EJR European Journal of Rheumatology

DOI: 10.5152/eurjrheum.2017.160085

Case Report

Anti-TNFα therapy and switching in severe uveitis related to Vogt-Koyanagi-Harada syndrome

Bryan Josue Flores Robles[1], Juan Blanco-Madrigal[2], Abel Alejandro Sanabria Sanchinel[3], Dixie Huntley Pascual[4], Rosario Demetrio-Pablo[5], Ricardo Blanco[3]

Abstract

The study aimed to describe the effectiveness of switching the anti-TNFα agent when an acceptable clinical response has not been obtained with the first anti-TNFα agent in patients with uveitis in VKH syndrome. Patients diagnosed with VKH syndrome being evaluated from the uveitis unit of a single tertiary hospital from January 1, 2000, to October 30, 2015. Patients who presented uveitis with an inadequate response to a first anti-TNFα and required switching to a second anti-TNFα were selected. Complete clinical response was assumed in patients whose visual acuity was normal and those who showed absence of inflammatory findings (inflammatory cells in the anterior chamber and vitritis) or absence of macular thickening in upon OCT. A systematic review of the literature of anti-TNFα agents in VKH syndrome was performed. Five patients met the criteria of VKH syndrome. Two cases of VKH syndrome with uveitis and inadequate clinical response to an initial anti-TNFα (both IFX) were presented. After switching to Adalimumab (ADA), a satisfactory clinical response was noted in the first month. For the first time, we present two patients with severe uveitis due to VKH syndrome who after inadequately responding to the first anti-TNFα agent showed complete and maintained clinical improvement when switched to a second anti-TNFα agent.

Cite this article as: Flores-Robles BJ, Blanco-Madrigal J, Sanabria Sanchinel AA, Huntley Pascual D, Demetrio-Pablo R, Blanco R. Anti-TNFα therapy and switching in severe uveitis related to Vogt-Koyanagi-Harada syndrome. Eur J Rheumatol 2017; 4: XX-XX.

[1]Division of Rheumatology, Hospital Universitario Puerta de Hierro, Madrid, Spain
[2]Division of Rheumatology, Hospital Universitario Basurto, Bilbao, Spain
[3]Division of Neurology, Hospital Universitario Lozano Blesa, Zaragoza, Spain
[4]Department of General Medicine, Universidad Complutense, Madrid, Spain
[5]Division of Ophtalmology, Hospital Universitario Marqués de Valdecilla, Santander, Spain

Address for Correspondence: Bryan Josué Flores Robles, Division of Rheumatology, Hospital Universitario Puerta de Hierro, Madrid, Spain

E-mail: rblanco@humv.es

Submitted: 20.10.2016
Accepted: 17.02.2017
Available Online Date: 21.06.2017

Introduction

The Vogt-Koyanagi-Harada (VKH) disease is a multisystem autoimmune disorder mediated by T cells directed against the antigens of melanin-containing tissues, such as the eye, inner ear, meninges, and skin (1). Clinically, it is characterized by diffuse bilateral granulomatous panuveitis with exudative retinal detachment that can be associated with auditory, neurological, and cutaneous manifestations (1). Chee et al. (2) observed that more than one-half of the patients, despite receiving prompt and adequate immunomodulatory treatment, developed chronic disease, and in some cases, blindness occurred due to cataracts, glaucoma, cystoid macular edema, choroidal neovascularization. Anti-tumor necrosis factor alpha (anti-TNFα) agents have improved the prognosis of inflammatory uveitis, including the VKH syndrome. According to the "expert panel recommendations for the use of anti-TNFα drugs in patients with ocular inflammatory disorders," the use of infliximab (IFX, Inflectra, Pfizer) or adalimumab (ADA, Humira, Abbvie) may be considered in VKH disease patients intolerant or unresponsive to traditional immunosuppressive therapies (3). There is no information regarding switching to a second anti-TNFα agent when faced with an inadequate response to the first anti-TNFα drug. The objective of this study was to describe the effectiveness of switching to another anti-TNFα drug when an acceptable clinical response has not been obtained with the use of the first anti-TNFα drug in patients diagnosed with VKH disease.

Case Presentation

A review of all the patients diagnosed with VKH disease being evaluated from the uveitis unit of one tertiary hospital was carried out from January 1, 2000, to October 30, 2015. Patients who presented severe ocular involvement with inadequate response to a first anti-TNFα drug and required switching to a second anti-TNFα agent were selected. The diagnosis of VKH was performed in accordance with the criteria suggested by an international committee on nomenclature (4). Uveitis was classified anatomically and the degree of intraocular inflammation was evaluated according to the Standardization of Uveitis Nomenclature (SUN) Working Group (5). As previously described, patients were defined as having refractory uveitis when it was not in remission despite having received immunosuppressive drugs or when the use of these drugs was not sufficient to maintain the disease under control in the first 6 months (6-8). A complete clinical response to the treatment was assumed in those patients whose visual acuity was normal in both eyes and showed absence of inflammatory findings in the ocular fundus exam (inflammatory cells in the anterior chamber, vitritis, and choroiditis) or absence of macular/choroidal thickening in optical coherence tomography

(OCT). Since uveitis is an off-label indication for anti-TNFα therapy, written and informed consent was obtained from all patients.

Five patients met the criteria of complete diagnosis of VKH disease. Two of them required treatment with one anti-TNFα agent and later needed switching to a second anti-TNFα drug. In both cases, intravenous pulses of 1 g of methylprednisolone a day for 3 days were administered at the time of diagnosis. Subsequently, corticosteroids were used at a dose of 30 mg/day of prednisone with decreasing dosage along with cyclosporine. In both patients, adverse effects were observed related to the use of cyclosporine. In the two cases, IFX 5 mg/kg was the first anti-TNFα agent administered at weeks 0, 2, and 6 and then every 8 weeks. A switch was conducted to subcutaneous ADA standard dose 40 mg injection every 2 weeks, observing complete clinical response after up to 12 and 24 months of follow-up, respectively.

Patient 1

The first case was of a 38-year-old male with decrease in his visual acuity due to bilateral exudative retinal detachment and panuveitis. Once the patient met the diagnostic criteria for VKH disease, treatment with cyclosporine was initiated at 100 mg every 12 hours. However, 3 months later, he experienced nausea and occasional vomiting with cyclosporine; hence, it was suspended, and treatment with azathioprine with a progressive dose of 3 mg/kg/day was initiated. A month later, due to the persistence of active uveitis, IFX 5 mg/kg was added to the treatment at weeks 0, 2, and 6 and then every 8 weeks. Complete clinical response and visual acuity improvement (from the first month until normal values are attained) were observed. During follow-up (2 years later), the patient presented with left eye choroiditis thus leading to IFX suspension and initiation of subcutaneous ADA 40 mg every 2 weeks with complete clinical remission from the first month and up to 2 years after the initiation of treatment.

Patient 2

The second case was of a 42-year-old female who was admitted with decrease in visual acuity due to bilateral exudative retinal detachment and panuveitis. During her hospital stay, the patient reported bilateral hearing loss. Due to initial suspicion of the VKH disease, a lumbar puncture was performed and noticeable pleocytosis was detected. She met the diagnostic criteria for VKH, and treatment was initiated with intravenous pulses of methylprednisolone 1 g once a day for 3 days and then continued with prednisone 30 mg a day of (reducing dosage to 2.5 mg until present day) and of cyclosporine 5 mg/kg/day, showing progressive clinical improvement. However, 4 months later during follow-up, the patient presented with hirsutism and bilateral anterior uveitis, therefore leading to cyclosporine suspension and initiation of IFX 5 mg/kg at weeks 0, 2, and 6 and then every 8 weeks combined with azathioprine 3 mg/kg/day. Clinical response was observed from the first month until it progressively became complete response. After 5 years of effectiveness, IFX was suspended because of severe fatigue and dizziness. Treatment with subcutaneous ADA was then initiated at 40 mg injections every 2 weeks, maintaining complete clinical response for the next 12 months. No adverse effects were observed in any of the two patients included in this study.

Discussion

Two cases of VKH disease with severe ocular involvement and inadequate clinical response to an initial anti-TNFα drug were presented. After switching to ADA and after the first month of treatment, a satisfactory clinical response is noted. Switching between anti-TNFα biologic agents has been described as successful in other inflammatory disorders, such as rheumatoid arthritis, psoriasis, ankylosing spondylitis or juvenile idiopathic arthritis. However, no information was found in the existing literature related to switching between anti-TNFα agents in VKH disease. The VKH disease etiology remains unknown. High levels of TNFα have been detected in patients with autoimmune uveitis (9). Therefore, the main objective is to suppress intraocular inflammation and prevent visual acuity loss. Thus, early and aggressive administration of corticosteroids is the most widely accepted treatment, and specific guidelines regarding immunosuppressive therapy have not been established, rendering that part of treatment to individual assessment. A variety of immunosuppressive drugs has been used in the treatment of VKH disease. Cyclosporine A is probably the most accepted medication as the first-line treatment. Azathioprine is another drug proven efficient, and in severe cases, azathioprine plus cyclosporine have been used. Other drugs that have been used less successfully are methotrexate and chlorambucil (10). Despite these treatment options, refractory cases have been reported, and anti-TNFα drugs could be an adequate alternative. A review of patients with VKH disease treated with anti-TNFα therapy was conducted in PubMed, Embase, and Medline. Nine articles were found in which a total of twenty-five patients with VKH disease treated with anti-TNFα drugs (16 with ADA and 9 with IFX) were described. In all the cases, patients were refractory to conventional immunosuppressive treatments. Clinical response was observed in 15 of 16 patients (94%) treated with ADA and eight of nine patients (89%) treated with IFX. There is no reference to switching from one anti-TNFα drug to another in any of the articles. The benefit of a second anti-TNF drug could be because some patients present secondary failure to the first anti-TNF either by the production of anti-drug antibodies or by loss of efficacy. For the first time, we present two patients with severe uveitis due to VKH disease who after inadequately responding to a first anti-TNFα agent show complete and maintained clinical improvement upon switching to a second anti-TNFα drug. In both cases, the switching was performed from IFX to ADA.

Ethics Committee Approval: The ethics committee approval for this study was obtained from the ethics committee of Hospital Marqués de Valdecilla, Santander.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.J.F.R.; Design - R.B.; Supervision - R.B.; Resources - A.A.S.S., R.D-P.; Data Collection and/or Processing - J.B., B.J.F.R.; Analysis and/or Interpretation - J.B., B.J.F.R., R.B.; Literature Search and/or Interpretation - J.B., B.J.F.R., R.B.; Writing Manuscript - D.H.P.; Critical Review - R.A.B.; Other - R.D-P.

Acknowledgements: The authors would like to thank Carlos Díaz.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Greco A, Fusconi M, Gallo, Turchetta R, Marinelli C, Macri GF, et al. Vogt-Koyanagi-Harada syndrome. Autoimmun Rev 2013; 12: 1033-8. [CrossRef]
2. Chee SP, Jap A, Bacsal C. Spectrum of Vogt-Koyanagi-Harada disease in Singapore. Int Ophthalmol 2009; 27: 137-42. [CrossRef]
3. Levy-Clarke G, Jabs DA, Read RW, Rosenbaum JT, Vitale A, Van Gelder RN. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. Ophthalmology 2014; 121: 785-96. [CrossRef]
4. Read RW, Holland GN, Rao NA, Tabbara KF, Ohno S, Arallanes-García, et al. Revised diagnostic criteria for Vogt-Koyanagi-Harada disease: report of an international committee on nomenclature. Am J Ophthalmol 2001; 131: 647-52. [CrossRef]

5. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of uveitis nomenclature for reporting clinical Data. Results of the First International Workshop. Am J Ophthalmol 2005; 140: 509-16. [CrossRef]
6. Calvo-Río V, Blanco R, Beltrán E, Sánchez-Bursón J, Mesquida M, Adán A, et al. Anti-TNF-α therapy in patients with refractory uveitis due to Behçet's disease: a 1-year follow-up study of 124 patients. Rheumatology (Oxford) 2014; 53: 2223-31. [CrossRef]
7. Riancho-Zarrabeitia L, Calvo-Río V, Blanco R, Mesquida M, Adan AM, Herreras JM, et al. Anti-TNF-α therapy in refractory uveitis associated with sarcoidosis: Multicenter study of 17 patients. Semin Arthritis Rheum 2015; 45: 361-8. [CrossRef]
8. Calvo-Río V, de la Hera D, Blanco R, Beltrán-Catalán E, Loricera J, Cañal J, et al. Golimumab in uveitis previously treated with other anti-TNF-alpha drugs: a retrospective study of three cases from a single centre and literature review. Clin Exp Rheumatol 2014; 32: 864-8.
9. Santos-Lacomba M, Martín MC, Gallardo Galera JM, Gómez Vidal MA, Collantes Estévez E, Ramírez Chamond R, et al. Aqueous humor and serum tumor necrosis factor alpha in clinical uveítis. Ophthalmic Res 2001; 33: 251-5. [CrossRef]
10. Kaçmaz RO, Kempen JH, Newcomb C, Daniel E, Gangaputra S, Nussenblatt RB, et al. Cyclosporine for ocular inflammatory diseases. Ophthalmology 2010; 117: 576-84. [CrossRef]