

The Risk Factors and Causes for Blindness in Behcet's Disease

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Abstract

Purpose: To investigate the risk factors and causes for blindness in Behcet's disease (BD).

Methods: In this preliminary retrospective case series we have investigated 27 BD patients (54 eyes), legally blind (vision 0.1 or less) at least in one eye at the last visit (2006), and compared them with 54 eyes of 27 non-blind patients (control group), matched individually and consequently in terms of duration of BD follow-up and treatment.

Results: Eighteen (66.6%) of our blind patients were male versus thirteen (48%) of the control group ($p=0.167$). Low vision (0.1 or less) at the first consultation, 23 eyes (42.6%) in the blind group versus three eyes (5.6%) in the control group ($p=0.001$), higher number of uveitis in the main group 51 eyes (94.4%) versus 35 eyes (64.8%) in the control group ($p=0.007$), Longer duration of uveitis (10.3 ± 4.8 vs. 5.1 ± 3.97 years, $p<0.001$), longer duration of retinal vacuities (10.9 ± 5.1 vs. 5.6 ± 3.7 years, $p<0.001$) in the blind group under investigation were the four major risk factors in the poor outcome of ocular disease, $P\leq 0.000$ in all cases. At the last visit 42 eyes (77.8%) of the main group were legally blind. The main cause of blindness was chorioretinal vasculitis in 32 eyes (20 patients), and its consequences: optic atrophy, macular scar, chorioretinal atrophy and vascular necrosis. In ten remaining blind eyes the causes for impaired vision were: 3 retinal detachments, 3 optic atrophies \pm macular scars, 1 macular scar, 1 macular and disc edema, 1 phthisis bulbi, 1 disc neovascularization and vitreous hemorrhage.

Conclusion: Higher frequency of uveitis and longer duration of uveitis and retinal vasculitis, and also the initial low vision at the presentation were the main blinding risk factors and the main cause of blindness was retinal vasculitis and its consequences.

Keywords: Behcet's disease, ocular Behcet, blindness, uveitis, retinal vasculitis, optic atrophy, retinal detachment

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Introduction

Behcet's disease is a chronic inflammatory disease with remissions and exacerbations. It is a vasculitis causing obliteration, and fibrinoid necrosis of the veins and arteries of nearly all organs, including the eyes.¹ The disease is particularly propagated at Far East, Middle East and the Mediterranean region. The prevalence of the disease is reported to be 68, 13.2, and 80 to 370 per hundred thousand inhabitants in Iran,² Japan³ and Turkey,^{4,5} respectively.

The etiopathogenesis of the disease is uncertain. The diagnosis is achieved by the clinical findings, the major criteria of the disease: oral aphthosis, genital ulceration, skin lesions, and ocular manifestations (uveitis, chorioretinal vasculitis) and along with the minor criteria of the disease: articular, digestive, neurologic, vascular, etc. The complementary examinations such as HLA-B51 typing and skin pathergy test may be helpful but not pathognomonic for the disease, and in fact, there are no specific paraclinical tests for the diagnosis of the disease.

The rate of the ocular involvement is variable in different countries. It is reported to be 55.9% in Iran,⁶ 69% in Japan⁷ and 47% in Turkey.⁸ Despite modern treatments, the disease still carries a poor visual prognosis with about one quarter of the patients going blind, after years of therapy.⁹

In this preliminary study of 27 legally blind patients at least in one eye, and 27 nonblind cases we have tempted to find out the blinding risk factors, and the causes of blindness in BD.

Methods

In this preliminary, retrospective, comparative case series study of 27 consecutive patients, legally blind (visual acuity=0.1 or less) at least in one eye, and 27 consecutive nonblind BD patients, matched one by one in terms of duration of BD, follow-up and treatment. The patients who had consulted our multidisciplinary Behcet's clinic of Shariati Hospital of Tehran University of Medical Sciences, in July and August 2006 were enrolled in this investigation. They had a complete ocular and general examination. Their medical records were reviewed to extract the required information. The patients

were the customary cases of the clinic, being visited at least twice yearly.

The visual acuity was taken by Snellen chart. The eyes were examined by Haag-Streit biomicroscopy, and 3 mirrors of Goldmann. If necessary, the ocular ultrasonography, fluorescein angiography and optical coherence tomography were performed at Farabi Eye Hospital of Tehran.

The diagnosis of BD was made by the classification tree of BD¹⁰ and confirmed by the international Classification of BD.¹¹

The patients had been treated by corticosteroid ± immunosuppressors.

The mean age of the patients was calculated at the first visit to our clinic. The duration of BD was considered from the appearance of the first symptoms to 2006. With respect to our baseline characteristics, we applied student t test or Mann-Whitney U test for quantitative variables and Chi-square test or Fisher's exact test for categorical variable, $p \leq 0.05$ was considered statistically significant.

Results

Twenty seven patients (54 eyes), 18 men and 9 women in our consecutively selected blind cases, and 27 patients (54 eyes), 13 men and 14 women in our control group were enrolled. 66.6% (n=18) of our blind cases were male versus 48% (n=13) of our control group, $X^2=1.89$, $p=0.167$.

The mean age of our main group was 35.5 ± 8.4 years (range 22-54) versus 32.5 ± 7.8 years (range 21-47) of our control group, $p=0.180$.

At presentation the mean duration of the disease (delayed diagnosis) in our blind cases was 3.9 ± 3.9 years versus 6.3 ± 5.5 years in our control group, $p=0.070$, and already 23 eyes (42.6%) of our main group under investigation had impaired vision (0.1 or less) versus 3 eyes (5.6%) in our control group, $p < 0.001$.

At the last visit (2006), the mean duration of BD in blind group was 15.4 ± 6.8 years and the mean-duration of follow-up and treatment was 11.5 ± 5.6 years, matched with our control group.

In our investigation, uveitis was documented in 51 eyes (94.4%) of our selected blind cases and 35 eyes (64.8%) of nonblind patients, $p=0.007$. The duration of

uveitis in the two groups was 10.3 ± 4.8 years and 5.1 ± 3.97 years, respectively, $p < 0.001$. Uveitis appeared periodically with remissions and exacerbations. Retinal vasculitis was present in 42 eyes (77.8%) of the blind cases versus 46 eyes (85.2 %) of our control group. The duration of vasculitis was 10.9 ± 5.1 years in our blind group, and 5.6 ± 3.7 years in the control group $t=5.9$, $p < 0.001$.

At the last visit, 32 eyes in our main group presented active or sequellar retinal vasculitis, 17 eyes had none, and 5 eyes were not explorable, and only 8 eyes in our control group presented vasculitis. One eye in our main group had active uveitis and none was registered in the control group.

At the last visit, 42 eyes (77.8%) in our main group were legally blind, the main cause was chorioretinal vasculitis and its consequences: optic atrophy, macular scar, chorioretinal atrophy which was observed in 32 eyes (76.2%) (Photo I), and in ten eyes (23.8%) the causes of blindness were: in 3 eyes (5.6%) retinal detachment, 3 eyes (5.6%) optic atrophy \pm macular scar, 1 eye macular scar + macular edema, 1 eye macular and disc edema, 1 eye phthisis bulbi, and 1 disc neovascularization and vitreous hemorrhage.

Discussion

Despite all the intensive treatments, in many cases of BD the ocular outcome is unfavorable. In an international survey in 25 eye centers and analysis of 1465 ocular BD patients, 23% of the cases had visual acuity equal to or worse than 0.1 at the final visit.⁹ In a report from China¹² on 437 patients, 20.4% of the eyes became legally blind despite aggressive treatments and it was estimated that the risks of loss of useful vision to be 6.4%, 10.7%, 24.5%, and 62.2% at 1, 3, 5, and 10 years respectively.

The ocular BD can be sight-threatening by its undesirable evolution and its consequences^{13,14} the chorioretinal vascular necrosis, optic atrophy, macular scar, macular edema, cataract, and glaucoma have been claimed to be the main causes of this event.

For some authors,^{12,15-17} the severe and blinding BD is more frequent in the male

population. In our investigation the predominance of male in the severe cases of BD was demonstrated but it was statistically nonsignificant, $p=0.167$. Tugal-Tutkun et al¹⁵ in their study of 880 BD patients with uveitis reported that the risk of visual loss was more prominent in the male population, after 5 years (21% vs. 17%). In Tunisia also¹⁶ the ocular disease has been reported to be more frequent and severe in men (37.5% vs. 17.9%). In the report of Bang et al¹⁷ risk of losing useful sight at 5 and 10 years for males and females was 29% versus 6% and 65% versus 33%, respectively.

In our investigation high frequency of uveitis, longer duration of uveitis and longer duration of retinal vasculitis were three major risk factors in the blinding outcome of the disease, $p < 0.001$, in all cases. The existence of low vision at presentation was also found to predict the poor outcome of the ocular disease, $p < 0.001$.

The main cause of blindness in our patients was chorioretinal vasculitis and consequently, chorioretinal vascular necrosis, optic atrophy, macular scar and chorioretinal atrophy. The other causes of blindness were retinal detachment, neurogenic optic atrophy, macular edema and scar, phthisis bulbi and vitreous hemorrhage.

In our investigation there has been sources of bias that may distort the results. Although the patients have been enrolled consecutively, and the investigation could be designed on a randomized basis, but this has been a pilot study for a larger investigation. On the other hand, most patients were unaware of the duration of their ocular disease, declaring it as a recent phenomena, while retinal vasculitis was well advanced at the presentation.

Conclusion

This study showed that higher frequency and longer duration of uveitis and retinal vasculitis, and also the initial low vision at the presentation were the main risk factors for blinding and the main cause for blindness was retinal vasculitis and its consequences.

Table 1: Characteristic of 27 patients (54 eyes) of BD cases legally blind at least in one eye.

Num	Age	sex	Duration of dis.	Duration of F/U	Duration of Tx	Duration of Ret. Vasculitis		Duration of uveitis		first vision		last vision		Causes of blindness	
						Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt
1	35	F	11.5	10	10	10ys	10ys	4ys	4ys	3m	3m	1m	3m	V	V
2	25	F	19	16	9	16ys	10ys	11ys	11ys	1.0	1.0	0.1	2m	V	V
3	40	F	22	7	7	7ys	7ys	7ys	7ys	0.5 m	LP	NLP	HM	V	V
4	31	F	6	6	6	6ys	6ys	6ys	6ys	2m	1m	3m	NLP	V	V
5	53	F	18	5	5	None	none	5ys	5ys	LP	0.6	LP	0.9	RD	None
6	33	F	23	20	19	20ys	20ys	20ys	20ys	LP	5m	NLP	3m	V	V
7	54	F	20	20	15	12ys	12ys	10ys	10ys	0.1	0.1	6m	NLP	V	V
8	46	F	24	16	16	16ys	16ys	16ys	10ys	0.5 m	3m	HM	0.2	V	None
9	27	F	18	14	14	None	none	14ys	14ys	HM	50cm	0.3	LP	None	OA
10	36	M	7	5	5	None	none	5ys	5ys	0.8	1.0	LP	1.0	RD	None
11	32	M	30	20	7	18ys	18ys	20ys	20ys	0.8	0.6	LP	LP	V	V
12	31	M	18	17	15	18ys	18ys	17ys	17ys	0.4	1m	NLP	1m	V	V
13	37	M	14	8	8	8ys	6ys	8ys	8ys	1.0	1.0	1m	0.5	NVD-Hx	none
14	28	M	7	7	3	2ys	2ys	7ys	7ys	3m	1.0	0.5m	1.0	OA	None
15	24	M	9	4	3	None	none	none	3ys	1.0	1.0	0.7	0.5m	none	OA
16	36	M	11	8	8	6ys	none	8ys	8ys	2m	0.9	NLP	1.0	V	None
17	37	M	11	9	1	9ys	9ys	9ys	9ys	0.3	1.0	NLP	LP	V	V
18	37	M	10	9	8	9ys	Phit	9	Phit	0.2	HM	LP	NLP	V	Phthisis
19	49	M	19	16	7	16ys	0	16ys	10ys	0.2 m	0.6	NLP	0.7	V	None
20	36	M	12	10	10	10ys	10ys	10ys	10ys	1m	0.5	NLP	0.9	V	None
21	26	M	8	7	7	7ys	7ys	7ys	7ys	1.0	1.0	LP	LP	V	V
22	39	M	29	24	18	18ys	18ys	18ys	18ys	0.1	0.2	0.1	0.5m	V	V
23	33	M	5	5	5	5ys	5ys	5ys	5ys	0.2	0.1	LP	NLP	V	RD
24	22	M	11	11	11	6ys	6ys	11ys	11ys	1.0	1.0	0.1	NLP	Mac. Ed + Disc Ed	V
25	35	M	17	9	9	9ys	9ys	9ys	9ys	1.0	1.0	1.0	3m	None	Mac Scar + Edema
26	47	M	17	12	5	12ys	12ys	12ys	12ys	0.3	3m	0.1	2m	V	V
27	31	M	18	15	15	15ys	0ys	15ys	0ys	HM	1.0	NLP	1.0	V	None

OA = Optic atrophy
RD = Retinal detachment
V = Vascular necrosis, optic atrophy

Rt = Right
Lt = Left
Tx = Treatment

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