Relief of Intractable Pruritus in Polycythemia Vera With Recombinant Interferon Alfa

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Following reports that recombinant interferon alfa (rIFNa), besides inducing clinical and hematologic remission in polycythemia vera (PV), can also resolve intractable pruritus, we used rIFNa to treat 13 PV patients complaining of severe pruritus refractory to conventional treatment (venesection and/or cytostatics). rIFNa was administered intramuscularly three times a week at a dosage of $3.0 \times 10^6$ U. Eight patients (61.5%) reported a $>50\%$ reduction of pruritus, which occurred within 2–8 weeks from the start of rIFNa treatment, leading to a substantial improvement in their quality of life. Three patients had to stop rIFNa within the first month of therapy because of unacceptable side effects. Thus rIFNa seems to be capable of providing considerable relief of otherwise intractable pruritus in a good proportion of PV patients.

Key words: polycythemia vera (PV), recombinant interferon alfa (rIFNa), pruritus

INTRODUCTION

The problem of identifying the best form of management for polycythemia vera (PV) is far from being solved. In fact, whereas venesection alone does not seem to be sufficient to prevent vascular occlusive episodes, especially in higher risk patients, radioactive phosphorus and cytotoxic drugs appear to cause a higher incidence of leukemic or myelofibrotic transformation [1,2].

Recent reports indicate that in PV patients recombinant interferon alfa (rIFNa) is capable of inducing and maintaining complete hematologic remission [3,4]. Moreover, sporadic cases of intractable pruritus associated with PV have been found to benefit from rIFNa therapy [5,6].

On the basis of these findings, we undertook a study to evaluate the effect of rIFNa on a selected population of PV patients complaining of severe pruritus despite having reached hematologic remission by means of conventional treatment (venesection and/or cytostatics).

MATERIALS AND METHODS

Thirteen PV patients (7 males and 5 females), aged 49–83 (median 68) years, were selected from the overall population of 128 subjects regularly followed at our outpatient clinic. The only criterion for selection was the presence of severe pruritus, resistant both to cytoreduction (by phlebotomy and/or cytostatics) and to symptomatic drugs (antihistamines), that was significantly affecting quality of life (e.g., work, sleep, bathing, social activity). All the patients gave informed written consent after being acquainted with the possible problems and side effects of rIFNa.

Although in all cases bathing worsened the itching, in other respects the characteristics of the pruritus varied considerably. In seven subjects this symptom presented throughout the daytime, gravely impairing their regular activities; two had prevalent difficulty in sleeping at night; in the remaining four the discomfort was constant.

The patients, all in hematologic remission at the start of the study (i.e., hematocrit $\leq 45\%$ and platelet count $\leq 600 \times 10^9/l$), were treated with intramuscular rIFNa at a dose of $3 \times 10^6$ U three times per week. In order to control a flu-like syndrome, acetaminophen was always given at the start of treatment and was thereafter pursued as and when necessary. Cytostatics were stopped in all

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cases, and phlebotomies were allowed only in cases where the hematocrit level increased to >45%.

Patients were followed every 2 weeks: a careful assessment by the same physician of PV-related symptoms and of rIFNα-related side effects was made, along with physical examination, full blood counts, and control of liver and renal functions.

Responsiveness to treatment was defined as a ≥50% reduction of pruritus, with a substantial improvement in the quality of life. After reaching clinical remission, responder patients were administered rIFNα at a lower dosage (3.0 × 10⁶ U once-twice a week) as a maintenance treatment.

RESULTS

The results of the study are summarized in Table I. Eight patients (61.5%) reported a ≥50% reduction of itching after 2–8 weeks of treatment. In particular, on social grounds, patient no. 6, a 49-year-old teacher, indicated a major improvement in her professional life.

rIFNα-related flu-like syndrome occurred in all patients, but in most cases was mild and acceptably controlled by acetaminophen. However, two patients (nos. 2 and 4) had to stop rIFNα at the first and fourth week, respectively, owing to severe flu-like symptoms, so they were considered not evaluable. Another patient (no. 10) had to discontinue rIFNα after achieving response, as the discomfort of side effects (fever, bone pain, headache, mental confusion) outweighed the advantages.

In all but two of the patients, hematologic remission was maintained throughout the course of rIFNα treatment. Patient no. 6 showed a progressive increase in splenomegaly, with increasing abdominal discomfort, after 2 months of therapy, requiring the addition of hydroxyurea, and patient no. 7 was submitted to three phlebotomies throughout a 40-week-period.

DISCUSSION

In our series of 13 PV patients with intractable pruritus, as well as maintaining hematologic remission, rIFNα treatment led to an effective reduction in this disturbing symptom in 61.5% of the cases. The results from this relatively short and uncontrolled, but accurately selected, group of patients reinforce the positive reports of Ariad et al. [6] and de Wolf et al. [5] in one and five patients, respectively.

Pruritus of varying severity, possibly related to histamine release from basophils [7], is a common symptom in PV and usually improves as the red cell mass is reduced by means of venesection or cytostatics. However, a minority of patients complain of severe itching even after reaching hematologic remission [8]. Histamine and H2 antagonists, aspirin, cholestyramine, and oral iron in the past have all been employed in an attempt to relieve pruritus, but although occasionally of value, they are generally not very helpful [rev. in 8].

rIFNα seems to be effective in relieving intractable pruritus in a consistent percentage of PV patients and at the same time is capable of maintaining hematologic remission. Even though the therapeutic employment of rIFNα in PV has so far been held back owing to the high cost and the frequently unpleasant side effects, its use seems warranted in case of severe and refractory itching, as this symptom may considerably worsen the quality of life of PV patients.
REFERENCES


