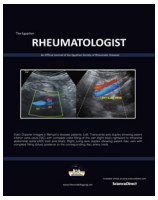
The Egyptian Rheumatologist xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

The Egyptian Rheumatologist

journal homepage: www.elsevier.com/locate/ejr



Original Article

Efficacy of infliximab in refractory posterior uveitis in Behcet's disease patients

Ayman K. El Garf [a], Amira A. Shahin [a,*], Sherif A. Shawky [b], Mohammed A. Azim [b], Dina A. Effat [a], Sherry K. Abdelrahman [c]

[a] Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University, Egypt
[b] Agouza Rheumatology & Rehabilitation Military Centre, Giza, Egypt
[c] Rheumatology and Rehabilitation Department, Benha Teaching Hospital, Benha, Egypt

ARTICLE INFO

Article history:
Received 1 August 2017
Accepted 1 August 2017
Available online xxxx

Keywords:
Behçet's disease
Posterior uveitis
Retinal vasculitis
Infliximab

ABSTRACT

Aim of the work: Ocular manifestations are the main cause of morbidity in Behcet's disease (BD). Infliximab (IFX), a chimeric monoclonal antibody directed against tumor necrosis factor-alpha, may be efficient in refractory uveitis due to BD. The aim of this study was to assess the efficacy and safety of IFX in the treatment of patients with BD-associated refractory posterior uveitis (PU).

Patient and Methods: Twenty patients with refractory Behcet's PU received IFX therapy as intravenous infusions at the dose of 5 mg/kg at weeks 0,2, 6 (induction) and every 8 weeks for a maximum of 6 infusions.

Results: The mean age of the patients was 31.8 ± 9.1 years, disease duration was 8 ± 6 years and 17 (85%) were males. After the third IFX infusion (week 8) a complete remission of PU was recorded in 8/20 (40%) patients and partial remission in 12/20 (60%) patients. At the end of week 32 a complete remission of PU was recorded in a total of 14 (70%) patients. The visual acuity of the 36 affected eyes (16 bilateral and 4 unilateral) showed a significant improvement at the week 8, and at week 32, while there was no additional improvement at week 56. Relapse occurred in 6 patients (30%) between week 9 and week 18 with a mean of 13.5 weeks.

Conclusion: IFX infusion should be considered for the control of acute PU, whereas repeated long-term IFX infusions were effective in reducing the number of episodes in refractory PU with fast regression and complete remission of complications.

1. Introduction

Behcet's disease (BD) is a chronic, relapsing, systemic form of primary vasculitic disorder of unknown cause, mainly characterized by recurrent aphthous oral ulcers, genital ulcers and ocular inflammation [1]. The prevalence of BD is the highest in the Middle East, Mediterranean region and Asia. The usual age of onset is around 30 [2]. Ocular manifestations are the main cause of morbidity in BD [3]. The risk is highest in young men and lowest in women with late onset disease [4]. The disease can affect the anterior and/or posterior segment of the eye. The main manifestations include iridocyclitis, hypopyon, mild to moderate vitreitis, retinal vasculitis and occlusion of retinal vessels, optic disc hyperemia, and macular edema [5], and if not treated may cause blindness. The risk of blindness increases progressively reaching 25% at 10 years and remains constant thereafter [6]. Patients were observed to become blind in an average of 3.36 years after the onset of eye symptoms [7]. Visual acuity (VA) was reported to be affected in 50%–90% of cases to reach 6/60 or worse within four years after the onset [8]. Visual acuity affection differs significantly between patients from different geographical areas [9].

On treating posterior uveitis (PU) in Egyptian BD patients, intravitreal methotrexate (MTX) and retrobulbar steroids had a comparable efficacy with a high frequency of relapse [10]. Patients with poor vision were more frequently in India, Iran and Japan [11]. Although there are no controlled trials, the existing evidence suggests efficacy of infliximab (IFX) in treating BD patients with refractory uveoretinitis, entero-Behçet, neuro-Behçet, vascular BD and arthritis [12]. The aim of this study was to assess the efficacy

Peer review under responsibility of Egyptian Society of Rheumatic Diseases.
* Corresponding author.
E-mail address: amirashahin@hotmail.com (A.A. Shahin).

http://dx.doi.org/10.1016/j.ejr.2017.08.001
1110-1164/

Please cite this article in press as: El Garf AK et al. Efficacy of infliximab in refractory posterior uveitis in Behcet's disease patients. The Egyptian Rheumatologist (2017), http://dx.doi.org/10.1016/j.ejr.2017.08.001

and safety of IFX in the treatment of refractory PU in BD patients and to investigate its efficacy to reduce disease flare-up.

2. Patients and methods

Twenty BD patients who met the criteria of The International Criteria for Behçet's Disease (ICBD) [13], with refractory PU, attending the rheumatology clinic in Agouza Rheumatology & Rehabilitation Military Centre were involved in the current study. The study was approved by the local ethics committee and conforms to the declaration of Helsinki. All subjects gave informed consent and patient anonymity has been preserved.

At baseline all patients underwent the following investigations: history taking, physical examination, purified protein derivative (PPD) test, laboratory tests including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), blood cell count with differential count, renal and liver function and antinuclear antibody (ANA) titer were evaluated. Moreover, a careful screening for tuberculosis was made by detailed medical history, chest X-rays and PPD test.

Ophthalmologic evaluation consisted of a complete ocular examination including best-corrected Visual Acuity (Snellen chart of 0.1–1.0), slit-lamp biomicroscopy, tonometry and ophthalmoscope, optical coherence tomography (OCT), and fundus fluorescein angiography (FFA).

Inclusion criteria: Patients included were BD with chronic PU, with or without retinal vasculitis, resistant to a dose of prednisone $\geq$10 mg/day, and at least one immunosuppressive drug e.g. MTX, azathioprine (AZA), cyclosporine (CsA), or cyclophosphamide (CYC), after at least 12 months of treatment. *Exclusion criteria*: Patients with permanent blindness, a history of recent infections, malignancies or tuberculosis, positive PPD test and radiographic signs that would be considered contraindications to therapy with Tumor necrosis factor antagonists were excluded from the study. Pregnancy and breast feeding were additional exclusion criteria; contraception was recommended to females of childbearing potential.

The response to therapy was calculated by a composite score (0–7) obtained by the sum of the grade of severity of inflammatory infiltrate and retinal vasculitis [14] and graded as follows: *Complete remission*: presence of <1 cellular reaction (scale 0–4), and remission of vasculitis (0–3 score) at fundus examination and FFA (0 absence of vasculitis, 1 vasculitis of peripheral retinal vessels, 2 posterior pole vasculitis and 3 vasculitis with evidence of areas of retinal necrosis). *Partial remission*: improvement of at least 50% of inflammation and retinal vasculitis scores. Absent: absence of any improvement or <50% of uveitis scores.

Treatment regimen: At baseline, all patients suspended the current immunosuppressive therapy, except the corticosteroids (CS). All patients were on CS 20-40 mg/day at enrollment in the study. AZA 100–150 mg/day was started. In addition, all subjects received IFX 2-h intravenous infusions at the dose of 5 mg/kg at weeks 0,2,6 (induction) and every 8 weeks for a maximum of 6 infusions after induction i.e. follow up period is 12 month after induction. IFX-dose escalation through infusion-interval shortening to 6 weeks was allowed in non responders or in those with partial remission according to the judgment of the physician. In responders, CS dose was tapered till withdrawal. Other immunosuppressant agents (other than AZA) and concomitant local CS injections were not allowed. Patients failing to achieve at least a partial remission after the third infusion of IFX withdrew from the study were planned to receive prednisone 1 mg/kg/day and an immunosuppressant different from that employed before the study entry.

All patients had a complete evaluation by an ophthalmologist, a rheumatologist and at baseline and over the follow-up visits that were scheduled after the first, third IFX infusion (week 8) and then every 8 weeks or before in case of relapse. FFA examination was scheduled at baseline, week 8, 32, and 56, and when needed.

Statistical analysis: The Statistical Package of Social Science Software program, version 15 (SPSS) was used for statistical analysis. Data was summarized using mean or median and standard deviation for quantitative variables and frequency and percentage for qualitative variables. Comparison between groups was done using independent sample t-test and repeated measures ANOVA (with Bonferroni multiple comparison adjustment) for quantitative variables, chi square test or Fisher's exact test for qualitative variables. P values $\leq$0.05 were considered statistically significant.

3. Results

Seventeen patients were males (85%), with female: male ratio 1:5.6. The mean age of the patients was 31.8 ± 9.1 years, with mean disease duration of 8 ± 6 years, while the mean age of onset of the uveitis in those patients was 23.7 ± 6 years. Uveitis was the presenting symptom preceding the other symptoms of BD in 2 (10%) patients, appeared with other manifestations of the disease in 12 (60%) patients, and followed the other manifestations in 6 (30%) patients. Disease manifestations of all patients are presented in Table 1. Central nervous system manifestations in the form of headache, seizures, dural sinus thrombosis, ataxia, aphasia, pseudo bulbar palsy, hemiplegia, were found in 6 (30%) patients; one of them had history of stroke. Skin lesions in the form of erythema nodosum, pseudofolliculitis and papulopustular lesions occurred in 11 (55%) patients. Uveitis in the 16 patients was bilateral (80%). Thirteen patients (65%) had PU only, while 7 patients (35%) had panuveitis.

History of immunosuppressive treatments that were given to the patients before inclusion into the study included MTX as weekly injection in 2 patients at a dose of 25 mg/week for 24 months, AZA orally at a dose of 100–150 mg/day in 3 patients for a mean duration of 24.3 ± 1.5 months, CsA orally in 9 patients at a dose of 100-300 mg/day for a mean duration of 21.8 ± 11.3 months and CYC in one patient as I.V. monthly (0.75 mg/cm^3) for 6 months and every 3 months for 6 times. CsA and AZA were used orally in 5 patients for a mean duration of 22.6 ± 2.9 months.

After the third IFX infusion (week 8) a complete remission of PU was recorded in 8/20 (40%) patients, partial remission in 12/20 (60%) patients. 2/8 patients with complete remission after induction went into relapse, after 12 and 16 weeks. They received extra two infusions (6 weeks apart) to get into a remission again. At the end of week 32 a complete remission of PU was recorded in other 6/12 patients, partial remission in 6/12. 4/6 patients that showed complete remission after week 32 went into a relapse, after 9, 12, 17, and 18 weeks, at weeks 41, 44, 49 and 50. They received

Table 1
Disease manifestations of the Behçet's disease patients.

Manifestation n (%)	BD patients (n = 20)
Oral ulcers	20 (100)
Genital ulcers	17 (85)
Fever	5 (25)
Fatigue	6 (30)
Arthritis	12 (60)
Arthralgia	11 (55)
Eye involvement	20 (100)
Skin involvement	11 (55)
CNS involvement	6 (30)
Arterial thrombosis	1 (5)
Venous thrombosis	4 (20)
Superficial thrombophlebitis	6 (30)

BD: Behçet's disease, CNS: central nervous system.

Please cite this article in press as: El Garf AK et al. Efficacy of infliximab in refractory posterior uveitis in Behcet's disease patients. The Egyptian Rheumatologist (2017), http://dx.doi.org/10.1016/j.ejr.2017.08.001

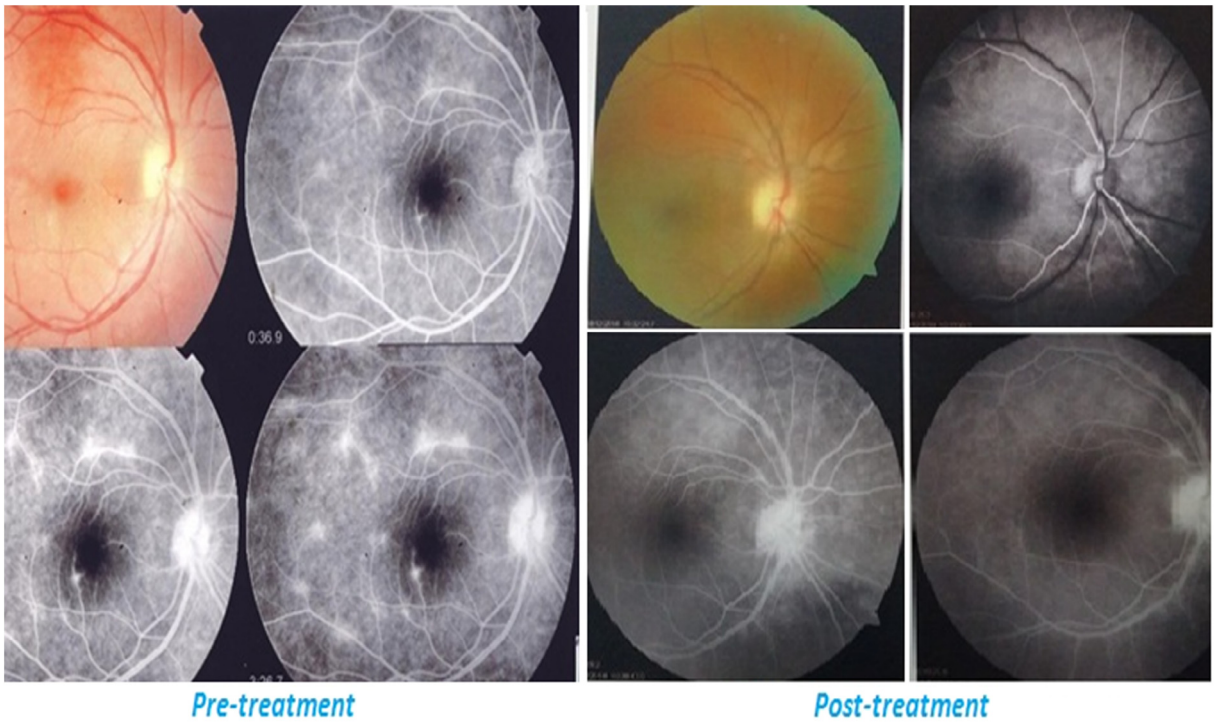


Fig. 1. Fundus fluorescein angiography (FFA) of a Behçet's disease patient with retinal vasculitis showing leakage of the dye indicating active inflammation. Leakage has largely decreased at week 32 post-treatment.

two infusions (6 weeks apart) to get in a remission. A favorable response to IFX was seen in all patients with cessation of concomitant corticosteroid treatment by week 22. At the end of week 32, improvement of the retinal vasculitis (Fig. 1), and cystoid macular edema was recorded (Table 2).

The VA of the 36 affected eyes (16 bilateral and 4 unilateral) showed a significant improvement at the week 8, and at week 32, while there was no additional improvement at week 56 (Table 3). 10 patients had VA ≥6/9 (≥0.9) or better, and the other 10 had VA <6/9 (<0.9) down to 6/60 (=0.1). Comparison of demographic data and pattern of uveitis according to the VA is shown in Table 4. Relapse occurred in 6/20 (30%) patients between week 9 and week 18 with a mean of 13.5.weeks. None of the patients had worsening of VA or new onset ocular complications including retinal detachment, papillitis, intra- or sub retinal hemorrhage, intravitreal hemorrhage, and optic atrophy during the follow-up.

Table 4
Comparison of demographic data and pattern of uveitis in Behçet's disease patients according to the visual acuity.

Parameter mean ± SD or n(%)	VA in BD patients (n = 20)		p
	≥6/9 (0.9) (n = 10)	<6/9 (0.9) (n = 10)	
Age (years)	25.2 ± 4.2	38.4 ± 7.7	**<0.05**
Duration (years)	3.8 ± 1.5	12.2 ± 5.8	**<0.05**
Bilateral uveitis	7 (70)	9 (90)	>0.05
Unilateral uveitis	3 (30)	1 (10)	>0.05
Posterior uveitis	8 (80)	5 (50)	>0.05
Pan uveitis	2 (20)	5 (50)	>0.05

VA: visual acuity, BD: Behçet's disease. Bold values are significant at p < 0.05.

Regarding drug tolerability and safety, mild infusion reactions were recorded in four (20%) patients, frequent urinary tract infections in one (5%) patient, frequent upper airway infection in three

Table 2
Ocular findings and response during infliximab therapy in the Behçet's disease patients.

Ocular finding/response n (%)	Infliximab therapy in BD patients (n = 20)			
	Baseline	week 8	week 32	week 56
Complete remission	–	8 (40)	14 (70)	14 (70)
Partial remission	–	12 (60)	6 (30)	6 (30)
Cystoid macular edema	5 (25)	3 (15)	2 (10)	0 (0)
FFA retinal vasculitis	11(55)	7 (35)	4 (20)	0 (0)

BD: Behçet's disease, FFA: fundus fluorescein angiography.

Table 3
Visual acuity of Behcet's disease patients at baseline and after infliximab treatment.

	VA in BD patients (36 eyes) (n = 20)				
	Baseline	week 8	week 32	p	week 56
VA	0.1 ± 0.09	0.6 ± 0.2	0.8 ± 0.2	**<0.05**	0.8 ± 0.2

VA: visual acuity, BD: Behçet's disease. Bold values are significant at p < 0.05.

Please cite this article in press as: El Garf AK et al. Efficacy of infliximab in refractory posterior uveitis in Behcet's disease patients. The Egyptian Rheumatologist (2017), http://dx.doi.org/10.1016/j.ejr.2017.08.001

patients (15%), with no severe adverse events requiring IFX interruption.

ANA positivity was observed in two (10%) patients during the whole period of follow-up; however no patients developed signs or symptoms of lupus- like syndrome.

4. Discussion

In the present study uveitis preceded the other clinical manifestations of BD in 10% of patients, and was diagnosed with other manifestations of disease in 60%. The detection of uveitis was reported as the initial manifestation in around 10–15% of the patients with ocular manifestation [15]. Behçet's uveitis was suggested to be recognized as a distinct entity that can be diagnosed in the absence of other manifestations [16].

The mean age of patients with uveitis in this study was 23.7 ± 6 years. This is younger than that reported in other parts of the world; 30 years for both genders in American cohort [16] and 34 years in Japan [17]. Seventeen of the 20 involved patients in our study were males, with female: male ratio 1:5.6. This showed more male preponderance than previous studies from different countries. An American study did not observe a strong male preponderance [16], as well as report from Italy which had an even gender distribution (50%) [17].

In this study, before starting IFX all patients received immunosuppressives including MTX, AZA, CsA or CYC as treatment for their uveitis, but they all showed recurrence of the condition with worsening of the visual acuity on repeated attacks. Jabs et al. [18] found that early AZA treatment was effective in improving the long-term visual prognosis of ocular BD patients and preventing new ocular involvement. Although AZA was suggested to be an effective and safe treatment in BD patients with severe uveitis [19], in our study, AZA failed to be that effective in controlling severe uveitis as a monotherapy or in combination with other conventional therapy before starting IFX. It was given in all patients in association with IFX. The young age and the short duration of the disease were found in this study to be associated with better visual acuity after IFX therapy.

A favorable response to IFX was seen in all patients with cessation of concomitant corticosteroid treatment by week 22. Concerning visual acuity, by the end of week 8 (induction), a highly significant improvement in VA of the 36 affected eyes was observed. This is consistent with the results of Sfikakis et al. [20] who reported a dramatic improvement of ocular inflammatory changes and VA after the third infusion in the majority of the patients (78%). In the study of Markomichelakis et al. [21] IFX used (in 19 eyes) was significantly faster than CSs (intravenously in 8 eyes and intra-vitreal in 8 eyes) in clearing retinal vasculitis, in resolution of retinitis and cystoid macular oedema. Moreover, a significantly faster regression of cystoid macular oedema was observed with IFX compared with CSs.

In this study, after the third infusion, 60% of patients were still in partial remission, and by the end of 32 week, other 30% of patients showed a complete remission with improvement in VA, i.e., 70% had complete remission by the end of the follow up. Tabbara and Hemidan [22] found that IFX (10 patients for 30 months) was significantly superior to the conventional therapy (33 patients for 36 months) including oral prednisone, CsA, AZA or MTX in decreasing inflammation, improving the visual acuity at 24 months follow up and in decreasing the number of relapses. When compared with a traditional drug (CsA), Yamada et al. [23] reported that IFX was more effective in reducing the number of acute uveitis episodes in ocular BD, at least during the initial 6-month treatment period. Adan et al. [24] have demonstrated that long-term 12-month repeated IFX infusions until complete remission of refractory PU were effective in Ocular BD, and were sustainable upon discontinuation of the drug in half of patients. Giardina et al. [25] supported previous reports and demonstrated that repeated IFX infusions in Behcet's uveitis refractory to at least one immunosuppressant (CsA, MTX, AZA, and CYC) revealed a total remission in about 85% of cases. Moreover, Cantini et al. [26] showed in a long-term, prospective study of IFX effect in refractory PU in BD, improvement of VA in 82% patients, with significant improvement of mean VA values at the end of follow up compared to baseline. In another study on Egyptian BD patients, infliximab was reported to be safe and effective in controlling PU and inducing remissions if given in a regimen before and after vitrectomy [27]. The results of our study and the above mentioned studies concerning long-term use of IFX confirm that IFX has a rapid and sustained efficacy in a high proportion of patients with BD-associated refractory PU.

In this study, relapse occurred in 30% patients between week 9 and week 18 with a mean of 13.5 weeks. Yukiko et al. [28] reported recurrent episodes of uveitis in approximately half of his 23 patients after 6 months of IFX treatment. Everekliogl [29] reported that ocular inflammation relapsed only in 3/50 patients just before the next scheduled IFX infusion (every 8 weeks). He claimed that shorter periods between infusions are needed for some young patients to maintain complete remission. In this study, all the patients were either complete or partial responders. This is in contrast to Cantini et al. [26] who reported 5/50 patients with refractory uveitis as non responders to IFX, and withdrew them from the study after the third infusion. Yukiko et al. [28] also reported 3/23 patients not responsive to IFX.

In our study, the dose of IFX was 5 mg/kg which is consistent with most of the studies in the literature. Cantini et al. [26], Khalil et al. [27] and Everekliogl [29] used 5 mg/kg. Adan et al. [24] used 3 mg/kg. In case of relapse, patients received extra two infusions (6 weeks apart) to get into remission. On contrast, Sukumaran et al. [30] suggested that dose escalation up to 4 times above the approved dose is often necessary to achieve disease control in patients with uveitis. None of the patients in this study had new onset ocular complications including retinal detachments, papillitis, intra- or sub retinal hemorrhage, intravitreal hemorrhage, and optic atrophy during the follow-up. A reduction of ocular complications (retinal vasculitis, and cystoids macular) edema was recorded. These results were in agreement with previous studies [24,25,28] that did not report, any new onset ocular complication after IFX therapy.

In conclusion, IFX is a useful alternative therapy for patients with sight-threatening uveitis unresponsive to the standard immunosuppressive therapy. Three pulses of IFX infusion should be considered for the control of acute PU, whereas long-term IFX infusions were proved to be effective in reducing the number of episodes in refractory uveitis with fast regression and complete remission of complications.

Conflict of interest

None.

References

[1] Tugal-Tutkun I, Mudun A, Urgancioglu M, Kamali S, Kasapoglu E, Inanc M, et al. Efficacy of infliximab in the treatment of uveitis that is resistant to treatment with the combination of azathioprine, cyclosporine, and corticosteroids in Behcet's disease: an open-label trial. Arthritis Rheum 2005;52:2478–84.

[2] Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med 1999;341:1284–91.

[3] Yurdakul S, Hamuryudan V, Yazici H. Behçet syndrome. Curr Opin Rheumatol 2004;16(1):38–42.

[4] Everekliogl C. Current concepts in the etiology and treatment of Behcet disease. Surv Ophthalmol 2005;50:297–350.

Please cite this article in press as: El Garf AK et al. Efficacy of infliximab in refractory posterior uveitis in Behcet's disease patients. The Egyptian Rheumatologist (2017), http://dx.doi.org/10.1016/j.ejr.2017.08.001

[5] Takeuchi M, Hokama H, Tsukahara R, Kezuka T, Goto H, Sakai J, et al. Risk and prognostic factors of poor visual outcome in Behçet's disease with ocular involvement. Graefes Arch Clin Exp Ophthalmol 2005;243:1147–52.
[6] Tugal-Tutkun I, Onal S, Altan-Yaycioglu R, Huseyin Altunbas H, Urgancioglu M. Uveitis in Behçet disease: an analysis of 880 patients. Am J Ophthalmol 2004;138(3):373–80.
[7] Mamo JG. The rate of visual loss in Behçet's disease. Arch Ophthalmol 1970;84:451–2.
[8] Cho YJ, Kim WK, Lee JH, Byeon SH, Koh HJ, Kwon OW, et al. Visual prognosis and risk factors for korean patients with behcet uveitis. Ophthalmologica 2008;222(5):344–50.
[9] Muhaya M, Lightman S, Ikeda E, Mochizuki M, Shaer B, McCluskey P, et al. Behçet's disease in Japan and in Great Britain: a comparative study. Ocul Immunol Inflamm 2000;8:141–8.
[10] Khalil HE, El Gendy HA, Youssef HA, Haroun HE, Gheita TA, Bakir HM. The effectiveness of intraocular methotrexate in the treatment of posterior uveitis in Behçet's disease patients compared to retrobulbar steroids injection. J Ophthalmol 2016;2016:1678495.
[11] Kitaichi N, Miyazaki A, Iwata D, Ohno S, Stanford MR, Chams H. Ocular features of Behçet's disease: an international collaborative study. Br J Ophthalmol 2007;91(12):1579–82.
[12] Saleh Z, Arayssi T. Update on the therapy of Behçet disease. Ther Adv Chronic Dis 2014;5(3):112–34.
[13] Davatchi F, Assaad-Khalil S, Calamia KT, Crook JE, Sadeghi-Abdollahi B, Schirmer M, et al. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatol Venereol 2014;28(3):338–47.
[14] Niccoli L, Nannini C, Benucci M, Chindamo D, Cassarà E, Salvarani C, et al. Long-term efficacy of infliximab in refractory posterior uveitis of Behçet's disease: a 24-month follow-up study. Rheumatology (Oxford) 2007;46(7):1161–4.
[15] Tugal-Tutkun I. Behçet's uveitis. Middle East Afr J Ophthalmol 2009;16:219–24.
[16] Kaçmaz RO, Kempen JH, Newcomb C, Gangaputra S, Daniel E, Levy-Clarke GA, et al. Ocular inflammation in Behçet disease: incidence of ocular complications and of loss of visual acuity. Am J Ophthalmol 2008;146:828–36.
[17] Salvarani C, Pipitone N, Catanoso MG, Cimino L, Tumiati B, Macchioni P, et al. Epidemiology and clinical course of Behçet's disease in the Reggio Emilia area of Northern Italy: a seventeen-year population-based study. Arthritis Rheum 2007;57:171–8.
[18] Jabs DA, Rosenbaum JT, Foster CS, Holland GN, Jaffe GJ, Louie JS, et al. Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel. Am J Ophthalmol 2000;130:492–513.
[19] Saadoun D, Wechsler B, Terrada C, Hajage D, Le Thi Huong D, Resche-Rigon M, et al. Azathioprine in severe uveitis of Behçet's disease. Arthritis Care Res (Hoboken) 2010;62(12):1733–8.
[20] Sfikakis PP. The first decade of biologic TNF antagonists in clinical practice: lessons learned, unresolved issues and future directions. Curr Dir Autoimmun 2010;11:180–210.
[21] Markomichelakis N, Delicha E, Masselos S, Fragiadaki K, Kaklamanis P, Sfikakis PP. A single infliximab infusion vs corticosteroids for acute panuveitis attacks in Behçet's disease: a comparative 4-week study. Rheumatology (Oxford) 2011;50(3):593–7.
[22] Tabbara KF, Al-Hemidan AI. Infliximab effects compared to conventional therapy in the management of retinal vasculitis in Behçet disease. Am J Ophthalmol 2008;146:845–50.
[23] Yamada Y, Sugita S, Tanaka H, Kamoi K, Kawaguchi T, Mochizuki M. Comparison of infliximab versus ciclosporin during the initial 6-month treatment period in Behcet disease. Br J Ophthalmol 2010;94:284–8.
[24] Adán A, Hernandez V, Ortiz S, Molina JJ, Pelegrin L, Espinosa G, et al. Effects of infliximab in the treatment of refractory posterior uveitis of Behçet's disease after withdrawal of infusions. Int Ophthalmol 2010;30(5):577–81.
[25] Giardina A, Ferrante A, Ciccia F, Vadalà M, Giardina E, Triolo G. One year study of efficacy and safety of infliximab in the treatment of patients with ocular and neurological Behcet's disease refractory to standard immunosuppressive drugs. Rheumatol Int 2011;31:33–7.
[26] Cantini F, Niccoli L, Nannini C, Kaloudi O, Cassarà E, Susini M, et al. Efficacy of infliximab in refractory Behçet's disease-associated and idiopathic posterior segment uveitis: a prospective, follow-up study of 50 patients. Biologics 2012;6:5–12.
[27] Khalil HEDM, Gendy HAE, Raafat HA, Haroun HE, Gheita TA, Bakir HM. The effectiveness of pre- and postoperative infliximab in controlling Behçet's disease posterior uveitis in patients undergoing vitrectomy: a preliminary study. J Ophthalmol 2017;2017:8168369.
[28] Yamada Y, Sugita S, Tanaka H, Kamoi K, Takase H, Mochizuki M. Timing of recurrent uveitis in patients with Behcet's disease receiving infliximab treatment. Br J Ophthalmol 2011;95:205–8.
[29] Evereklioglu C. Ocular Behçet disease: current therapeutic approaches. Curr Opin Ophthalmol 2011;22:508–16.
[30] Sukumaran S, Marzan K, Shaham B, Reiff A. High dose infliximab in the treatment of refractory uveitis: does dose matter? ISRN Rheumatol 2012;2012:765380.

Please cite this article in press as: El Garf AK et al. Efficacy of infliximab in refractory posterior uveitis in Behcet's disease patients. The Egyptian Rheumatologist (2017), http://dx.doi.org/10.1016/j.ejr.2017.08.001