purine analogs[6,7].

We describe our experience with seven patients presenting to our ward with the diagnosis of HCL in a 30 month period from August 2008 to January 2011. Their clinical presentation, hematological picture and treatment with different chemo-therapeutic drugs as well as their outcome will be discussed.

METHODOLOGY AND RESULTS

Seven patients were diagnosed with HCL at Medical Oncology Ward, Hayatabad Medical Complex Peshawar since August 2008. Six patients were male while one was female (M : F ratio = 6 : 1). Median age at diagnosis was 44 years (range 37–59). The most common presenting complaints in all our patients were recurrent fevers, pallor, palpitations, fatigue and pain left upper abdominal quadrant. All seven patients had spleenomegaly at presentation. All except one patient had an initial Hb count < 10 gm/dl (mean 8.1 gm/dl) while all seven patients had an initial platelet count of < 100000/mm^3 (mean 45285/ mm^3). After excluding the two patients who presented with blast crisis after splenectomy, all the remaining five patients had an initial WBC count < 3500/ mm^3 (mean 2600/ mm^3). Details of initial clinical presentation and treatment outcome of our patients are shown in Table 1 while hematological picture at presentation of these patients is presented in Table-2. All patients had morphological features of HCL on light microscopy while the immuno-histochemical stains found positive in these patients included CD11c, CD103 and Cd25.

Two of the seven patients had a prior splenectomy and both presented to us with a recurrence in the form of increased WBC and

Table 1: Initial Clinical Presentation of HCL Patients

Patient	Age	Sex	Spleenomegaly	Fever	Treatment
Patient 1	38 yrs	Male	Yes	Yes	Cladribine*
Patient 2	59 yrs	Male	Yes	Yes	Cladribine*
Patient 3	37 yrs	Male	#	Yes	IFN*
Patient 4	45 yrs	Male	Yes	Yes	IFN*
Patient 5	50 yrs	Male	Yes	Yes	IFN+
Patient 6	38 yrs	Male	#	Yes	IFN*
Patient 7	40 yrs	Female	Yes	Yes	IFN¶

Abbreviations: IFN: interferon
These two patients had prior splenectomy and presented with a recurrence .
* Patients are in complete remission after at least 18 months of follow-up.
+ Patient had a relapse one year after interferon therapy.
¶ Patient lost to follow-up after one month on IFN therapy.

Table 2: Hematological profile of HCL patients at presentation

Patient	Hb	WBC	Platelets
Patient 1	7.0	2700	91000
Patient 2	8.5	2900	40000
Patient 3 #	11	375000[1]	15000
Patient 4	7.0	1700	51000
Patient 5	7.8	2500	30000
Patient 6 #	7.8	44000[2]	42000
Patient 7	7.6	3200	48000

Abbreviations: Hb: hemoglobin level; WBC: white blood cell count
These two patients had prior splenectomy and presented with a recurrence along with increased WBC and blasts in the peripheral smear and bone marrow ([1] 90% blasts; [2] 30% blasts).

blasts in the peripheral blood and bone marrow. Both were treated with Interferon (IFN) 3 mIU on alternate days for six months. Both patients were in complete remission after eighteen months of follow-up. Three of the remaining five patients were treated with IFN (3 mIU alternate days for six months). One patient was still in remission after 18 months of follow-up, one patient had a relapse after 12 months of treatment while the third patient was lost to follow-up after one month of IFN therapy. All four eligible patients (100%) treated with IFN showed complete response (clinically and hematologically) while three out of four IFN treated patients (75%) followed for 18 months were in remission. The remaining two patients received 2-chlorodeoxyadenosine (Cladribine) 0.1 mg/kg/day for 7 days (one course each). Both these patients were in complete remission (clinical and hematological) after 18 months of follow-up.

DISCUSSION

HCL is a relatively rare disorder of the elderly representing 2% of all leukemias. Our study also shows an incidence of 2% of all leukemias in our unit while in another study in Pakistan the morphological pattern of 234 consecutive cases of various leukemias was studied and they reported 2 cases of HCL among the 234 cases, an overall incidence of 1%[8]. Although western literature reports median age at diagnosis of HCL patients in the mid to late fifties[3] but our study shows the age at presentation for HCL patients in our population as 44 years. This younger age at presentation of HCL has also been reported in Indian patients with HCL where the median age at diagnosis was 47 years[9]. The result of our study and the one conducted in India suggests that HCL is diagnosed at a relatively younger age in our population compared to western countries. This trend towards diagnosis in younger age in Asian population has also been reported for other leukemias including chronic myeloid leukemia[10,11].

The higher male to female ratio in HCL patients was also confirmed in our study. HCL has been reported to be characterized by peripheral cytopenias resulting in weakness, fatigue and recurrent infections with fever in HCL patients[3,12,13]. All patients in our study also had pancytopenia along with a history of recurrent infections and fever. All our patients presented with spleenomegaly (two had prior splenectomy for grossly enlarged spleens) as has been reported in literature. Thus our study is in agreement with the literature from western countries regarding presentation and manifestation of the disease except for the fact that in our population the age at diagnosis of HCL patients is at least a decade younger.

Outcome of HCL has changed dramatically with the introduction of interferon and nucleoside analogs since the mid eighties. Prior to this, splenectomy was the treatment of choice that resulted in only 50% survival at 4 years[14]. With interferon 3 mIU three times week for six months followed by a tapering off dose in the next six months, an overall response rate of 91% and a complete response rate of 13-40% has been reported with only 17% of patients requiring nucleoside analogs[14,15,16]. In case of recurrence with interferon, purine analogs can be used as salvage regimens. Currently, nucleoside purine analogs cladribine and pentostatin are the first line treatment of choice for HCL. Cladribine has shown a complete response rate of 95% and overall survival of 97% at 9 years[6]. Similar responses have also been reported for pentostatin[17]. The superior complete remission rates and overall survival rates with nucleoside analogs has therefore resulted in recommendation of these agents as the treatment of choice for HCL. Our study also shows a medium term complete clinical and hematological response to cladribine confirming its efficacy in our population.

CONCLUSION

In summary, treatment with purine nucleoside analogs has made HCL a potentially curable disease. Although more expensive (total cost Rs. 280000) compared to 12 months of interferon (total cost Rs. 140000), the impressive response rates and overall survival dictates the use of purine analogs over interferon. However, in case of financial difficulties, interferon for 6 months followed by 6 months of tapering/maintenance dose may also give acceptable results. Currently, splenectomy is not the treatment of choice.

REFERENCES

1. Bouroncle BA, Wiseman BK, Doan CA. Leukemic endotheliosis. Blood 1958;13:609-30.
2. Dores GM, Matsuno RK, Weisenburger DD, Rosenberg PS, Anderson WF. Hairy cell leukemia: a heterogeneous disease? Br J Haematol 2008;142:45-51.
3. Wanko SO, DeCastro C. Hairy cell leukemia: an elusive but treatable disease. Oncologist 2006;11:780-9.
4. Chen YH, Tallman MS, Goolsby C, Peterson L. Immunophenotypic variations in hairy cell leukemia. Am J Clin Pathol 2006;125:251-9.
5. Malfuson JV, Gisserot O, Cremades S, Doghmi

K, Fagot T, Souleau B, et al. Hairy-cell leukemia: 30 cases and a review of literature. Ann Med Interne 2003;154:435-40.

6. Goodman GR, Burian C, Koziol JA, Saven A. Extended follow up of patients with hairy cell leukemia after treatment with cladribine. J Clin Oncol 2003;21:891-6.
7. Else M, Dearden CE, Matutes E, Garcia-Talavera J, Rohatiner AZ, Johnson SA, et al. Long term follow up of 233 patients with hairy cell leukemia, treated initially with pentostatin or cladribine, at median of 16 years from diagnosis. Br J Haematol 2009;145:733-40.
8. Hassan K, Ikram N, Shah SH. A morphological pattern of 234 cases of leukemias. J Pak Med Assoc 1994;44:145-8.
9. Chatterjee T, Panigrahi I, Mahapatra M, Pati HP, Kumar R, Naithani R, et al. Hairy cell leukemia: clinical, pathological and ultrastructural findings in Asian-Indians. Indian J Cancer 2008;45:41-4.
10. Jameel A, Jamil SN. Clinico-pathological profile of chronic myeloid leukemia. J Postgrad Med Inst 2006;20:235-8.
11. Syed NN, Usman M, Khaliq G, Adil SN, Khurshid M. Clinici-pathologic features of chronic myeloid leukemia and risk stratification according to Sokal score. J Coll Physicians Surg Pak 2006;16:336-9.
12. Grever MR. How I treat hairy cell leukemia. Blood 2010;115:21-8.
13. Kraut E. Infectious complications in hairy cell leukemia. Leuk Lymphoma 2011;52:50-2.
14. Golomb HM, Catovsky D, Golde DW. Hairy cell leukemia: a clinical review based on 71 cases. Ann Intern Med 1978;89:677-83.
15. Damasio EE, Clavio M, Masoudi B, Isaza A, Spriano M, Rossi E, et al. Alpha-interferon as induction and maintenance therapy in hairy cell leukemia: a long-term follow-up analysis. Eur J Haematol 2000;64:47-52.
16. Benz R, Sicilliano RD, Stussi G, Fehr J. Long term follow-up of interferon alpha induction and low-dose maintenance therapy in hairy cell leukemia. Eur J Haematol 2009;82:194-200.
17. Kraut EH, Grever MR, Bouroncle BA. Long-term follow-up of patients with hairy cell leukemia after treatment with 2-deoxycofomycin. Blood 1994;84:4061-3.

CONTRIBUTORS

AJ conceived the idea, collected & analyzed data, wrote the manuscript. SC helped in writing and revising manuscript, literature search & patient care. SI & MF did data collection & helped in patient follow-up.