Introduction

Hairy cell leukemia (HCL) is a chronic lymphoproliferative disorder characterized by abnormal mononuclear cells of B lymphocyte origin infiltrating bone marrow and spleen. Patients often present with some combination of anemia, neutropenia, thrombocytopenia and splenomegaly (1,6,11). Anemia is very common and is observed in 75 to 80 percent of patients (3,9,12). The mechanism of anemia has been attributed to the splenic sequestration with a substantial increase in splenic volume (13) and to the reduced red-cell production due to diffuse bone marrow infiltration by tumor cells and bone marrow fibrosis (4,15). Erythron studies revealed that in addition to splenic sequestration and reduced red-cell production there is some reduction in red cell-survival (5). The anemia is usually normocytic or macrocytic with slight anisocytosis and poikilocytosis. The mean cell volume (MCV) is nearly always toward the upper limit of normal and often elevated (6). We have observed that red cell distribution width, which is indicative of anisocytosis, reflects in HCL the disease's activity (7).

Patients and Methods

The RDW values were assessed in 18 patients with hairy cell leukemia (HCL) treated with 2-chlorodeoxyadenosine (2-CdA), in 5 patients treated with Interferon alpha (IFN-alpha) and in 9 patients subjected to splenectomy. Out of 18 patients treated with 2-CdA one patient was excluded from the study because of association of HCL with acquired sideroblastic anemia. In the remaining 17 patients the mean value of RDW before therapy was 18.8% (range 13.5% to 25.0%) and dropped after successful therapy after 6 to 12 months to the mean value of 13.6% (range 11.2% to 17.9%) and after 18 months to 13.4% (range 12.6% to 14.7%) (p = 0.00015 and p = 0.00049 respectively). The hemoglobin level increased from the mean value of 119 g/l (range 99 g/l to 157 g/l) before therapy to the mean value of 145.9 g/l (range 127 g/l to 172 g/l) after 6 to 12 months and after 18 months to 147.8 g/l (range 132 g/l to 168 g/l) (p = 0.000017 and p = 0.00036 respectively). The same trend was observed in the group of patients treated with IFN-alpha. The RDW decreased from the mean value of 21.3% (range 18.8% to 28.7%) to the mean value of 15.3% (range 12.4% to 16.7%), (p = 0.031). The hemoglobin level increased in this group of patients from the mean value of 115 g/l (range 98 g/l to 127 g/l) to the mean value of 136 g/l (range 127 g/l to 146 g/l) (p=0.031). In 9 patients in complete hematologic remission 34 to 293 months after splenectomy the mean value of RDW was 13.9% (range 13.0% to 15.5%). Conclusion: Increased RDW in HCL is associated with active disease and is reversible after successful therapy. This phenomenon has not been reported in the literature yet. Preliminary results show that the increase of RDW may be due to the dyserythropoiesis.

Key words: HCL; RDW; Dyserythropoiesis

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normal interdigitating mononuclear cells and the presence of blood-filled spaces lined by hairy cells, so called pseudosinuses (14).

Response criteria to the therapy
Complete hematologic remission (CR) required all of the following:
1) Complete absence of hairy cells in the peripheral blood.
2) Normalization of peripheral blood counts (hemoglobin level ≥120 g/l, white cell count ≥3x10^9/l, absolute neutrophil count ≥1.5x10^9/l, platelet count ≥100x10^9/l, disappearance of retroperitoneal lymphadenopathy and hepatosplenomegaly by CT or US scan.

Partial remission (PR) required
1) Failure of normalization in one of low peripheral blood counts.
2) Reduction grater than 50% of lymphadenopathy and/or hepatosplenomegaly. The Red Cell Width (RDW in %) was determined using Coulter JT3 or Coulter STKS. Normal value 11.5-14.5%.

Patients
Group 1 (see table 1): consisted of 18 patients treated by 2-chlorodeoxyadenosine (2-CdA). All patients received a single cycle of 2-CdA at a dose of 0.1 mg/kg/d by continuous intravenous infusion for 7 days. Out of 18 patients there were 14 male and 4 female with an age range 39 to 82 years (median, 61.5 years). 11 patients were previously treated: 7 by splenectomy, 2 by splenectomy and IFN-alpha, 2 by repeated course of IFN-alpha because of relapse, in remaining 7 patients the 2-CdA therapy was the first treatment. All 18 patients responded to the therapy, in 16 complete hematologic remission was achieved, in one patient (M.W. No 11) the remission was partial because the platelet count increased after therapy only to 90x10^9/l, but the hemoglobin level after therapy was within normal limits. Patient V.J. (No 15) reached the normal hemoglobin level after 18 months. Patient V.M. (No 6) was excluded from further assessment because of associated acquired sideroblastic anemia and will be considered separately.

Group 2 (see table 2) consisted of 5 patients treated by Interpheron-alpha. 3 patients were previously treated by splenectomy. 1 patient received the second course of IFN-alpha because of relapse. Out of 5 patients there were 4 male and 1 female with an age range of 39 to 78 years (median, 58 years).

Group 3 (see table 3) consisted of 9 patients treated by splenectomy with the follow up period after splenectomy between 34 and 293 months (median, 193 months). Out of 9 patients there were 5 male and 4 female with an age range between 51 to 71 years (median, 60 years). Bone marrow biopsy reveiled interstitial infiltration by hairy cells in all patients. All patients have been after splenectomy in complete hematologic remission.

### Table 1: Hemoglobin levels and RDW in Patients with hairy cell leukemia treated with 2-chlorodeoxyadenosine

| Name         | Age/Sex | Previous therapy | Before therapy | After 6 months | After 18 months |
|--------------|---------|------------------|---------------|----------------|----------------|
| L.O.         | 56/M    | SPL              | SPL           | SPL            | SPL            |
| J.S.         | 56/M    | SPL              | SPL           | SPL            | SPL            |
| M.H.         | 59/M    | SPL              | SPL           | SPL            | SPL            |
| T.S.         | 56/M    | SPL              | SPL           | SPL            | SPL            |
| V.J.         | 63/M    | SPL              | SPL           | SPL            | SPL            |
| M.L.         | 60/M    | SPL              | SPL           | SPL            | SPL            |
| V.M.         | 71/M    | IFN (2x)         | IFN (2x)      | IFN (2x)       | IFN (2x)       |
| S.V.         | 82/F    | IFN              | IFN           | IFN            | IFN            |
| J.V.         | 62/F    | SPL, INF         | SPL, INF      | SPL, INF       | SPL, INF       |
| M.O.         | 76/M    | SPL, INF         | SPL, INF      | SPL, INF       | SPL, INF       |
| L.Z.         | 63/M    | SPL              | SPL           | SPL            | SPL            |
| F.J.         | 71/M    |                  |               |                |                |
| M.W.         | 56/M    |                  |               |                |                |
| B.J.         | 49/M    | IFN (2x)         | IFN (2x)      | IFN (2x)       | IFN (2x)       |
| A.M.         | 39/M    | SPL              | SPL           | SPL            | SPL            |
| J.S.         | 56/M    | SPL              | SPL           | SPL            | SPL            |
| V.J.         | 62/M    | SPL, INF (2x)    | SPL, INF (2x) | SPL, INF (2x)  | SPL, INF (2x)  |
| K.A.         | 65/M    |                  |               |                |                |
| F.J.         | 59/M    | IFN (2x)         | IFN (2x)      | IFN (2x)       | IFN (2x)       |
| Z.J.         | 63/M    | IFN (2x)         | IFN (2x)      | IFN (2x)       | IFN (2x)       |

### Table 2: RDW and hemoglobin levels in patients with hairy cell leukemia treated with IFN-alpha

| Name         | Age/Sex | Previous therapy | Before therapy | After 6 months |
|--------------|---------|------------------|---------------|---------------|
| L.O.         | 56/M    | SPL              | SPL           | SPL           |
| J.S.         | 56/M    | SPL              | SPL           | SPL           |
| M.H.         | 59/M    | SPL              | SPL           | SPL           |
| T.S.         | 56/M    | SPL              | SPL           | SPL           |
| V.J.         | 63/M    | SPL              | SPL           | SPL           |
| M.L.         | 60/M    | SPL              | SPL           | SPL           |
| V.M.         | 71/M    | IFN (2x)         | IFN (2x)      | IFN (2x)      |
| S.V.         | 82/F    | IFN              | IFN           | IFN           |
| J.V.         | 62/F    | SPL, INF         | SPL, INF      | SPL, INF      |
| M.O.         | 76/M    | SPL, INF         | SPL, INF      | SPL, INF      |
| L.Z.         | 63/M    | SPL              | SPL           | SPL           |
| F.J.         | 71/M    |                  |               |                |
| M.W.         | 56/M    |                  |               |                |
| B.J.         | 49/M    | IFN (2x)         | IFN (2x)      | IFN (2x)      |
| A.M.         | 39/M    | SPL              | SPL           | SPL           |
| J.S.         | 56/M    | SPL              | SPL           | SPL           |
| V.J.         | 62/M    | SPL, INF (2x)    | SPL, INF (2x) | SPL, INF (2x) |
| K.A.         | 65/M    |                  |               |                |
| F.J.         | 59/M    | IFN (2x)         | IFN (2x)      | IFN (2x)      |
| Z.J.         | 63/M    | IFN (2x)         | IFN (2x)      | IFN (2x)      |

### Table 3: Hemoglobin levels and RDW in patients with hairy cell leukemia treated by splenectomy

| Name         | Age/Sex | Previous therapy | After splenec- tomy (months) | Bone marrow biopsy | Lymph nodes | RDW (%) | Hb (g/l) |
|--------------|---------|------------------|-----------------------------|-------------------|-------------|---------|---------|
| L.R.         | 71/F    | SPL              | 293                         | INT               | 0           | 13.9    | 158     |
| V.J.         | 63/M    | SPL              | 214                         | INT               | 0           | 13      | 146     |
| J.V.         | 62/F    | SPL              | 198                         | INT               | 0           | 13      | 130     |
| K.J.         | 60/M    | SPL              | 194                         | INT               | 0           | 14.2    | 173     |
| H.J.         | 51/M    | SPL              | 193                         | INT               | 0           | 14      | 150     |
| V.J.         | 54/M    | SPL              | 181                         | INT               | 0           | 15.5    | 177     |
| J.W.         | 53/F    | SPL              | 175                         | INT               | 0           | 13.6    | 129     |
| V.J.         | 62/M    | SPL              | 84                          | INT               | 0           | 13.1    | 159     |
| V.J.         | 53/F    | SPL              | 34                          | INT               | 0           | 15.1    | 135     |

### Statistical analysis:
For the statistical analysis of RDW and hemoglobin concentration procedures described in (10) were used. As we have two measurements on the same individual at different times two statistical tests were used. In the case when normality of differences could be accepted (by means of D’Agostino skewness, kurtosis and omnibus normality tes-
Results

Group 1 (see table 1): Out of 17 assessed patients the RDW values before therapy were increased in 13 patients, within normal limits in 4 patients with a range between 13.5 to 25.0% (mean, 18.8%). After 6 to 12 months of therapy the mean value of RDW was 13.6% (range 12.6 to 17.9%), (p=0.00015) it was normal in 14 patients, slightly above the upper limit of normal value in 3 patients (14.6%, 14.8, 17.3%) and in the forth patient (V.J.,No 17: RDW 17.9%) the normal RDW 13.7% was reached after 18 months. The After 18 months RDW was within normal limits in 14 patients and only slightly above the upper limit of normal values in 3 (14.7%, 14.7%, 14.7%). The mean value of RDW after 18 months was 13.4% (range 12.4% to 14.7%), (p=0.00049).

The hemoglobin level simultaneously increased from the mean value of 119 g/l (range 99 g/l to 157 g/l) before therapy to the mean value of 145.9 g/l (range 127 g/l to 172 g/l) after 6 to 12 months and to 147.8 g/l (range 132 g/l to 168 g/l) after 18 months (p=0.00049 and p=0.00036 respectively).

Group 2 (see table 2): In the group of 5 patients treated with Interferon-alpha the RDW dropped from the mean value of 21.3% (range 18.8% to 28.7%) before therapy to the mean value of 15.3% (range 12.4% to 16.7%) after six months of therapy (p=0.031).

The hemoglobin level simultaneously increased from the main value of 115 g/l (range 98 g/l to 127 g/l) to the main value of 136 g/l (range 127 g/l to 146 g/l), (p=0.031).

Group 3 (see table 3): In the group of 9 patients treated by splenectomy all patients were in complete hematologic remission. Mean value of RDW was 13.9%. The RDW was slightly above the upper limit of normal value in two patients (15.1% and 15.5%) despite normal levels of hemoglobin 135 g/l and 177 g/l respectively. The RDW values before splenectomy were not accessible. The examination before splenectomy was performed with an automated instrument not giving RDW value.

Discussion

Anisocytosis is an increase in the variability of erythrocyte size beyond that which is observed in a healthy subject. In automated instruments the calculated value of RDW reflects very accurately the degree of anisocytosis and makes the comparison of its changes possible. RDW has been found to be increased in iron deficiency anemia, megaloblastic anemias, congenital and acquired dyserythropoietic anemias (1,2,16,17). We have found that increased RDW in HCL was present in patients with an active disease and subsided after successful therapy with 2CdA or IFN-alpha with a simultaneous rise of the hemoglobin levels. This phenomenon as far as we know has not been reported in the literature yet. Preliminary data show that the increased RDW may be due to the dyserythropoiesis (8). This finding is the subject of a further study and will be reported separately in more details.

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