Treatment of ocular symptoms of Behçet’s disease with interferon α2a: a pilot study

Ina Köttter, Anja K Eckstein, Nicole Stübiger, Manfred Zierhut

Abstract

Aim—To study long term effects of interferon α2a (IFNα2a) on panuveitis in seven patients with Behçet’s disease in a prospective, open clinical trial.

Methods—Seven patients were treated with IFNα2a for a mean of 23.6 months (14–37 months). They received an initial dose of IFNα2a of 6×10^6 IU/day, followed by 3×10^6 IU/day after 1 month and 3×10^6 IU every other day after 3 months. Two patients received low dose prednisolone (between 0.2 and 0.4 mg/kg/body weight) additionally at the beginning of the therapy. Complete cessation of IFNα2a was possible in three patients (observation period 22, 6, and 4 months).

Results—Marked improvement occurred in six patients who had ocular manifestations of Behçet’s disease for the first time or with minor damage during their course of chronic relapsing panuveitis. In one patient with advanced ocular Behçet’s disease, new relapses were prevented. Retinal infiltrates resolved within 2 weeks; vasculitis, macular oedema, infiltration of the anterior chamber and vitreous resolved within 4 weeks. Mean posterior uveitis score before treatment (nine affected eyes) was 6.6, 4 weeks after IFN α it was reduced to 0.4. The mean observation period is 27.6 months, ranging from 14 to 42 months.

Conclusion—Treatment of ocular symptoms of Behçet’s disease with IFNα2a alone or in combination with low dose steroids led to complete remission of ocular vasculitis in all patients treated in this open, uncontrolled trial. Treatment with IFNα2a may prevent permanent retinal or optic nerve damage due to vascular occlusion. No severe side effects occurred. Controlled randomised studies are warranted in order to prove the efficacy of IFNα2a in ocular Behçet’s disease and to compare it with other, established treatments such as azathioprine or cyclosporin A.

Behçet’s disease is a multisystem inflammatory disorder. In addition to oral aphthosis, which is the hallmark of Behçet’s disease, frequent clinical manifestations comprise skin lesions, genital ulcers, arthritis, subcutaneous and deep vein thrombophlebitis. Ocular involvement occurs in 60–80%. In most cases a panuveitis with primary manifestation on average 8 years after disease onset and with a chronic relapsing course. Ocular manifestations are bilateral in most of the patients. Visual loss is mainly caused by retinal vasculitis involving superficial capillaries at the optic disc, macula, and retinal periphery and leading to occlusive vasculopathy. Perivenous and capillary leakage are the most common ocular findings, and sometimes only visible on fluorescein angiography. The central feature of the histopathology of Behçet’s disease is a systemic occlusive vasculitis (arteries and veins) with a tendency to venous thrombus formation. The underlying aetiology is not yet known. HLA-B51 association hints at a genetic component in the development of Behçet’s disease.

The poor ocular prognosis of Behçet’s disease has improved over recent years with the increasing use of immunosuppressive agents. In particular, young male patients are at increased risk for ocular complications and require aggressive medical management. Azathioprine has been shown to maintain visual acuity (VA) and prevent the development of eye disease. Cyclosporin A is also an effective and rapidly acting drug for the treatment of eye disease in Behçet’s disease. Nephrotoxicity, particularly at doses higher than 5 mg/kg/day, relapses after cessation of therapy, and the high costs limit its use. Cytotoxic agents such as chlorambucil, and cyclophosphamide are also used but have been less well studied. Colchicine is effective for mucocutaneous and articular manifestations, but only partially effective for posterior uveitis. Brief courses of corticosteroids may shorten the duration of the attacks but they are not effective for long term treatment, probably because the dose necessary for maintenance of remission would be very high with unacceptable side effects.

Up to now, interferons have only been used in relatively small patient groups with Behçet’s disease. A few open studies with up to 20 patients excluding ocular disease, showed efficacy of IFNα2a and γ in different dosages. Recently, there have been case reports on four patients with severe refractory eye disease successfully treated with steroids, immunosuppressants, and IFNα in various combinations.

Patients and methods

Patients
We studied a total of seven patients. All were diagnosed as having Behçet’s disease according to the international study group criteria. First symptoms of the disease occurred approximately 3–14 years before ocular manifestation. All patients had clinical evidence of vision threatening retinal or optic nerve vasculitis. Each patient was admitted to hospital and,
after initiation of IFN \( \alpha \) therapy, examined daily for 10–14 days and then examined weekly for a period of 1 month. During remission patients were examined at intervals ranging from 1 to 3 months.

**Evaluation**

All patients underwent ophthalmological examination including visual acuity, measurement of intraocular pressure, slit lamp examination of the anterior segment, and indirect ophthalmoscopy of the posterior segment. A general examination was performed at the department of internal medicine. Visual fields, fluorescein angiography, and fundus photography were performed at regular intervals, as well as laboratory tests including routine laboratory variables—erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and autoantibody testing. Complete HLA typing was done at initiation of the therapy.

**Criteria for Efficacy**

The uveitis scoring system 20 which includes visual acuity, reduction of anterior and posterior activity scores, reduction of inflammatory activity in the fluorescein angiogram and reduction of inflammatory activity in the laboratory values (ESR, CRP) have been used as criteria for efficacy.

**Dosage of IFN \( \alpha \)**

\( \text{IFN}_{\alpha} \times 10^6 \) IU/day was administered initially. Depending on efficacy this dosage was tapered to \( 3 \times 10^6 \) IU/day after 4–8 weeks and to \( 3 \times 10^6 \) IU every other day after 3–4 months. In one patient with Kaposi’s sarcoma, therapy was started with \( 18 \times 10^6 \) IU/day, which is the clinical standard therapy for this disease. IFN\( \alpha \) was always injected subcutaneously before bedtime.

Concomitant low dose oral prednisolone in doses between 0.2 and 0.4 mg/kg body weight was given to two patients on steroid therapy at the time of exacerbation which could not be stopped promptly. Dosage was not changed in the first 2 months.

**Exclusion Criteria and Cessation of Therapy**

In case of inefficacy after 4 weeks or further deterioration, therapy was to be changed to CSA at the standard dosage of 3 mg/kg daily.\(^1\)\(^2\)

**Results**

**Case Reports**

**Case 1**

A 30 year old man of Turkish origin had suffered from Behçet’s disease since the age of 19. The first symptom was oral aphthosis; since June 1989 he had also had chronic relapsing panuveitis. Diagnosis of Behçet’s disease was made in February 1990. HLA-B51 was positive. Previous treatments were cyclosporin A (CSA, 5 mg/kg/day) plus low dose systemic steroids from July 1990 to November 1992, with several relapses of bilateral uveitis with persistent visual loss (chronic macular oedema, vascular occlusion, optic atrophy). In November 1992,
Behçet's disease diagnosed in 1986. At that time a skin biopsy revealed a leucocytoclastic vasculitis. First clinical symptoms had occurred at the age of 17 (arthritis, oral aphthosis, and skin lesions). HLA-B51 was negative. Previously, from 1986 to 1990, interferon γ was successfully applied to treat mucocutaneous symptoms and arthritis. This case has been described in detail previously. In September 1993 she presented with an acute localised field defect in the right eye and ophthalmological examination revealed a large peripapillary retinal infiltrate in the left eye with otherwise normal fundus appearance in both eyes. VA was normal in both eyes. In the anterior chamber no cells or flare were detectable. There was a vitreous haze scoring 0–1 in both eyes but more pronounced in the left eye. Fluorescein angiography revealed a local blockage due to the nerve fibre oedema in the left eye without signs of vasculitis elsewhere. Systemic steroids were not effective (prednisolone 1 mg/kg), but when treated with higher doses of IFNα2a (6×10^6 IU/day), reperfusion occurred and the large retinal infiltrate resolved within 4 weeks. There was no loss of VA or persistent visual field defects. The patient was in stable remission on 3×10^6 IU IFNα2a twice weekly, which was tapered completely to zero by November 1995. No ocular relapses have occurred (22 months).

Case 2

A 31 year old woman of German origin had Behçet's disease diagnosed in 1986. At that time a skin biopsy revealed a leucocytoclastic vasculitis. First clinical symptoms had occurred at the age of 17 (arthritis, oral aphthosis, and skin lesions). HLA-B51 was negative. Previously, from 1986 to 1990, interferon γ was successfully applied to treat mucocutaneous symptoms and arthritis. This case has been described in detail previously. In September 1993 she presented with an acute localised field defect in the right eye and ophthalmological examination revealed a large peripapillary retinal infiltrate in the left eye with otherwise normal fundus appearance in both eyes. VA was normal in both eyes. In the anterior chamber no cells or flare were detectable. There was a vitreous haze scoring 0–1 in both eyes but more pronounced in the left eye. Fluorescein angiography revealed a local blockage due to the nerve fibre oedema in the left eye without signs of vasculitis elsewhere. Systemic steroids were not effective (prednisolone 1 mg/kg), but when treated with higher doses of IFNα2a (6×10^6 IU/day), reperfusion occurred and the large retinal infiltrate resolved within 4 weeks. There was no loss of VA or persistent visual field defects. The patient was in stable remission on 3×10^6 IU IFNα2a twice weekly, which was tapered completely to zero by November 1995. No ocular relapses have occurred (22 months).

Case 3

A 30 year old woman of Greek origin had Behçet's disease diagnosed in December 1994 at the time of her first ocular manifestation. At the age of 25 she already had the first symptoms of Behçet's disease (oral aphthosis). Previous treatment consisted of CSA (4 mg/kg body weight) in December 1994 with good effect but was stopped by the patient after 3 months because of hirsutism. HLA-B51 was positive. At presentation in February 1995 with an acute onset of floaters and black patches in the visual field and pain of the right eye, together with a flare of oral and genital ulcers and arthritis of the right wrist, ophthalmoscopic examination revealed anterior chamber cell score and flare scores of 3 in the right eye. Vitreous haze scored 3. Funduscopically, there was a panuveitis with retinal vasculitis and retinal infiltrates in the mid periphery of the two lower retinal quadrants (posterior uveitis score 9) of the right eye. VA was reduced to 0.6 in the right eye. Fluorescein angiography disclosed vasculitis predominantly of the veins in the two lower quadrants and a mild macular oedema. The left eye was completely normal. IFNα2a therapy was started with 6×10^6 IU/day. Retinal infiltrates resolved within 2 weeks and vasculitis within 4 weeks. Vitreous flare persisted between score 0–1. After 2 months, the dosage was reduced to 3×10^6 IU/day and after 6 months to 3×10^6 IU every other day. After reduction to 3×10^6 IU every other day a discrete relapse, manifesting as a localised area of vasculitis occurred, which disappeared after 2 weeks without increase of the IFNα2a dosage. In May 1997 IFNα2a was completely tapered to zero. VA is still 1.0 both eyes and visual fields are normal (4 months).
Treatment of ocular symptoms of Behçet's disease with interferon α

The first symptoms occurred at the age of 12 (oral aphthosis). Erythema nodosum lesions occurred for the first time in April 1995 and genital aphthosis in December 1995. HLA-B51 was positive. He had been effectively treated with IFN-γ as far as the arthritic and mucocutaneous symptoms were concerned. This therapy was discontinued 2 years ago. In November 1995 he presented with acute reduction of VA and central field defects of the left eye together with dermal papulopustules, bilateral gonarthrosis, and orogenital aphthosis. VA was 0.2 in the left eye and normal in the right eye. Ophthalmological examination revealed an anterior chamber cell score of 3 and flare score of 1 in the left eye, but anterior chamber of the right eye was free of inflammation (score 0). Vitreous haze scored 2 in the left and 0 in the right eye. Funduscopy revealed papillitis with a disc edema of 2 dioptres, nerve fibre layer bleeding at the rim of the disc, and sheathing of more than half of the vessels at the disc in the left eye (Fig 2A). There was retinal vasculitis with infiltrates and slight macular edema with small hard exudates (retina score 7). Fluorescein angiography showed disc leakage and localized late staining of the vessels in the left eye (Fig 3A) but no changes in the right eye. Therapy with 6×10^6 IU IFNα2a/day was initiated. Because of marked, flu-like side effects and mental depression the dosage was tapered to 3×10^6 IU/day after 1 week. Retinal infiltrates resolved within 2 weeks, vasculitis disappeared within 6 weeks (Fig 2B). After 2 months, fluorescein angiography did not show any leakage of the disc and almost normal venous filling (Fig 3B). Vitreous flare persisted between 0–1. VA improved to 0.7 after 3 months, fluorescein angiography did not show any leakage of the disc and almost normal venous filling (Fig 3B). Vitreous flare persisted between 0–1. VA improved to 0.7 after 3 months of therapy. Currently, the patient has been free of any recurrence for 20 months.

Case 5

A 36 year old male patient of Italian origin had Behçet’s disease diagnosed in 1990 when he had orogenital aphthosis and arthritis of the right knee. The first symptoms had occurred at the age of 31 (oral aphthosis). HLA-B51 was positive. He had been effectively treated with IFN-γ as far as the arthritic and mucocutaneous symptoms were concerned. This therapy was discontinued 2 years ago. In November 1995 he presented with acute reduction of VA and central field defects of the left eye together with dermal papulopustules, bilateral gonarthrosis, and orogenital aphthosis. VA was 0.2 in the left eye and normal in the right eye. Ophthalmological examination revealed an anterior chamber cell score of 3 and flare score of 1 in the left eye, but anterior chamber of the right eye was free of inflammation (score 0). Vitreous haze scored 2 in the left and 0 in the right eye. Funduscopy revealed papillitis with a disc edema of 2 dioptres, nerve fibre layer bleeding at the rim of the disc, and sheathing of more than half of the vessels at the disc in the left eye (Fig 2A). There was retinal vasculitis with infiltrates and slight macular edema with small hard exudates (retina score 7). Fluorescein angiography showed disc leakage and localized late staining of the vessels in the left eye (Fig 3A) but no changes in the right eye. Therapy with 6×10^6 IU IFNα2a/day was initiated. Because of marked, flu-like side effects and mental depression the dosage was tapered to 3×10^6 IU/day after 1 week. Retinal infiltrates resolved within 2 weeks, vasculitis disappeared within 6 weeks (Fig 2B). After 2 months, fluorescein angiography did not show any leakage of the disc and almost normal venous filling (Fig 3B). Vitreous flare persisted between 0–1. VA improved to 0.7 after 3 months of therapy. Currently, the patient has been free of any recurrence for 20 months.

Case 6

A 38 year old male patient of Turkish origin had Behçet’s disease diagnosed in 1984, when he was suffering from recurrent panuveitis of both eyes. The first symptoms of Behçet’s disease occurred at the age of 16 (oral aphthosis). HLA-B51 was positive. He had been effectively treated with IFN-γ as far as the arthritic and mucocutaneous symptoms were concerned. This therapy was discontinued 2 years ago. In November 1995 he presented with acute reduction of VA and central field defects of the left eye together with dermal papulopustules, bilateral gonarthrosis, and orogenital aphthosis. VA was 0.2 in the left eye and normal in the right eye. Ophthalmological examination revealed an anterior chamber cell score of 3 and flare score of 1 in the left eye, but anterior chamber of the right eye was free of inflammation (score 0). Vitreous haze scored 2 in the left and 0 in the right eye. Funduscopy revealed papillitis with a disc edema of 2 dioptres, nerve fibre layer bleeding at the rim of the disc, and sheathing of more than half of the vessels at the disc in the left eye (Fig 2A). There was retinal vasculitis with infiltrates and slight macular edema with small hard exudates (retina score 7). Fluorescein angiography showed disc leakage and localized late staining of the vessels in the left eye (Fig 3A) but no changes in the right eye. Therapy with 6×10^6 IU IFNα2a/day was initiated. Because of marked, flu-like side effects and mental depression the dosage was tapered to 3×10^6 IU/day after 1 week. Retinal infiltrates resolved within 2 weeks, vasculitis disappeared within 6 weeks (Fig 2B). After 2 months, fluorescein angiography did not show any leakage of the disc and almost normal venous filling (Fig 3B). Vitreous flare persisted between 0–1. VA improved to 0.7 after 3 months of therapy. Currently, the patient has been free of any recurrence for 20 months.

Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Patient Details</th>
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<tbody>
<tr>
<td>1</td>
<td>Male, 22, German origin</td>
</tr>
<tr>
<td>2</td>
<td>Male, 38, Turkish origin</td>
</tr>
<tr>
<td>3</td>
<td>Male, 36, Italian origin</td>
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<tr>
<td>4</td>
<td>Male, 38, Turkish origin</td>
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<td>5</td>
<td>Male, 36, Italian origin</td>
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<tr>
<td>6</td>
<td>Male, 38, Turkish origin</td>
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</table>
In summary, in all seven patients, ocular manifestations of Behçet’s disease entered complete remission after treatment with IFNα. In five patients (nos 2, 3, 5, 6, 7) IFNα monotherapy was effective. In another two combination with 2–10 mg of prednisolone daily was required (patients 1 and 4). Under IFNα therapy, retinal infiltrates resolved after approximately 2–3 weeks in all patients, and active vascular sheathing disappeared after approximately 4–6 weeks. Most of the occluded vessels were reperfused, and only localised small areas of non-perfusion persisted. Vitreous opacity persisted longer but signs of active disease disappeared after 4 weeks. Anterior segment inflammation, additionally treated with local steroids, completely resolved within 4 weeks.

In the patients who had a short history of ocular involvement with good visual acuity before outbreak or relapse of the uveitis only minor damage persisted (patients 2–7).

Five patients have had no relapses up to now (patient 1, duration of remission 40 months; patient 2, 22 months; patient 4, 20 months; patient 5, 20 months; patient 7, 6 months). Patients 3 and 6 relapsed 4 weeks after discontinuation of IFN) with a visual acuity of 1.0 (R/L).

The patients’ data are summarised in Table 1, the results of the ophthalmological examinations in Table 2.

In summary, in all seven patients, ocular manifestations of Behçet’s disease entered complete remission after treatment with IFNα. In five patients (nos 2, 3, 5, 6, 7) IFNα monotherapy was effective. In another two combination with 2–10 mg of prednisolone daily was required (patients 1 and 4). Under IFNα therapy, retinal infiltrates resolved after approximately 2–3 weeks in all patients, and active vascular sheathing disappeared after approximately 4–6 weeks. Most of the occluded vessels were reperfused, and only localised small areas of non-perfusion persisted. Vitreous opacity persisted longer but signs of active disease disappeared after 4 weeks. Anterior segment inflammation, additionally treated with local steroids, completely resolved within 4 weeks.

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tapered to zero without relapse of uveitis up to now (observation period since cessation of therapy 22, 4, and 6 months, respectively). Mean posterior uveitis score before treatment (nine affected eyes) was 6.6; 4 weeks after initiation of IFNα therapy it was reduced to 0.4. The mean observation period is 27.6 months, ranging from 14 to 42 months.

**Discussion**

All seven patients treated with IFNα entered complete remission of ocular vasculitis/panuveitis. In three of the patients, complete cessation of IFN therapy was possible without relapse of uveitis. An effective maintenance dose of IFNα seems to be $3 \times 10^6$ IU daily with the possibility of complete cessation of therapy in at least some of the patients.

It may be that some of the remissions in our patients were the result of the natural undulating course of Behçet’s disease, but the close temporal relation of remissions to initiation of IFN therapy and relapses in some patients to dose reductions strongly suggests a therapeutic effect of IFNα.

Long term treatment (five patients now for more than 2 years) did not cause serious side effects and in this respect IFN may be superior to immunosuppressants. In all patients flu-like symptoms following the first injections were treated with paracetamol. With $6 \times 10^6$ IU/day and above, slight thrombocytopenia and leucopenia occurred. However, patient 1 tolerated the high dose of $18 \times 10^6$ IU/day very well. All patients experienced a mild alopecia and reddening at the site of injection. One patient had moderate gastrointestinal side effects (diarrhoea) and one patient had temporary mental depression; one patient developed antinuclear antibodies and dsDNA antibodies and one antithyroid antibodies without clinically overt autoimmune disease. The induction of autoantibody production by IFNα and even autoimmune disease, especially autoimmune thyroid disease, has been observed in patients with chronic hepatitis C or malignant haematological diseases. Another, less frequent side effect described in literature is an interferon induced retinopathy with retinal infiltrates similar to those occurring in Behçet’s disease itself, which also mainly has been observed in patients with chronic hepatitis and an anterior ischaemic optic neuropathy. The development of cutaneous leucocytoclastic vasculitis and even Behçet’s disease itself during IFNα treatment has been described.

We did not observe retinopathy, vasculitis, or worsening of Behçet’s disease in our patient group during the observation period of 3 years. This, of course, could be due to the small number of patients treated or the shortness of the observation period. In our opinion, the development of retinopathy in hepatitis C could possibly be explained by autoimmune phenomena due to the chronic viral infection. A retinopathy also exists in chronic myelogenous leukaemia and hairy cell leukaemia as a disease related phenomenon. Thus, studies comparing patients with hepatitis C without interferon treatment are necessary to evaluate whether retinopathy really is more frequent in patients on IFNα treatment. We also believe that the development of Behçet’s disease during IFNα treatment for chronic myelogenous leukaemia (CML) either may be hazardous, because the three cases described by now were all observed in areas where Behçet’s disease is endemic (Japan and Turkey) or the result of disease specific reactions in CML—for example, a specific change in adhesion status of the CML clones which, in genetically susceptible individuals, consecutively leads to symptoms of Behçet’s disease.

One rationale for using interferons in Behçet’s disease is their efficacy in other immune complex associated vasculitides, in which an infectious trigger is known—for example, cryoglobulinaemia (hepatitis C) and polyarteritis nodosa (hepatitis B). The possibility that viral infections may have an aetiological role in Behçet’s disease has been postulated previously by several investigators. The microbiological agents proposed include herpes simplex virus and parvovirus B19. Bacteria, mainly strains of streptococcus, have also been suggested as candidate infectious agents. Recently, hepatitis C virus was implicated in the aetiology of Behçet’s disease, but preliminary results of one group were not proved by another. Of our patients, none was serologically positive for hepatitis C (results not shown). Additionally, there is evidence for a polarisation towards the Th1 functional profile in Behçet’s disease. A substitution with IFNα further diverts the T cell response in the

### Table 2 Visual acuity and uveitis scores before and 4 weeks after (in parentheses) initiation of IFNα therapy

<table>
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<tr>
<th>Case no</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<td>Visual acuity</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>R</td>
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<td>1.0 (1.25)</td>
<td>0.6 (1.0)</td>
<td>0.2 (0.8)</td>
<td>1.25 (1.25)</td>
<td>0.6 (1.0)</td>
<td>1.0 (1.0)</td>
</tr>
<tr>
<td>L</td>
<td>0.2 (0.2)</td>
<td>0.8 (1.25)</td>
<td>1.25 (1.25)</td>
<td>0.2 (1.0)</td>
<td>1.0 (1.0)</td>
<td>0.6 (1.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Anterior chamber**

| Cells | 5 (0) | 0 (0) | 3 (0) | 1 (0) | 0 (0) | 0 (0) | 1 (0) |
| Flare | 5 (0) | 0 (0) | 0 (0) | 1 (0) | 3 (0) | 0 (0) | 1 (0) |

**Vitreous haze**

| R       | 5 (0) | 0 (0) | 3 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| L       | 5 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) | 0 (0) | 0 (0) |

**Posterior**

| R       | 8 (0) | 0 (0) | 0 (0) | 0 (0) | 19 (0) | 0 (0) | 4 (0) |
| L       | 7 (0) | 2 (0) | 0 (0) | 0 (0) | 2 (0) | 7 (0) | 2 (0) |

**Notes:**

- Values are in parentheses.
- R: Right eye, L: Left eye.
- Flare: Flare in the anterior chamber.
- Vitreous haze: Vitreous haze.
- Posterior: Posterior segment.
- Values are given in decimal form.

**References:**

1. [Interferon α](#)
2. [Tapered zero without relapse of uveitis](#)
3. [Mean posterior uveitis score before treatment](#)
4. [Complete cessation of IFN therapy](#)
5. [Effective maintenance dose](#)
6. [Observation period since cessation of therapy](#)
7. [Mean observation period](#)
8. [Seven patients treated with IFNα](#)
9. [Complete remission of ocular vasculitis/panuveitis](#)
10. [Three of the patients](#)
11. [Possible cessation of therapy](#)
12. [Effect of IFN therapy](#)
13. [Temporal relation of remissions](#)
14. [Dose reductions strongly suggest a therapeutic effect](#)
15. [Long term treatment](#)
16. [Five patients now for more than 2 years](#)
17. [Caused serious side effects](#)
18. [Immunosuppressants](#)
19. [Paracetamol](#)
20. [Thrombocytopenia](#)
21. [Leucopenia](#)
22. [Patient 1 tolerated](#)
23. [High dose of $18 \times 10^6$ IU/day](#)
24. [All patients experienced](#)
25. [A mild alopecia](#)
26. [Reddening at the site of injection](#)
27. [Moderate gastrointestinal side effects](#)
28. [Diarrhoea](#)
29. [One patient had temporary mental depression](#)
30. [One patient developed antinuclear antibodies](#)
31. [Antinuclear antibodies](#)
32. [dsDNA antibodies](#)
33. [One antithyroid antibodies](#)
34. [Without clinically overt autoimmune disease](#)
35. [Induction of autoantibody production](#)
36. [By IFNα and even autoimmune disease](#)
37. [Especially autoimmune thyroid disease](#)
38. [Has been observed in patients](#)
39. [With chronic hepatitis C](#)
40. [Malignant haematological diseases](#)
41. [Another, less frequent side effect](#)
42. [Described in literature](#)
43. [Interferon induced retinopathy](#)
44. [Retinal infiltrates](#)
45. [Similar to those occurring in Behçet’s disease](#)
46. [Behçet’s disease itself](#)
47. [Also mainly has been observed in patients](#)
48. [With chronic hepatitis](#)
49. [And an anterior ischaemic optic neuropathy](#)
50. [The development of cutaneous leucocytoclastic vasculitis](#)
51. [And even Behçet’s disease itself](#)
52. [During IFNα treatment](#)
53. [Recent studies](#)
54. [Hepatitis C virus](#)
55. [Implicated in the aetiology](#)
56. [Behçet’s disease](#)
57. [Preliminary results](#)
58. [One group were not proved by another](#)
59. [Of our patients, none](#)
60. [Was serologically positive for hepatitis C](#)
61. [Results not shown](#)
62. [Additional evidence](#)
63. [Polarisation towards the Th1 functional profile](#)
64. [Behçet’s disease](#)
65. [Substitution with IFNα](#)
66. [Further diverts the T cell response](#)
direction of Th1. This and some other immunomodulatory actions of IFN-α as enhancement of HLA class I antigen expression on lymphoid cells and of T and NK cell cytotoxicity may be helpful in improving elimination of foreign antigens.

We therefore conclude that IFN-α, alone or in combination with low dose steroid therapy may be effective in treating ocular Behçet’s disease. Of note, randomised controlled studies are necessary to further prove this. Optimal dosage also has to be evaluated. Our current recommendation is 600 IU IFN-α2b/day for the first month with consecutive tapering to 3x10^6 IU/day, later every other day to three times weekly. The most frequent side effects are flu-like symptoms, mild alopecia, and development of autoantibodies without clinically overt autoimmune disease.

We thank Dr Graham Pawelec for his critical review of our manuscript.