Longterm Visual Prognosis of Patients with Ocular Adamantiades-Behçet's Disease Treated with Interferon-α-2a

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ABSTRACT. ***Objective.*** Relapsing ocular involvement is one of the major manifestations in Adamantiades-Behçet's disease (ABD). Combining systemic corticosteroids with cyclosporin A is currently the treatment of choice. Interferon-α (IFN-α) has proven to be effective in mucocutaneous ABD and has been reported to improve ocular lesions. We examined the longterm effects of IFN-α-2a in a case series of 45 patients with ocular involvement.

Methods. Since 1988, 45 patients (79 eyes of 90 eyes) with ocular involvement in ABD have been treated with IFN-α (3 × 6–9 Mio IU per wk). In the initial acute phase of the disease, patients additionally received short-term corticosteroids (oral prednisolone 100 mg/day), tapered to a maintenance dose of 10 mg/day within 2 weeks. IFN-α-2a was administered as longterm therapy with a mean duration of 30 months (range 1.1–101 mo).

Results. IFN-α-2a/prednisolone treatment was effective against vasculitis, optic nerve neuropathy, and iritis. Sixty-four eyes had no recurrence under therapy. To date, recurrences have been seen in 26 eyes under IFN-α treatment. Flu-like symptoms were recorded in nearly all patients (n = 43). Further side effects were dose-dependent reversible thrombocytopenia (n = 1), psychosis (n = 3), depression (n = 13), thyroiditis (n = 1), and reversible diffuse alopecia (n = 7). In our series, 92% of all eyes showed stable or improved visual acuity in longterm followup.

Conclusion. Longterm remission of ocular inflammation can be achieved with the combination of IFN-α and low-dose corticosteroids. (First Release April 15 2008; J Rheumatol 2008;35:896–903)

Key Indexing Terms:
ADAMATIADES-BEHÇET'S DISEASE INTERFERON-α UVEITIS

Adamantiades-Behçet's disease (ABD) is a chronic relapsing multisystemic vasculitis involving small and large vessels. This inflammatory disorder is characterized by the classic clinical signs of recurrent oral ulcers, genital ulcers, and uveitis, whereas mucocutaneous lesions exhibit histological changes consistent with vascular reaction or vasculitis. The disease is found throughout the world, although mainly among individuals of Mediterranean or East Asian descent. Its etiology remains unknown. A number of factors have been implicated and studied intensively: genetic factors, infectious agents, environmental pollution, immunological mechanisms, and endothelial and clothing factors. The strong influence of ethnicity and the wide geographic variations of prevalence in the same ethnic group indicate environmental triggering of a genetically determined disorder[1,2].

Relapsing ocular involvement is one of the major manifestations in ABD, found in 60%–80% of patients[3]. It is characterized by iritis, uveitis, occlusive retinal vasculitis, and optic nerve neuropathy, which all lead to blindness in up to 50% of patients within 5 years, if left untreated[3,4]. Retinal detachment and secondary glaucoma are severe complications of occlusive retinal vasculitis. Although cyclosporin A combined with systemic corticosteroids is the treatment of choice for ocular ABD, it can cause severe side effects such as Cushing's syndrome, osteoporosis, or renal failure[3,5]. Other drugs such as azathioprine, cyclophosphamide, or chlorambucil are also used, but do not act rapidly enough or have not yet been studied in detail. Colchicine is less effective for posterior uveitis[4,6,7].

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Interferon-α (IFN-α) has proved to be effective in treating mucocutaneous ABD[8] and has also been suggested as a means to improve ocular lesions[9-13]. Although IFN-α has been successfully used in ocular therapy, limited information is available on longterm treatment. We evaluated the longterm effects of IFN-α (6–9 Mio IU 3 times/wk) in a large series of 79 eyes of 45 patients with ocular involvement.

MATERIALS AND METHODS

We retrospectively analyzed data from 45 patients (28 male, 17 female) receiving subcutaneous IFN-α for ocular involvement of ABD in 79 eyes (Table 1). Most patients were Turkish (n = 27; 14 male, 13 female), 5 were from Germany (4 male, 1 female), 4 from Lebanon, 2 from Italy, and one each from Cuba, Greece, Iran, Kosovo, Morocco and Serbia, the last being of African origin (Table 2). The patients from Germany had no genetic connections or relatives from countries in the Near East. All patients fulfilled the criteria of the International Study Group for Behçet's Disease[14]. We first used IFN-α for treating ocular ABD in 1988. Patients had a mean followup of 6.67 years (range 0.3–22.3 yrs). The mean age was 22 years (range 3–46 yrs) at disease onset and 28.6 years (range 12.5–50 yrs) at initial ocular involvement. Onset manifestations were oral aphthous ulcers (n = 27, 60%) and eye involvement (n = 8, 18%) in the majority of patients. Second signs occurring at a mean age of 28 years (range 13–46 yrs) were oral aphthous ulcers (n = 12, 27%), genital ulcers (n = 6, 13%), and skin lesions (n = 6, 13%). The mean age at the time of diagnosis was 31 years (range 15–50 yrs). All patients except one were typed for HLA, and 29 (64.4%) were HLA-B51-positive (Table 1). Pathergy testing was performed in 37 patients and yielded a positive result in 17 (46%). Only 5 Turkish patients had a positive family history.

The following were present at initiation of treatment: oral aphthous ulcers in 44 (98%) patients, genital ulcerations in 28 (62%), arthritis in 39 (87%), folliculitis in 31 (67%), and erythema nodosum in 26 (58%).

Table 1. Clinical characteristics of patients.

Characteristic	Data
No. of patients	45 (90 eyes)
No. of involved eyes	79 (88%)
Female/male	17/28
Followup, yrs (range)	6.67 (0.3–22.3)
Mean age at disease onset, yrs (range)	22 (3–46)
Mean age at initial ocular involvement, yrs (range)	28 (12.5–50)
HLA-B51-positive, n (%)	29 (64.4)

Table 2. Ethnic origin of 45 patients.

Country of Origin	N (%)
Turkey	27 (60)
Germany	5 (11)
Lebanon	4 (9)
Italy	2 (4)
Cuba	1 (2)
Greece	1 (2)
Iran	1 (2)
Kosovo	1 (2)
Morocco	1 (2)
Serbia	1 (2)
Africa	1 (2)

Patients' followup included a complete eye examination comprising the best-corrected visual acuity tested on a Snellen chart, slit-lamp examination, and binocular indirect ophthalmoscopy. Seventy-nine eyes (88%) of the 45 patients developed ocular involvement during the course of the disease. The complete eye examination detected iritis (n = 11, 14% of the affected eyes), hypopyon (n = 6, 8%), panuveitis (n = 53, 91%), occlusive retinal vasculitis (n = 29, 37%), retinitis (n = 17, 19%), optic nerve neuropathy (n = 10, 13%), and chorioretinal infiltrates (n = 1, 1%) (Table 3).

All patients received subcutaneous IFN-α-2a (6–9 Mio IU 3 times/wk) as longterm therapy.

IFN-α-2a is a commercial human recombinant IFN-α with highly purified protein containing 165 amino acids and a molecular weight of 19,000 Da.

Treatment was initiated on relapse of ocular disease. Additionally administered corticosteroids (oral prednisolone 100 mg/day) were tapered to a maintenance dose of 10 mg/day within 2 weeks. Dose of IFN-α-2a was lowered to 6 and subsequently to 3 Mio IU 3 times/week after a 4-month period, without ocular inflammation (Table 4). Corticosteroids were discontinued after a 6-month inflammation-free period. The mean duration of IFN-α treatment was 30 months (range 1.1–101 mo).

RESULTS

The IFN-α-2a/prednisolone treatment was effective against vasculitis, optic nerve neuropathy, and iritis. IFN-α treatment led to a response within 2 weeks after initiation. Sixty-two eyes (78% of the affected eyes) showed no recurrence under the therapy. Twenty-six eyes (32% of the affected eyes) had recurrences during followup. One female patient discontinued the treatment on her own decision (Figure 1), and another because of pregnancy. Six patients (13%) were considered to be nonresponders. They had several recurrence episodes under IFN-α treatment, and 2 also had recurrences under cyclosporin A, chlorambucil, and the tumor necrosis factor-α (TNF-α) antagonist etanercept. We were able to discontinue IFN-α in 9 patients (20%) who had achieved complete remission after a mean treatment period of 33 months (range 8–67 mo). These patients remained recurrence-free for 37 months (range 2–113 mo) with no additional medication. However, IFN-α had to be reinitiated in 9 patients because of recurrences. Therapy was changed to cyclosporine in 3 patients because of side effects and in

Table 3. Clinical signs at initiation of treatment.

Clinical sign	N (%)
Oral aphthous ulcers	44 (98)
Genital ulcerations	28 (62)
Arthritis	39 (87)
Folliculitis	31 (67)
Erythema nodosum	26 (58)
Iritis	11 (14)
Hypopyon	6 (8)
Panuveitis	53 (91)
Occlusive retinal vasculitis	29 (37)
Retinitis	17 (19)
Optic nerve neuropathy	10 (13)
Chorioretinal infiltrates	1 (1)

Table 4. Steroid dosages (mg/day) and interferon (IFN) dosages (Mio IU/week).

	Steroid Dose					IFN Dose				
	Beginning	After 3 mo	After 6 mo	After 12 mo	After 24 mo	Beginning	After 3 mo	After 6 mo	After 12 mo	After 24 mo
Median (SD)	80 (78.420)	20 (20.047)	5.00 (19.042)	0.00 (21.519)	0.00 (8.694)	27.00 (8.115)	27.00 (8.437)	27.00 (7.634)	18.00 (9.802)	9.00 (9.196)

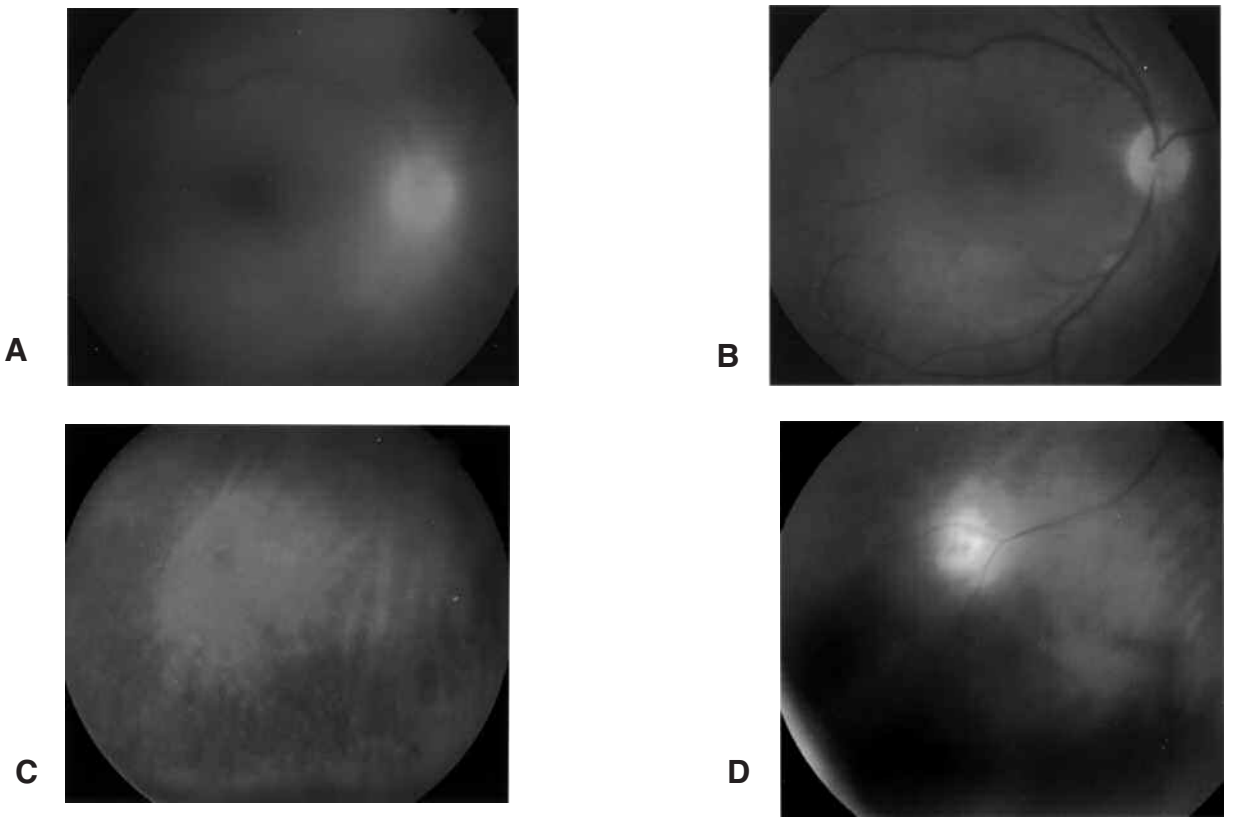

Figure 1. Observations in a female patient. A. Acute vasculitis with vitreous infiltration prior to IFN-α treatment. B. Intraocular findings after one week of IFN-α treatment. C. One week after discontinuation of IFN-α treatment on the patient's decision. There is recurrence with chorioretinal infiltration in the lower periphery. D. Chorioretinal infiltration in the other eye.

one patient because of central nervous system involvement. The additional prednisolone therapy was discontinued in 33 (73%) patients. Two patients (4%) are still taking additional prednisolone.

Visual acuity remained stable (± 2 lines) in 48 eyes (61% of affected eyes) and improved by > 2 lines in 24 eyes (30% of affected eyes). It decreased by > 2 lines in 7 eyes (9% of affected eyes) due to the development of cataract, retinal scars, maculopathy, or neuropathy. Nineteen percent of eyes had a final visual acuity < 0.1. Altogether, 91% of all affected eyes achieved stable or improved vision (Figure 2). All except one patient with deteriorated vision were nonresponders to IFN-α treatment. Three eyes developed optic neuropathy. Clinical findings and visual results of each patient are summarized in Table 5.

Response of extraocular manifestations. At the initiation of treatment oral aphthous ulcers occurred in 44 (98%) patients, genital ulcerations in 28 (62%), arthritis in 39 (87%), folliculitis in 31 (67%), and erythema nodosum in 26 (58%). During the treatment, therapy did not have to be changed in any patient because of missing response of extraocular manifestations. All patients except one with additional arthritis had a remission of their symptoms under IFN-α. These findings were different in mucocutaneous manifestations. Remission was found in genital ulcerations in 86%, but only in 73% of cases with oral ulcers.

Side effects. Flu-like symptoms were recorded in 43 patients. Further side effects were dose-dependent reversible thrombocytopenia (n = 1), psychosis (n = 3), depression (n = 13), thyroiditis (n = 1), and reversible diffuse alopecia (n = 7). The flu-like symptoms were well tolerated under additional treatment with nonsteroidal antiphlogistics.

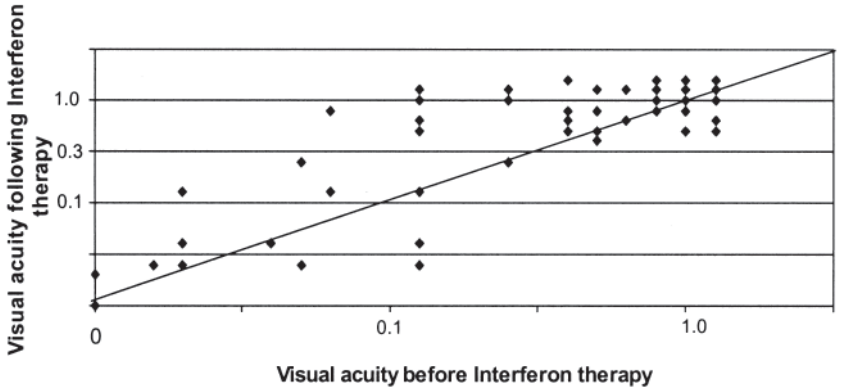

Figure 2. Visual acuity before and after IFN-α therapy.

DISCUSSION

Eye involvement is a serious manifestation of ABD, with a prevalence of up to 70% and bilateral involvement in up to 90% of patients. Recurrent intraocular inflammation often leads to irreversible retinal vascular changes, vitreous hemorrhage, secondary cataract, glaucoma, and optic nerve atrophy with reduced vision. Blindness occurs in 20%–50% of affected eyes[2,3,8,15].

Cyclosporin A combined with corticosteroids is the current treatment of choice for ocular ABD. Both drugs may cause severe side effects during longterm therapy. Cyclosporin A is associated with dose-dependent nephrotoxic effects, while corticosteroids can lead to adrenal suppression, Cushing's syndrome, osteoporosis, severe skin atrophy, and vascular rigidity[3,5]. Other drugs such as azathioprine, cyclophosphamide, or chlorambucil are also used but do not act rapidly enough (azathioprine) or have not been adequately studied. Colchicine is effective for mucocutaneous manifestations and arthritis, but less effective for posterior uveitis[5-7].

Interferons have immunoregulatory, antiproliferative, antineoplastic, and antiviral effects. Natural killer cell activity was found to be significantly lower in patients with active ABD than in those with inactive disease or in normal controls. IFN-α was shown to restore natural killer cell activity in ABD and to suppress enhanced interleukin 8 synthesis and secretion by microvascular endothelial cells challenged with patients' serum[16,17]. IFN-α therapy has been used to treat mucocutaneous ABD for over 10 years, although patients with ocular involvement were initially excluded[13]. High response rates were reported in previous case series and noncontrolled studies. Recent reports suggest that IFN-α is also effective in ocular ABD, and our data confirm its impressive effect[9-13].

In 2004, Deuter, *et al*[18] published the results of a 5-year followup (Table 6). A visual acuity < 0.1 was seen in 40% of all eyes at initiation of treatment, and in only 13.3% after mean treatment duration of 40.6 months. During a 5-year followup, visual acuity remained stable in 33% (n = 5) of the eyes and improved in 66.6% (n = 10).

In a series published by Kötter, *et al*[10], only 12% of the patients had recurrences under therapy, and visual acuity showed a mean 2-line improvement after a treatment duration of 24 months. Visual acuity remained stable in 22% of the eyes, improved in 75%, and deteriorated in 2.7%. In that study, 3 eyes had amaurosis at the beginning, and 7 eyes (7%) still had a visual acuity of 0.1.

In a study from Turkey by Tugal-Tutkun, *et al*[19], more than 90% of the treated eyes showed improved visual acuity. Additional steroid therapy could be stopped in 46%.

Bodaghi, *et al*[20] reported that 76.3% in a series of 23 patients receiving IFN-α for ocular ABD had stable or improved visual acuity. The mean steroid dose could be tapered from 20.8 mg/day to 9.7 mg/day. In our experience corticosteroids were tapered slowly in contrast to other studies[10,18]. In 52.6% of the patients, IFN-α could be discontinued; 40% of these patients developed recurrences. Their encouraging results with IFN in ABD led them to also use this treatment modality in other chronic uveitis cases, but with less effectiveness.

In our series, 92% of all eyes showed stable or improved visual acuity in the longterm followup. A visual acuity < 0.1 was found in 28% at the beginning, but in only 19.7% at the end of therapy. Visual acuity remained stable in 61%, improved in 30%, and deteriorated by more than 2 lines in only 9% of all eyes. Table 4 compares our results to those of other studies. An improvement of visual acuity was achieved by us in one-third of the affected eyes, by Deuter, *et al*[18] in 66%, and by Tugal-Tutkun *et al*[19] in 95%. This may be partly due to the fact that we start treatment early, and we found an initial visual acuity < 0.1 in only 28% of cases, in contrast to the 40% reported by Deuter, *et al*[18]. Most of our patients had stable visual acuity in the longterm followup.

In contrast to reports on the natural disease course or other treatment regimens that show a poor longterm visual prognosis and a loss of useful vision (i.e., visual acuity <

Table 5. Clinical findings and visual results.

Patient	F	Eye	Eye Manifestation	Y/B	Sex	Origin	FH	HLA	FS	SS	A1	A2	A3	A4	VA1	VA2	VA3	IFN	R
1	6.7	R	Irit, Vas	1979	M	Tur		Y	A	oI	19.1	23.9	24.1	22.1	HM	0.03	+	31.9	0
	6.7	L	Irit, Vas												0.8	1.0	+/–		0
2	6.4	R	Irit,Vas, Papil	1971	M	Tur	B	Y	oU	A	24.9	30.4	31.9	30.4	0.5	1.0	+	43.3	0
	6.4	L	Vas, Papil				B								0.8	1.0	+/–		0
3	4.1	R	Vas	1971	M	Tur	S	Y	oI	oU	25.5	35.1	32.5	25.5	0.3	0.6	+	8.7	1
	4.1	L	Vas				S								0.05	0.6	+		1
4	3.2	R	Irit, Vas	1957	F	Tur		Y	oU	oI	6.86	42.9	49.6	42.9	0.5	0.5	+/–	38.9	1
	3.2	L	Irit, Vas												0.8	0.6	+/–		2
5	7.1	R	Irit, Vas, Hypop	1968	F	Tur		Y	oU	oI	27.2	29.2	34.9	29.2	0.3	0.5	+/–	64.6	2
	7.1	L	Irit, Vas												0.6	0.6	+/–		1
6	8.9	R		1969	F	Tur		N	oU	gU	21.3	27.3	31.3	—	0.8	0.8	+/–	42.8	0
	8.9	L	Vas											27.3	0.1	0.8	+		0
7	3.9	R	Vas	1977	M	Leb		Y	oU	oI	26.3	26.8	29.3	29.4	0.8	1.0	+/–	49.2	0
	3.9	L	Irit, Vas											26.3	HM	CF	+/–		0
8	3.8	R	Irit, Vas	1969	M	Ger		N	oU	gU	17.1	36.5	36.5	36.5	0.5	1.0	+	27.2	0
	3.8	L	Vas											36.7	1.0	1.0	+/–		0
9	2.8	R	Irit, Vas	1969	M	Ital		Y	oU	oI	24.8	35.8	36.8	36.8	0.1	0.8	+	25.0	0
	2.8	L	Irit, Vas											35.8	LP	CF	+/–		0
10	3.9	R	Irit, Vas	1974	M	Cuba		Y	oU	gU	5.63	27.6	25.6	31.2	1.0	1.0	+/–	50.5	0
	3.9	L	Irit, Vas											31.2	0.6	1.0	+/–		0
11	5.1	R	Irit, Vas	1960	M	Ger		N	oU	A	3.15	37.1	37.1	37.1	0.04	0.2	+	30.9	5
	5.1	L	Irit											37.1	0.5	1.0	+		0
12	2.5	R	Irit, Vas	1965	M	Kos		Y	oU	A	37.1	42.3	42.4	42.3	HM	0.1	+	8.2	0
	2.5	L												—	1.0	0.8	+/–		0
13	7.1	R	Vas, Ret	1976	M	Tur	S	Y	gU	oU	17.7	26.2	22.7	26.2	1.0	0.5	–	32.6	5
	7.1	L	Vas, Ret				S							29.7	1.0	0.8	+/–		3
14	1.2	R	Vas	1985	M	Tur		Y	oU	oI	9.8	23.9	23.9	22.8	0.8	1.0	+/–	10.0	0
	1.2	L	Vas											24.4	0.8	1.0	+/–		2
15	5.8	R	Vas, Irit	1982	F	Tur	B	N	oU	oI	18.9	19.9	19.9	19.9	0.1	0.1	+/–	64.1	0
	5.8	L	Vas				B							19.9	0.1	CF	–		0
16	6.5	R	Irit, Vas	1971	F	Tur		N	oI	oU	32	32.2	32.3	32	0.2	0.8	+	21.4	3
	6.5	L	Irit, Vas											32	0.1	1.0	+		3
17	2.3	R	Irit, Vas, Ret	1965	M	Tur		Y	oU	gU	31.9	32.9	32.9	32.9	0.04	CF	–	32.7	1
	2.3	L	Irit, Vas, Ret											32.9	0	0	+/–		1
18	4.9	R	Vas, Ret	1970	M	Tur		N	oU	oI	22.4	23.4	33.9	23.4	0.6	1.0	+/–	66.5	1
	4.9	L	Vas, Ret											23.4	0.4	1.0	+		0
19	0.3	R	Vas	1974	M	Tur			A	gu	28.4	30.4	33.7	29.4	1.0	1.0	+/–	3.4	0
	0.3	L	Vas											29.4	1.0	1.0	+/–		0
20	6.3	R		1964	F	Tur	O	N	oU	oI	38.4	39.4	39.4		0.8	1.0	+/–	12.9	0
	6.3	L	Irit, Vas, Papil, Hypop				O							39.4	0.2	0.8	+		0
21	8.0	R	Irit, Vas, Papil	1974	M	Ger		Y	A	oU	23.6	25	25	25	0.3	1.0	+	32.8	0
	8.0	L													1.0	1.0	+/–		0
22	4.7	R	Irit, Vas, Ret	1976	F	Iran		Y	A	oI	16	27.6	29.1	27.6	LP	0.02	+	61.5	4
	4.7	L	Irit, Vas											27.6	0.6	0.6	+/–		2
23	4.8	R		1973	F	Tur		Y	oU	oI	2.76	31	31.5		1.0	1.0	+/–	62.9	0
	4.8	L	Vas, Ret											31	0.2	1.0	+		0
24	10.3	R	Papil	1953	M	Tur		Y	A	oU	45.6	46.3	46.3	46.2	0.6	0.8	+/–	39.3	0
	10.3	L													1.0	0.8	+/–		0
26	9.1	R	Irit, Vas	1969	M	Ger		N	EN	ep	30.7	31.2	31.2	31.2	1.0	1.0	+/–	31.6	0
	9.1	L													1.0	1.0	+/–		0
27	4.1	R	Irit, Vas, Hypop	1972	F	Mali		N	oU	EN	17.3	29.3	33.2	29.3	0.5	0.5	+/–	1.6	0
	4.1	L	Irit, Vas, Hypop											29.3	0.1	0.1	+/–		0
28	2.1	R	Vas	1973	M	Ital		Y	oU	oI	13.7	30.1	30.1	30.1	0.4	0.6	+/–	23.5	0
	2.1	L	Vas											30.1	0.3	0.4	+/–		0
29	6.6	R	Irit, Vas	1970	M	Leb		Y	oU	EN	29.1	29.6	29.6	33.1	0.8	0.6	+/–	83.8	0
	6.6	L	Irit											29.6	0.8	1.0	+/–		0
30	8.6	R	Vas, Ret	1972	M	Leb		N	oI	oU	28.6	30	31.6	28.6	0.1	0.03	–	3.9	3
	8.6	L	Vas, Ret												1.0	0.5	–		2

Table 5. Continued.

Patient	F	Eye	Eye Manifestation	Y/B	Sex	Origin	FH	HLA	FS	SS	A1	A2	A3	A4	VA1	VA2	VA3	IFN	R
31	2.0	R	Irit, Vas, Ret	1980	M	Ger		N	CNS	oU	25.9	27.8	27.8	27.8	0.8	0.6	+/–	8.0	1
	2.0	L	Irit, Vas, Ret												0.4	0.3	+/–		5
36	7.3	R	Papil	1975	M	Mor		Y	oU	A	26.4	26.5	26.5	26.5	1.0	1.0	+/–	11.4	0
	7.3	L	Papil												1.0	1.0	+/–		0
39	19.1	R	Vas	1957	F	Tur		N	A	oU	28.9	34	33.3	33.3	0.8	0.8	+/–	1.1	0
	19.1	L												—	0.8	0.8	+/–		0
42	14.8	R	Vas	1954	F	Tur		Y	oI	oU	12.5	40.6	40.6	12.5	1.0	0.8	+/–	49.0	0
	14.8	L	Vas												1.0	0.8	+/–		0
49	21.7	R	Irit, Vas, Hypop	1955	F	Serb		N	oU	oI	28.4	33.1	33.6	33.1	0.2	0.2	+/–	1.7	1
	21.7	L	Irit, Vas, Hypop												0	0	+/–		1
52	3.6	R	Irit, Vas, Papil, Ret	1976	F	Tur		Y	oU	EN	16	28	23	24	0.2	0.8	+	3.2	1
	3.6	L	Irit, Vas, Ret												1.0	0.4	–		1
57	4.7	R	Irit	1972	F	Tur		Y	oU	EN	26.6	33.1	33.2	30.6	1.0	1.0	+/–	22.0	0
	4.7	L	Irit												1.0	1.0	+/–		0
59	4.5	R		1973	M	Tur		N	oU	EN	24.2	26.1	27.8	—	1.0	1.0	+/–	32.5	0
	4.5	L	Irit, Vas											26.1	0.8	1.0	+/–		0
65	3.3	R	Irit, Ret	1986	M	Tur		Y	oU	gU	20.2	20.4	20.4	20.4	0.5	1.0	+	33.9	1
	3.3	L	Irit, Ret												0.1	1.0	+		0
70	7.9	R	Irit, Vas, Papil	1985	F	Ger		N	oI	CNS	12.8	15.3	15.3	12.8	1.0	1.0	+/–	1.9	0
	7.9	L	Irit, Vas, Papil												0.5	0.5	+/–		0
86	22.3	R	Irit, Vas, Retin	1963	M	Tur		Y	oI	oU	23.1	23.1	23.1	23.1	6	6	+/–	—	0
	22.3	L	Vas, Ret												0	0	+/–	—	0
92	17.2	R	Vas	1965	M	Tur		Y	oU	oI	25.2	27.2	27.2	26.2	0.4	0.4	+/–	1.4	0
	17.2	L	Vas												8	0.1	+		0
104	16.7	R	Irit, Vas, Hypop	1973	F	Tur		Y	oU	oI	18.3	19.2	19.2	19.2	0.8	0.4	–	101	0
	16.7	L	Irit, Vas, Hypop												0	0	+/–		0
130	6.1	R	Vas	1967	M	Leb		Y	oI	EN	29.3	34.3	35.9	29.3	0.1	0.5	+	27.4	0
	6.1	L	Vas												1.0	0.8	+/–		0
134	1.8	R	Vas	1975	M	Tur		Y	oI	oU	27.9	32.6	32.6	27.9	0.3	0.6	+	19.5	0
	1.8	L												—	1.0	1.0	+/–		0
139	1.4	R	Irit, Vas, Hypop	1963	F	Tur		Y	gU	oU	14.8	41.8	44.9	41.8	0.1	0.4	+	9.4	0
	1.4	L												—	0.8	0.8	+/–		0

Headings: F: Followup, yrs, Y/B: Year of birth, FH: Family history, HLA: HLA-B51+, FS: First Symptom, SS: Second symptom, A1: Age at first manifestation, yrs, A2: Age at full disease, yrs, A3: Age at diagnosis, yrs, A4: Age at Ocular involvement, yrs, VA1: VA pre-IFN (lines), VA2: VA post-IFN (lines), VA3: VA/IFN (> 2 lines), IFN: IFN therapy, mo, R: Recurrences. Key: Tur: Turkey, Leb: Lebanon, Ger: Germany, Ital: Italy, Kos: Kosovo, Mor: Morocco, Serb: Serbia. B: brother, S: sister, U: uncle, A: arthritis, oU: oral ulcers, gU: genital ulcers, EN: erythema nodosum, CNS: central nervous system, HM: hand movements, Orc: orchitis, oI: ocular involvement, ep: epididymitis, NT: not tested, Irit: iritis, Vas: vascular involvement, Papil: papillitis, Hypop: hypopyon. VA pre/post IFN: visual acuity before/after interferon therapy; VA/IFN: changes of visual acuity > 2 lines.

0.1) in most eyes, our results demonstrate the remarkable effectiveness of IFN in treating ocular ABD. A visual acuity < 0.1 was reported for 24% (n = 4) of patients in a study from Spain by Torres, *et al*[21], for about 41% (n = 647) of the eyes in a study from Turkey by Tugal-Tutkun, *et al*[22], for about 53% (n = 104) in a study from Taiwan by Chung, *et al*[23],and for 21%–49% (n = 128) of the patients in a study from Japan by Yoshida, *et al*[24]. In a longterm followup of 15 eyes, Deuter, *et al* found that about 13.3% of their patients had a final vision < 0.1 under IFN-α therapy[18]. In our series, only 9% of the affected eyes had deteriorated visual acuity, whereas 19% had a final visual acuity < 0.1. Thus 81% of all affected eyes had useful vision (visual acuity > 0.1) at the end of followup. In contrast to all other immunosuppressives used to treat ocular ABD, IFN-α has side effects that are tolerable and reversible. All side effects we observed in the followup period except thyroidism were dose-dependent and reversible. In particular, development of autoimmune phenomena had to be observed carefully during treatment with IFN-α. In published case series or studies of IFN-α and ABD these complications were rare, and the development in our series was similar to that described in the literature[9,10,13,19,20,25]. Psoriasis, for example, another possible complication under this treatment described in other series did not occur in this study[10]. Special care had to be taken in case of patients with depression and psychosis. These patients should not be treated with IFN because of the risk of suicide.

Compared to another group of "new" treatment modalities, the anti-TNF monoclonal antibodies infliximab and adalimumab and the soluble TNF receptor etanercept, the side effects of IFN seem to be tolerable. Side effects such as

Table 6. Studies on interferon treatment in ocular Adamantiades-Behçet's disease.

Feature	Kötter[10]	Deuter[18]	Yugal-Tutkun[19]	Alpsoy[25]	Bodaghi[20]	Current Study
No. of eyes	94	15	88	11	38	79
Mean treatment duration of, mo	6	41	12	3	30	30
Improved visual acuity, %	75	66	95	45	76.3	30
Stable visual acuity, %	22	33			76.3	61
Deteriorated visual acuity, %	2.7					9
Initial visual acuity ≤ 0.1, %	NG	40				28
Final visual acuity ≤ 0.1, %	NG	13.3				19.7
Stopping prednisolone, %			46			79
Flu-like symptoms, %	100		100	78		98
Alopecia, %	24		2	4		18
Depression, %	8		0		5	31
Psychosis, %						6
Thyroiditis, %	6				2.5	2
Allergy, %						2
Leukopenia, %	40		14	4	28.9	2
Fever, %						24
Emesis, %				4		11

NG: not given.

induction of infections or secondary malignancy are rare. Most patients with ABD treated with anti-TNF described in the literature were treated with infliximab in case of ocular involvement. It could be shown that infliximab is an effective and fast-acting medication in the treatment of ocular ABD, but as stated in the published recommendations it should be used in selected patients balancing the efficacy and the possible side effects[26-28]. The main advantage of IFN compared to all other drugs is the possibility of discontinuation of treatment. Another important fact is that in nearly all cases the steroid treatment and potential side effects, such as Cushing syndrome or osteoporosis, could be reduced or stopped. This was also shown in the study by Kötter, *et al* and in the study of Deuter, *et al*[10,18].

Remarkably, not all patients responded to IFN-α therapy. Some nonresponders are also resistant to other immunomodulatory or immunosuppressive agents, an observation for which no explanation has been offered.

IFN-α was markedly effective for ocular ABD, and should thus be regarded as a treatment option for this ABD manifestation.

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