

Hairy Cell Leukemia Treatment: Where We Are Now?

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SUMMARY

Hairy cell leukemia (HCL) is a very rare type of leukemia, in which abnormal B lymphocytes, present in the bone marrow, spleen, and peripheral blood stream, get worse slowly or do not get worse at all. HCL is the disease where patients have pancytopenia with splenomegalia over 90% percent, palpable lymphadenopathy occur in 35% of patients, some form of serious infection eventually developed in over 50% of patients and was the most common cause of death in patients. HCL is dominantly a male disease, with the male-female ratio, ranging from 4:1 to 7:1. Treatment and prognosis of HCL depends on: the number of HC in the peripheral blood or bone marrow, if the spleen is enlarged and on the existence of the visible leukemia infection symptoms. Prognostic factors are similar to the above mentioned and also if the basic disease HCL is aggressive or the number of HC grow slowly and there is no need for treatment. Starting from September 1985 till September 2010, we observed a group with total number of 28 patients (22 males and 6 females) at the age of 30-76 (median range 46 years), all with HCL disease. From the total number of participants, 20 patients (71,43%) received chemotherapy, Cladribine and 8 patients (28,57%) received different type of therapy, such as immunomodulator therapy, surgery or combination of both, without Cladribine. Most effective therapy for HCL, from all of the above mentioned was definitely Cladribine which is dominant with a resulting response rates of 80-100%, where 70-90% of patients were achieving a complete remission, as defined by a complete disappearance of hairy cells in the bone marrow.

Key words: 2-chlorodeoxyadenosine, cladribine, hairy cell leukemia

1. INTRODUCTION

Hairy cell leukemia is very rare type of leukemia in which abnormal B lymphocytes, covered with tiny hair-like projections are present in the bone marrow, spleen, and peripheral blood stream, get worse slowly or do not get worse at all (1, 2, 3, 4, 5, 6, 7, 8, 9, 10). The World Health Organisation has codified the appellation "hairy cell leukemia", "leukemic reticuloendotheliosis" was its historical reference in the literature (4, 11, 12, 13, 14, 15, 16). Ewald first used this term for a disease more consistent with acute monocytic leukemia. Hairy cell leukemia is disease where patients have pancytopenia with splenomegalia over 90% percent, palpable lymphadenopathy occur in 35% of patients, some form of serious infection eventually developed in over 50% of patients and was the most common cause of death in patients (2, 19) Laboratory findings are also abnormal like highest LAP score, accelerated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia (5, 10, 14, 19, 20) HCL is very rare disease, constitutes approximately 2% of all lymphoid leukemias (2). Dominantly is a male disease, with the male:female ratio ranging from 4:1 to 7:1.(2,19). The median age of onset is in the early fifth decade. Fluorescence in situ hybridisation techniques have detected clonal chromosomal abnormalities in up to 67% in HCL patients. (6). Most common cytogenetic abnormalities are 11q deletion,

17p deletion, trisomy 12, 13q deletion, also gain or loss of alleles on chromosome 5 and 14 were common findings (6). Hairy cells behave like monocytes, performing phagocytosis, producing fibronectin, displayed on his surface CD 19, CD 20, CD 22 like B lymphocyte but another markers typical for HCL were: CD 11c, CD 25, HC2, PCA1, CD 23, CD 103, HLA DR (1, 12).

Hairy cell leukemia expresses tartarate resistant acid phosphatase (TRAP), CD25, and PCA 1, while splenic marginal zone lymphoma does not.(17,18) DBA 44 and L 26 (an anti CD 20) antibody are fixative resistant monoclonal antibodies that were sensitive for hairy cells, although not specific. HCL is very similar disease with splenic lymphoma with villous lymphocytes (CD 11 c positive, CD 25 positive, CD 103 negative), HCL variant (CD 11 c positive, but CD 25 negative).(7,17) Possible clinical signs of HCL include tiredness and weakness (27%), infections, (29) bleeding complications, (16%) abdominal pain bellow the ribs, shortness of breath, weight loss for no known reason and painless stomach or grain (2, 5, 19).

Treatment and prognosis of HCL depends on the number of HC in the peripheral blood, or bone marrow, if the spleen is enlarged, are existing leukemia infection symptoms visible. Prognostic factors are similar to the above mentioned and also if the basic disease HCL is aggressive

or the number of HC grow slowly and there is no need for treatment.(8) Also is important if the HC are progressive and should there be a need for chemotherapy or surgery. There are several different types of treatments for HCL patients such as: watch and wait, chemotherapy (Cladribine and Pentostatine) biological therapy (the patients immune system is fighting the cancer by it self) Interferon Alpha is a common biological agent for HCL treatment, surgery, targeted therapy (Rituximab) (11, 13, 16).

Because of it we made a clinical research to find how far are we with handling the challenges of this illness due to the fact that we are a small single center in treatment for HCL.

2. MATERIALS AND METHODS

Starting from September 1985 till September 2010, we observed a group with total number of 28 patients (22 males and 6 females) at the age of 30-76 (median range 46 years) all with HCL disease. The entire group was medicated and treated on the University Clinic of Hematology in Skopje. Previous clinical research was established by the morphology from peripheral blood and bone marrow examination, immunophenotyping by flow cytometry, biochemical parameters, and sonography. Splenomegaly was present in 26 (92,86%) patients, hepatomegaly in 4 patients, lymphadenopathy in 6 patients, other (infective complications) – 1 patient, and 1 patient with no clinical presentation of clinical disease.

From the total number of participants, 20 patients (71,43%) received chemotherapy, Cladribine and 8 patients (28,57%) received different type of therapy such as immunomodulator therapy, surgery or combination of both without Cladribine. Nine (32,14%) patients from our group were pre-treated with another type of chemotherapy, non treated patients were 19 (67,86%) from which 20 patients (71,43%) received Cladribine, and the other 8 (28,57%) were treated differently. Surgery or splenectomy were used in 6 (21,43%) patients, only chemotherapy received 4 (14,28%) patients, and Interferon Alpha ± chemotherapy received 2 (7,15%) patients, Interferon Alpha alone received 4 (14,28%) patients, Interferon Alpha ± splenectomy received 2 (7,15%) patients. Number of non-treated patients were 10 (35,71%).

3. DISCUSSION

Complete or partial remission were shown in 16 patients (80%) and 4 patients (20%) didn't respond to the treatment at all. Leukopenia, sepsis, and insufficient cardiorespiratory were the main reason for the death of the patients. The number of patients that received Cladribine therapy but died from sepsis is 3, number of patients that didn't receive any kind of treatment and died from sepsis are 2, two patients died from the basic disease HCL due to the complications combined with leukopenia and sepsis.

Overall summary in patients which were treated with Cladribine—we had 15 (75%) survived patients and 5 (25%) which died. Patients treated with other therapy (immunomodulatory) we had 2 (25%) survived and 6 (75%) died. Response status was assessed at 4 weeks.

4. CONCLUSION

Most effective therapy for HCL from all the above mentioned was definitely Cladribine who is dominant resulting response rates of 80-100%, with 70-90% of patients achieving a complete remission as defined by complete disappearance of hairy cells in the bone marrow.(3) This kind of therapy is still controversial because its necessary long term follow up for secondary malignancies such as brain or pancreatic tumor, but our observed group (none of the patients) didn't show this kind of complication. Recent follow up of the patients found no hairy cells in bone marrow after treatment, indicating that some patients may perhaps be cured, but is not definitely proved.(15) Only one patient died from acute renal failure after Cladribine infusion one week later, but the patient was with low Karnofsky score (positive comorbidities and older age). Three of the patients died without Cladribine treatment or any other agent by the basic illness which was an aggressive form of HCL.

Data from numerous studies suggest that Cladribine is still a treatment of choice for HCL, like in our study in most studies the drug has been given i.v. but there are many studies that drug was given subcutaneous and gave better results. We can say the as a small center of hematology we are entering in the world level of treatments and results.

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