Treatment with Low Dose Human Recombinant Interferon-Alpha-2-ARG Induces Complete Remission in Patients with Hairy Cell Leukemia

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Key Words

Interferon
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Summary

Five cases with advanced hairy cell leukemia refractory to treatment with splenectomy and chemotherapy as well as one patient presenting with a stage-A response to splenectomy were treated with rhu-IFN- α_2 -arg. 5×10^6 were administered intramuscularly every day. Both patients, with advanced disease resistant to conventional therapy and treated for six or more months with rhu-IFN- α_2 -arg, achieved complete clinical remissions. Three further cases treated for less than half a year and also with advanced disease achieved partial remission states with marked reduction of circulating hairy cells and with recovery of normal hemopoiesis. Minimal residual disease in the remaining patient during a three-month period of treatment did not respond. Side effects of rhu-IFN- α_2 low dose therapy were minimal in 5 cases and comprised a severe leukopenia reversible after dose reduction in one patient.

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Schlüsselwörter

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Zusammenfassung

Fünf Haarzell-Leukämiepatienten in fortgeschrittenen, Splenektomie-bzw. Chemotherapie-resistenten Stadien der Erkrankung sowie ein Patient mit Stadium-A-Antwort nach Splenektomie wurden einer Behandlung mit rhu-IFN- α_2 -arg 5×10^6 U täglich intramuskulär unterzogen. Zwei Patienten mit fortgeschrittener Erkrankung und Resistenz gegenüber konventioneller Therapie wurden sechs und mehr Monate therapiert und erreichten eine komplette klinische Remission. Drei weitere Fälle, ebenfalls in späten Krankheitsstadien, erreichten innerhalb von sechs Monaten eine Teilremission mit ausgeprägter Reduktion von zirkulierenden Haarzellen und

weitgehender Rekonstruktion der normalen Hämatopoese. Ein Patient mit **minima-ler** Restinfiltration nach Splenektomie zeigte innerhalb der ersten drei Behandlungsmonate kein Ansprechen. Während bei fünf Patienten nur geringe Nebenwirkungen auftraten, führte die relativ niedrig dosierte **rhu-IFN- α** -Therapie bei einem Patienten zu einer schweren, aber nach Dosisreduktion reversiblen Leukopenie.

Introduction

Recently Quesada et al. reported on seven patients with hairy cell leukemia treated with partially purified human interferon- α [2]. They observed three complete and four partial remissions. This remarkable success in the management of a disease with otherwise still rather limited therapeutic options has attracted much attention and thus revived the search for the value of interferons in the treatment of malignant states. On the other hand their use of an only partially purified preparation did not enable them to conclude whether interferon itself or other contaminating constituents were responsible for the effects observed [2]. In this report we present data on the treatment of hairy cell leukemias with an almost pure preparation of human recombinant interferon- α (rhu-IFN- α).

Material and Methods

Six patients (4 male, 2 female) aged from 40 to 57 years entered the study. Diagnosis was established on the basis of morphology, immunocytology, cytochemical demonstration of acid phosphatase resistant to tartaric acid and was further supplemented by bone marrow biopsy. Details of the clinical findings and the previous treatment of these patients are given in table I.

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Treatment consisted of daily intramuscular injections of 5×10^6 U of rhu-IFN- α (Bender, Vienna). This dose in two patients was reduced to 5×10^6 U every alternate day (patients WA, PR). Details of the therapy are shown in table II.

Results

Five patients with advanced disease refractory to conventional treatment as well as one patient with a stage-A-response to splenectomy but still presenting minimal residual disease, were treated with daily doses of rhu-IFN- α using the low dose regimen given in table II. Time of therapy ranged from 3 to 10 months. As shown both patients receiving rhu-IFN- α for six or more months achieved complete clinical remissions documented by negative bone marrow biopsies (cases PR and WA, table II). Clinical improvement with almost complete disappearance of hairy cells from the peripheral blood and with recovery of normal hemopoiesis was seen in three further cases treated for less than half a year (patients RI, HIL and SC, table II). Residual minimal disease in case HI, however, did not respond to treatment during three months.

Side effects of rhu-IFN- α were minimal in five patients (patients RI, PR, WA, HI, SC) and mainly consisted of flulike symptoms during the first two weeks of therapy. Severe leukopenia associated with a septic episode was observed in patient HIL. This problem, however, rapidly resolved subsequent to dose reduction.

144 Gastl et al.: Alpha Interferon for Treatment of Hairy-Cell Leukemia

Table I. Clinical data of hairy cell leukemia patients before treatment with rhu-IFN- α

Patient

Age/Sex

Diagnosed Previous since therapy*)

BCC before rhu-IFN- α Hb WBCC

(g%) (x10⁻³)
arg
PMNC (x10⁻³)
HC
(x10⁻³)
PLTs (x10⁹)
Disease course

WA
49/♀

18 months Sx, stage
11.4
26.2
0.54
24.0
164
progressive
PR
45/♂

B response 12 months Sx, stage
9.2
0.8
0.48
0.1
14
progressive
HIL
40/♂

B response 30 months Sx, stage
5.9

32.1
0.19
27.4
78
progressive
RI
57/♂

C response 21 months Sx, stage
8.4
97.5
0.13
96.0
166
progressive
HI
51/♀

B response 21 months Sx, stage
12.7
5.1
2.74
0.1
261
stable
SC
40/♂

A response 2 months none
10.9
4.5
0.32 ;
3.2
57
progressive
*)Sx-
- splenectomy,

response to splenectomy assessed according to the criteria described by Jansen et al. [1]

Table II. Response of hairy cell leukemia patients to treatment with rhu-IFN- γ -arg
Patient rhu-IFN- γ -arg therapy
BCC before/after therapy
Response*)

WA

PR
HIL
RI
HI
SC

Hb
time
dose
/12.2
 5×10^6 U im qd/4w, 10 months 11.4
then $3 \times$ weekly
9.2
/13.2
 5×10^6 U im qd/4w, 6 months
then $3 \times$ weekly
5.9
 5×10^6 U im qd/12w, 4 months
then $3 \times$ weekly
8.4
 5×10^6 Uimqd 3 months
/10.5
3 months 12.7
/12.4
3 months
10.9
/13.2
 5×10^6 Uimqd 5×10^6 Uimqd
WBCC
26.2
/3.1
0.8
/3.2
32.1
/2.0
97.5
/3.7
5.1
/10.
4.5
/2.7
PBMNC
0.54
/2.13
/1.32
0.19

/0.34
 0.18
 /1.43
 2.74
 /7.12
 0.32
 /1.18
 HC
 24.0
 0.1
 27.4
 96.0
 0.1
 3.2
 /0
 /0
 /0.1
 /1.6
 /0.1
 /0
 PTLS
 164
 /297
 14
 /204
 78
 /181
 166
 /169
 261
 /269
 57
 /147
 BM-biopsy clinical

“) Response assessed using one criteria described by Quesada et al. [2]
 Discussion
 References

Using a low dose regimen of rhu-IFN- α for treatment of hairy cell leukemia cases results were obtained which were comparable to those achieved by Quesada et al. with partially purified natural interferon- α [2]. This clinical observation suggested that
 (i) interferon- α itself is in fact the active principle inducing remissions in hairy cell leukemia,

(ii) rhu-IFN- α is equally effective for treatment as natural interferon- α , and
(iii) the hairy cell leukemia among various malignancies is characterized by an outstanding sensitivity to treatment with alpha-interferons. Further studies, however, are clearly required to define the optimal dose and length of treatment. Such investigations are now in progress in our institutions.

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