We agree with these authors that the small volume of synovial fluid, the low leucocyte counts, the rapidity of accumulation, and the transient nature of the effusion support a pathogenic mechanism related to fluid shifts across the synovial vasculature. Although glucocorticoids are known to exert a membrane stabilising effect, our patient's fluid lost its own characteristics (colour, cells, chemical properties) and became similar to plasma as if it had been subjected to increased synovial capillary intravascular pressure. Synovial tissue permeability is markedly affected by increased vascular forces, which alter filtration pressure and synovial fluid production. Bertone *et al* showed, in an animal study, an increase in trans-synovial fluid flow associated with an increase in arterial and venous pressure.[6] Raised arterial pressure, which is a side effect of high dose corticosteroid treatment, and low oncotic pressure due to a low protein plasma concentration in a nephrotic patient, can increase the trans-synovial fluid flow at a lower arterial pressure than normal. This rare side effect of high dose corticosteroid treatment should not be forgotten.

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REFERENCES

1 **Woods JE**, Anderson CF, De Weerd JH, Johnson WJ, Donadio JV, Leary FJ, *et al*. High-dosage intravenously administered methylprednisolone in renal transplantation: a preliminary report. JAMA 1973;223:896–9.
2 **Bennet WM**, Strong D. Arthralgia after high-dose steroids. Lancet 1975;i:332
3 **Cathcart ES**, Scheinberg MA, Idelson BA, Couser WG. Beneficial effects of methylprednisolone "pulse" therapy in diffuse proliferative lupus nephritis. Lancet 1976;i:163–6.
4 **MacFarlane JD**, Filo RS, Brandt KD. Joint effusion after kidney transplantation. Arthritis Rheum 1979;22:164–9.
5 **Lally EV**. High-dose corticosteroid therapy: association with non-inflammatory synovial effusion. Arthritis Rheum 1983;26:1283–7 .
6 **Bertone AL**, Hardy J, Simmons EJ, Muir WW 3rd. Vascular and transsynovial forces of the isolated stationary equine joint. Am J Vet Res 1998;59:495–503.

Effects of interferon α treatment on the clinical course of refractory Behçet's disease: an open study

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Interferon α (IFNα) has recently been introduced in the treatment of uveitis, mucocutaneous lesions, and arthritis of Behçet's disease (BD).[1–6] To our knowledge, there is currently no clinical trial which has evaluated the efficacy of IFNα treatment in the vascular or neurological involvement in BD. In this open study we evaluated the efficacy, toxicity, and tolerability of IFNα in the management of BD with ocular, articular, vascular, or neurological manifestations which had previously been unsuccessfully treated conventionally.

PATIENTS AND METHODS

A total of 29 patients (17 men, 12 women; mean age 33.2 months, range 16–51) who were resistant to conventional treatments were treated with systemic IFNα. Previous conventional treatments had been colchicine, aspirin, and penicillin plus sulfasalazine for patients with arthritis; or colchicine, aspirin, and penicillin plus steroids and/or immunosuppressive agents, azathioprine, cyclosporin A, or cyclophosphamide for ocular, vascular, and/or neurological involvement. The mean duration of the disease was 8.86 years (range 1–30). Four patients were excluded from the statistical analysis because of the short duration of treatment (<4 months).

Seventeen patients had ocular inflammation. Eleven patients had arthritis. Ten patients had vascular disease (aneurisms in the internal cerebral and ophthalmic arteries; thrombosis of popliteal veins and left anterior descending coronary artery causing myocardial infarction; organised thrombus in superior and inferior caval, iliac, and femoral veins causing intractable ascites; thrombophlebitis; thromboses of internal jugular vein and sigmoid sinus; thrombosis of pulmonary arteries together with intracardiac thrombus in the right ventricle; thrombosis of popliteal vein and ulcerated erythema nodosum; thrombosis of deep veins of the lower extremities only; thromboses of superior vena cava, jugular, and brachiocephalic veins; and thrombosis of sagittal sinus). Four patients had parenchymal neurological complications which were diagnosed with physical examination and magnetic resonance imaging.

All patients were treated with colchicine 1.5 mg/day orally in three divided doses, aspirin 80 mg/day, and intramuscular benzathine penicillin 1.2 million units every three weeks. Thrombotic occlusions were also treated with anticoagulant agents. Cyclophosphamide was continued together with IFNα in one patient with neurological and vascular disease.

The patients were followed up regularly every 3–6 months. The IFNα dose was 5 million units subcutaneously three times a week, and this was tapered to 3 million units three times a week after 6–9 months as clinical response was achieved. The dose intervals were then gradually increased. The dose of IFNα was increased to 10 million units in one patient because of a lack of response.

Data were evaluated according to the following criteria: complete remission, disappearance of all manifestations during treatment; partial remission, >50% decrease in the number, severity, duration, and/or frequency of recurrence of the lesions; stable disease, <50% change in the manifestations; and progressive disease, >50% deterioration of existing manifestations or/and the development of new ones.[7]

The visual acuity of two patients had deteriorated severely before they were admitted to our clinic. The IFNα treatment prevented new relapses, and, moreover, after the treatment both patients regained a satisfactory visual acuity which was sufficient for the maintenance of daily activities. Another patient had had intractable ascites due to the organised thrombus in the superior and inferior caval, iliac, and femoral veins. Anticoagulation plus IFNα reduced the amount of ascitic fluid without additional vascular event and improved the general clinical condition of the patient. Those three patients were classified as "remission with sequela".

Table 1 Response rates for the distinct forms of clinical manifestations in our patients with Behçet's disease. Results are shown as No (%)

Type of clinical manifestation	Complete remission	Remission with sequela	Partial response	Progressive disease
Uveitis	13/17 (76)	2/17 (12)	1/17 (6)	1/17 (6)
Arthritis	11/11 (100)			
Vascular disease	9/10 (90)	1/10 (10)		
Neurological disease	4/4 (100)			

RESULTS

The mean duration of IFNα treatment was 22.2 months (range 5–72). The overall response rate was 96% (24/25). Table 1 shows the response rates for the distinct forms of clinical manifestations.

Flu-like symptoms were recorded in eight patients. Serum transaminase levels were reversibly raised in two patients. Although no patient had to discontinue IFNα, the dose was reduced to 3 million units three times a week in one patient because of intolerance.

DISCUSSION

IFNα has previously been given in the treatment of BD with mucocutaneous, articular, and/or ophthalmological manifestations.[1–6] Zouboulis and Orfanos extensively reviewed 144 patients with BD who were treated with IFNα.[7] Seventy four per cent (92/124) of these patients with mucocutaneous manifestations, 95% (37/39) with uveitis, and 93% (51/55) with arthropathy/arthritis showed a partial or complete response. We found similar response rates for uveitis (16/17, 94%) and arthritis (11/11, 100%) .

Although the therapeutic potential of IFNα in BD with vascular or neurological involvement has not been previously investigated, there are some anecdotal reports. In one study treatment with IFNα resulted in complete remission of ocular vasculitis with reperfusion of most of the occluded vessels.[2] One patient with BD with gastrointestinal vasculitis[8] and two patients with superficial thrombophlebitis improved after IFNα treatment.[4 5] Two patients with neuro-BD were reported to be responsive to treatment with IFNα.[1 9] In our study, IFNα produced remission in all patients with neurological or vascular disease (table 1), and, moreover, no recurrence or major toxicity was seen during the long term follow up.

There is no consensus on the dose of IFNα which should be used for the treatment of BD. In most trials the dose ranged between 3 and 9 million units daily or three times a week.[1–7] The risk of IFNα related retinopathy and splinter haemorrhages is increased at high doses.[10] Moreover, relatively low doses were found to be as effective as the high IFNα doses, with fewer side effects.[4] Therefore, we started the treatment with 5 million units three times a week. The duration of IFNα treatment is also controversial. Most studies have used the drug for a 3–6 month course, although shorter and longer treatments have also been reported.[1–7] Recurrences have been reported in a number of patients when treatment was stopped.[1–7] Accordingly, we continued the IFNα treatment with dose tapering and later increasing the intervals between doses. Evaluation of response to any treatment including IFNα is complicated and is usually based on the clinical features of BD. Therefore some of the criteria mentioned in the manuscript remain subjective. However, the results of this open study suggest that IFNα may be an effective, safe, and well tolerated therapeutic alternative in BD where sight or life is threatened. Controlled studies are needed to elucidate its possible role as a first line agent in BD and its optimal therapeutic dosage and duration of treatment.

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REFERENCES

1 **Pivetti-Pezzi P**, Accorinti M, Pirraglia MP, Priori R, Valesini G. Interferon alpha for ocular Behçet's disease. Acta Ophthalmol Scand 1997;75:720–2.
2 **Kötter I**, Eckstein AK, Stübiger N, Zierhut M. Treatment of ocular symptoms of Behçet's disease with interferon alpha 2a: a pilot study. Br J Ophthalmol 1998;82:488–94.
3 **O'Duffy JD**, Calamia K, Cohen S, Goronzy JJ, Herman D, Jorizzo J, *et al*. Interferon-alpha treatment of Behçet's disease. J Rheumatol 1998;25:1938–44.
4 **Georgiou S**, Monastirli A, Pasmatzi E, Gartaganis S, Goerz G, Tsambaos D. Efficacy and safety of systemic recombinant interferon-alpha in Behçet's disease. J Intern Med 1998;243:367–72.
5 **Azizlerli G**, Sarica R, Kose A, Ovul C, Kavala M, Kayabali M, *et al*. Interferon alfa-2a in the treatment of Behçet's disease. Dermatology 1996;192:239–41.
6 **Hamuryudan V**, Moral F, Yurdakul S, Mat C, Tuzun Y, Ozyazgan Y, *et al*. Systemic interferon alpha 2b treatment in Behçet's syndrome. J Rheumatol 1994;21:1098–100.
7 **Zouboulis CC**, Orfanos CE. Treatment of Adamantiades-Behçet disease with systemic interferon alfa. Arch Dermatol 1998;134:1010–16.
8 **Kötter I**, Stübiger N, Eckstein AK, Helligenhaus A, Günaydin I, Jacki SH, *et al*. Treatment of ocular Behçet's disease (BD) with recombinant human interferon alpha 2a (rhIFN-α2a): a three center pilot study [abstract]. Arthritis Rheum 1998;41(suppl):S355.
9 **Nichols JC**, Ince A, Akduman L, Mann ES. Interferon-alpha 2a treatment of neuro-Behçet disease. J Neuroophthalmol 2001;21:109–11.
10 **Guyer DR**, Tiedeman J, Yannuzzi LA, Slakter JS, Parke D, Kelley J, *et al*. Interferon-associated retinopathy. Arch Ophthalmol 1993;111:350–6.