KJO
pISSN: 1011-8942 eISSN: 2092-9382

Korean J Ophthalmol 2013;27(6):466-469
http://dx.doi.org/10.3341/kjo.2013.27.6.466

Case Report

Frosted Branch Angiitis as Ocular Manifestation of Behçet's Disease: Unusual Case Report and Literature Review

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We report an unusual case of unilateral frosted branch angiitis associated with Behçet's disease, including a review of previously reported cases. A 39-year-old male with history of recurrent oral and genital ulcers presented with visual loss in his left eye. Fundus findings demonstrated occlusive retinal vasculitis resembling acute frosted branch angiitis. Laboratory examinations including viral markers revealed no abnormal findings except positive HLA-B51. The patient was treated with systemic steroid and cyclosporine. Six months after presentation, new oral ulcers and pseudofolliculitis appeared, and he was diagnosed with Behçet's disease following rheumatology consultation. During follow-up, there was no change in visual acuity of hand movement, and disc neovascularization developed even after complete panretinal photocoagulation. Ocular manifestations of Behçet's disease can present as unilateral frosted branch angiitis, and may consecutively involve in both eyes. Early immunosuppressive treatment is recommended.

Key Words: Behçet's disease, Frosted branch angiitis, Occlusive retinal vasculitis

Behçet's disease is a systemic immune-mediated vasculitis of unclear origin [1]. Frosted branch angiitis (FBA), first described in 1976 by Ito et al. [2], is a retinal perivasculitis with severe sheathing of all retinal vessels, resembling the frosted branches of a tree [3]. The disease may be idiopathic in a majority of cases or may be associated with ocular and systemic pathology [4]. FBA in association with Behçet's disease is rare and there are only six reported cases of this uncommon combination [5-10]. In this article, an unusual case of unilateral occlusive retinal vasculitis resembling FBA in association with Behçet's disease is reported. In addition, the authors give a literature review of FBA as an ocular manifestation of Behçet's disease with a summary of previously reported cases.

Received: May 24, 2012 *Accepted*: December 12, 2012

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Case Report

A 39-year-old male presented with decreased vision in his left eye for two days. Visual acuity was 20 / 20 in the right eye and hand movement in the left eye. On slit lamp examination of the left eye, severe inflammation was seen in the anterior chamber (cells +4) and the vitreous (cells +4). Fundus examination of the left eye demonstrated thick, white, confluent sheathing surrounding the retinal veins and arteries from the posterior pole to the periphery with extensive retinal hemorrhages, optic disc swelling, and macular edema (Fig. 1A). The right eye was normal. B-scan ultrasonography and spectral-domain optical coherence tomography of the left eye showed a severely edematous and detached retina in posterior pole (Fig. 1B and 1D). Fluorescein angiography demonstrated a prolonged arteriovenous transit time, blockage of fluorescein corresponding to extensive retinal hemorrhage, widespread area of capillary non-perfusion, and extensive staining of sheathing veessels (Fig. 1G). A diagnosis of occlusive reti-

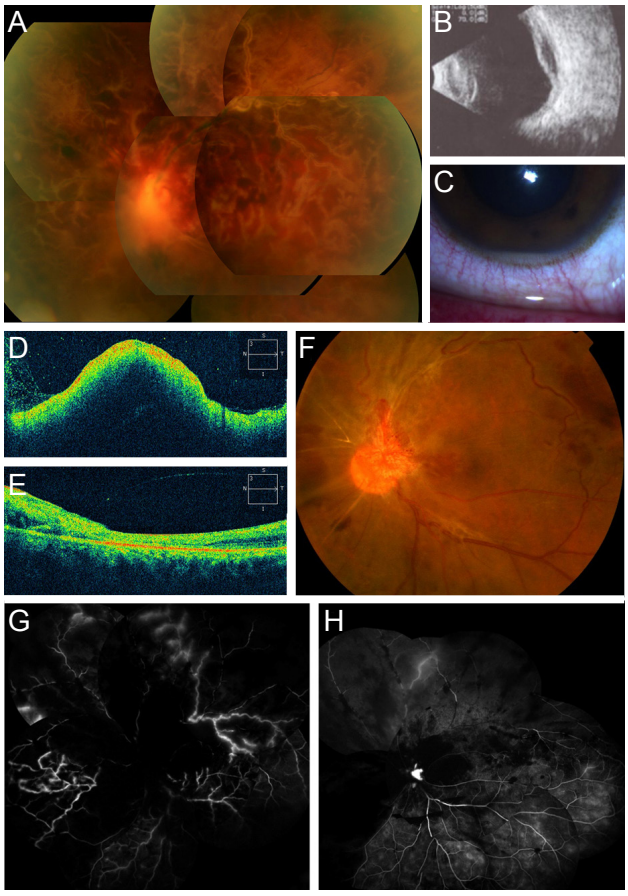

Fig. 1. (A) Initial fundus photograph of the left eye showed thick, white, confluent sheathing surrounding the retinal veins and arteries from the posterior pole to the periphery with extensive retinal hemorrhages, optic disc swelling, and macular edema. (B) Initial B-scan showed diffuse, thickened chorioretinal layer with retinal detachment of the posterior pole. (C) The next day after treatment, hypopyon in the anterior chamber appeared. (D) During the acute phase of inflammation, spectral-domain optical coherence tomography (OCT) showed a severely edematous and detached retina in the macular area. (E) Eight months after treatment, OCT image revealed an atrophied retina and disruption of the photoreceptor segment in the macular area. (F) Four months later, fundus photograph of the left eye showed that perivascular sheathing and macular edema disappeared, but neovascularization of the optic disc developed. (G) Initial angiography of the left eye demonstrated a prolonged arteriovenous transit time of 25 seconds, background blockage due to extensive retinal hemorrhage, widespread areas of capillary non-perfusion, and extensive staining of sheathing vessels. (H) Two months after treatment, angiography demonstrated a widespread non-perfusion area involving three quadrants of the retina, fluorescein blockage by retinal hemorrhage and dye leakage from neovascularization of the optic disc.

nal vasculitis resembling acute FBA was made and systemic evaluation for retinal vasculitis was performed. The patient had a history of recurrent genital and oral ulcers over two years, but no other systemic manifestations of Behçet's disease on presentation. The results of laboratory examinations, including serology for herpes virus, varicella zoster virus, and human immunodeficiency virus were normal or negative. Other examinations, including brain magnetic resonance imaging and polymerase chain reaction assay for varicella zoster virus and cytomegalovirus in the aqueous humor, were negative or normal. Human leukocyte antigen typing resulted in a positive HLA-B51.

The patient was started on intravenous methylprednisolone. Vitreous opacity progressed and angle hypopyon appeared until 24-hour after treatment initiation (Fig. 1C). However, during two weeks after treatment, the vascular sheathing and vitreous opacity gradually disappeared. Systemic steroids were slowly tapered during the next two months and cyclosporine 150 mg/day was added. Two months later, follow-up angiographic findings revealed a widespread area of non-perfusion in three retinal quadrants with neovascularization of the disc (Fig. 1H). Although panretinal photocoagulation for non-perfusion areas was performed, neovascularization progressed by four months (Fig. 1F). However, iris rubeosis and neovascular glaucoma had not developed by 10 months. Six months after his presentation, he developed two ulcers on oral mucosa and pseudofolliculitis on his face, along the hairline. A diagnosis of Behçet's disease was made using the international criteria following a rheumatology consultation. Eight months later, follow-up optical coherence tomography imaging revealed atrophy and disruption of the photoreceptor layer in the macular area (Fig. 1E). The final visual acuity was hand movement in the left eye. He is currently on maintenance cyclosporine therapy.

Discussion

FBA can be idiopathic or associated with various ocular and systemic disorders. In 1997, Kleiner [4] classified the patients who had the appearance of FBA into three subgroups. First are patients with lymphoma or leukemia whose disease is due to infiltration with malignant cells (frosted branch-like appearance). Second is the group of patients who have associated viral infections or autoimmune disease (secondary FBA). Cases associated with Behçet's disease such as this study can be classified into this subgroup. Finally, there is a group of otherwise healthy

young patients who develop acute visual loss (acute idiopathic FBA).

Our case can be classified into acute idiopathic FBA because systemic examination revealed no obvious abnormalities except positive HLA-B51 and ocular findings on presentation. However, the history of recurrent oral and genital ulcers over a period of two years and a positive HLA-B51 suggested the possibility of an underlying Behçet's disease [1,11]. Obliterative retinal vasculitis and hypopyon iritis on presentation also supports ocular manifestations of Behçet's disease [1,11]. Six months after his ocular presentation, he developed oral ulcers and pseudofolliculitis, which led the authors confirm the diagnosis of Behçet's disease with secondary FBA. The patient had severe occlusive vasculitis involving three quadrants of his retina, initial visual acuity was hand movement, and the patient had no visual improvement even with the proper treatment. For these reasons, the authors started early immunosuppressive treatment to prevent involvement of the contralateral eye before confirming the diagnosis of Behçet's disease.

The authors found six cases in PubMed using the search parameters of "frosted branch angiitis, Behçet's disease." Including this study, seven cases are discussed here [5-10]. Table 1 shows the characteristics of patients diagnosed as having secondary FBA associated with Behçet's disease. All cases aside from this study presented with improvement of visual acuity during the follow-up period, and three cases recovered their sight up to 20 / 20 or 10 / 10. Four cases presented with bilateral involvement, and while three cases presented with bilateral involvement initially, the other one was reported to affect both eyes, two years apart [5,8-10]. This case suggests that the subsequent involvement of the other eye could occur and early immunosuppressive treatment should be considered, especially in cases of initially unilateral involvement [9]. Three cases presented with neuro-Behçet's disease and two cases revealed typical hypopyon iritis. All patients had a history of recurrent oral or genital ulceration, and five of six cases had a positive HLA-B51. These findings suggest that both a careful history and a positive HLA-B51 can help make a diagnosis of underlying Behçet's disease.

In summary, this case revealed that FBA can be an ocular manifestation of Behçet's disease, which could initially be unilateral and result in blindness, particularly when combined with severe occlusive retinal vasculitis. This condition may consecutively involve both eyes and result in the deterioration of bilateral visual function. Thus, the authors recommend that Behçet's disease should be considered in a diagnostic workup for unilateral FBA, and a careful history and a positive HLA-B51 are helpful to establish an early diagnosis. In addition, it is recommended that patients with unilateral FBA with suspicion of Behçet's disease should be treated with the early immunosuppressive treatment in order to prevent the involvement of the contralateral eye.

Table 1. Characteristics in seven patients with frosted branch angiitis diagnosed as an ocular manifestation of Behçet's disease

	Sex/age (yr)	Country	Past history	Bilateralilty	Initial BCVA (OD / OS)	Final BCVA (OD / OS)	HLA-B51	Hypopyon	Neuro-Behçet
Reynders et al. (2005) [5]	F/31	Bellgium	OrU, GU, skin lesions	OU	1 / 20, CF	5 / 10, 1 / 10	Positive	(-)	(-)
Renard et al. (2009) [6]	M/30	France	OrU, skin lesions	OD	1 / 10	10 / 10	Positive	(-)	(-)
Jacson et al. (2011) [7]	M/51	UK	OrU, GU, arthritis	OS	HM	6 / 18	Positive	(-)	(-)
Portero et al. (2011) [8]	F/28	Spain	OrU, skin lesions	OU	20 / 200, 20 / 120	20 / 20, 20 / 20	Positive	(-)	(+)
Al-Mujaini et al. (2011) [9]	M/28	Oman	OrU, GU, skin lesions	OD / OS*	20 / 100, NA	Improved†	NA	(-)	(+)
Ramachandran et al. (2011) [10]	M/15	UK	OrU, GU	OU	NA	Improved†	Negative	(+)	(+)
Present case	M/39	Korea	GU, OrU	OS	HM	HM	Positive	(+)	(-)

BCVA = best-corrected visual acuity; OrU = oral ulcers; GU = genital ulcers; CF = count fingers; HM = hand movement; NA = not available.
*Involved in both eyes, two years apart; †In article, described as clinical improvement.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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