American Journal of Ophthalmology Case Reports 11 (2018) 139–141

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

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

Case report

Long term treatment with infliximab in pediatric Vogt-Koyanagi-Harada disease

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ARTICLE INFO

Keywords:
Anti TNF biological agents
Infliximab
Pediatric
Uveitis
Vogt-koyanagi-harada

ABSTRACT

Purpose: To report a case of pediatric Vogt-Koyanagi-Harada (VKH) successfully treated with infliximab and methotrexate for ten years.

Observations: A 9-year-old Hispanic girl with VKH disease, was successfully treated with oral methotrexate 15 mg/week and oral prednisone 40 mg/day (1mg/kg/day). But when oral prednisone was tapered to 10 mg/day over a 3-month period, inflammation recurred. Patient was considered as corticosteroid-dependent thus infliximab 7mg/kg/pulse was started on days 0, 15, 60 and every 60 days thereafter. Six months after, infliximab was increased to 10mg/kg/pulse as cells in the anterior chamber were still observed. After four months of treatment, ocular inflammation was fully controlled, oral prednisone was tapered to discontinuation over a period of 10 months and methotrexate was maintained at 15 mg/week. At 1-year follow up, infliximab was reduced to 6 mg/kg/pulse as patient remained stable on examination. After being treated for 3-years it was decided to discontinue infliximab however, 2 + anterior chamber cells recurred after a dose was skipped thus infliximab was restarted. After 10 years treatment with infliximab 6 mg/kg/pulse every 60 days and methotrexate 15 mg/week associated, no relapsing inflammatory episodes and resolution of physical features of Cushing's syndrome were observed.

Conclusion and importance: Combined therapy of infliximab and methotrexate for up to 10 years was efficacious in this girl in controlling recurrent inflammation without associated side effects. To the best of our knowledge, this is the longest reported clinical follow up of a pediatric VKH case supporting the use of infliximab and methotrexate without steroids treatment.

1. Introduction

Vogt-Koyanagi-Harada disease (VKH) is a chronic and systemic inflammatory disorder characterized by bilateral panuveitis, neurological manifestations, auditory and integumentary findings that mainly affects adults in the second to fifth decades of life. However, it represents an infrequent and often unrecognized cause of uveitis in childhood. Moreover, ocular complications observed in chronic stage are usually more severe in pediatric patients than in adults.[1] Frequent complications include glaucoma, cataract, retinochoroidal atrophy or subretinal fibrovascular membranes that can lead to blindness. The aim of treatment for VKH recurrences is to suppress anterior chamber inflammation as it is a clinical sign of active choroiditis.[2] High dose systemic corticosteroids in combination with steroids sparing agents are still the mainstay for treating recurrent disease. In children, long term treatment represents a therapeutic challenge as risks associated to prolonged corticosteroids therapy and immunomodulatory agents should be minimized. Infliximab is a chimeric biological agent that inhibits tumor necrosis factor-alpha (TNF-α) which is found at high concentrations in non-infectious uveitis.[3] Infliximab, demonstrated to be efficacious in the treatment of several pediatric inflammatory conditions including uveitis.[4] However, durability of clinical response and safety for the long-term management of pediatric VKH has not been communicated yet.

Herein, we report a case of refractory pediatric VKH disease successfully controlled with infliximab for 10 years without steroids requirement.

1.1. Case report

A 9-year-old Hispanic girl was referred for evaluation with diagnosis of bilateral panuveitis. Clinical examination revealed vitiligo at perioral and sacral regions, poliosis in eyelashes and scalp, and Cushing's syndrome. She had been treated with corticosteroids for the previous 7

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https://doi.org/10.1016/j.ajoc.2018.06.022
Received 21 February 2018; Received in revised form 22 April 2018; Accepted 29 June 2018
Available online 02 July 2018

months and was currently on prednisone 8 mg/day. Her ocular evaluation revealed best corrected visual acuities (BCVA) of 20/20 in both eyes (OU). Intraocular eye pressure (IOP) was 14 mmHg in the right eye (OD) and 16 mmHg in the left eye (OS). Biomicroscopic examination showed OD non-granulomatous keratic precipitates (KP), Köeppe nodules, 3 + cells in the anterior chamber and an incipient subcapsular posterior cataract and, OS 3 + cells in the anterior chamber without any other remarkable signs. Posterior pole examination demonstrated hyperemic optic discs, multiple punched-out retinochoroidal scars in the periphery, mid-periphery at 360° and near the central area and diffuse fundus depigmentation consistent with sunset glow fundus OU. The results of laboratory tests and chest X-ray were unremarkable as negative syphilis test, normal angiotensin converting enzyme (ACE) and chest CT scan; hepatogram, human immunodeficiency virus (HIV), antinuclear autoantibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), rheumathoid factor, erithocyte sedimentation rate (ESR), c-reactive protein, all of them were negative; PPD 2UT was anergic. A diagnosis of chronic, complete VKH disease was made.[5]

Treatment with oral methotrexate 15 mg/week was initiated and oral prednisone was increased to 40 mg/day (1mg/kg/day). Initial treatment response was satisfactory as evidenced by a preserved visual acuity (20/20 OU) with absence of cells in the anterior chamber. When oral prednisone was tapered to 10 mg/day over a 3-month period, inflammation recurred. Patient was considered as corticosteroid-dependent thus infliximab 7mg/kg/pulse was started. Infliximab off label use was discussed and informed consent obtained prior to starting treatment. Pulses were indicated on days 0, 15, 60 and every 60 days thereafter. Six months after, infliximab was increased to 10mg/kg/pulse as cells in the anterior chamber were still observed. After four months of treatment, ocular inflammation was fully controlled thus oral prednisone was tapered to discontinuation over a period of 10 months and methotrexate was maintained at 15 mg/week.

At 1-year follow up, infliximab was reduced to 6 mg/kg/pulse as patient remained stable on examination. After being treated for 3-years with combined therapy and without evidence of ocular inflammation it was decided to discontinue infliximab however, 2 + anterior chamber cells recurred after a dose was skipped thus infliximab was restarted. Same results were observed after a second attempt to discontinue infliximab after 4 years of treatment.

After 10 years treatment with infliximab 6 mg/kg/pulse every 60 days and methotrexate 15 mg/week associated, BCVA was 20/20 OU, no relapsing inflammatory episodes and resolution of physical features of Cushing's syndrome were observed. Treatment was well tolerated without any safety concerns.

2. Discussion

Although there is no consensus on VKH management there is general agreement that prompt diagnosis and aggressive treatment are usually associated to better prognosis. Long-term safety and efficacy of pediatric VKH treatment are important because of the chronic nature of the disease. Prolonged therapy with systemic corticosteroids have proven efficacy however its use in the pediatric population poses a dilemma since they can result in serious and, sometimes irreversible side effects. Thus, quickly tapering and discontinuation of corticosteroids is of outmost importance to minimize side effects. Soheilian et al. found that addition of methotrexate resulted in inflammation control which allowed tapering of systemic steroids in seven refractory pediatric cases.[6] Although other combinations of corticosteroids with azathioprine or cyclosporine have also been communicated, none of these combined treatments induced remission in VKH that allowed corticosteroid discontinuation.[7,8]

In the last 50 years, around 50 communications of VKH patients less than 16 years of age have been published and anti TNF-α agents have been used only in few refractory cases.[6,9]

Khalifa et al. reported two refractory VKH pediatric cases treated with intravenous infliximab in addition to systemic corticosteroids and methotrexate, only one patient had complete resolution of serous retinal detachment with subsequent discontinuation of corticosteroids within 4 months.[10] Infliximab efficacy was also demonstrated in a study including 17 pediatric cases with refractory uveitis. Two of these patients had a diagnosis of VKH disease and both showed good clinical response to infliximab however steroids could be discontinued only in one case.[4]

In our patient, recurrences were always evidenced by presence of cells in the anterior chamber without visual acuity reduction or other clinical manifestations. Addition of infliximab allowed safely tapering of corticosteroids. Moreover, inflammation recurred when infliximab was discontinued and fully controlled after treatment was restarted without steroids requirement for up to 10 years. Some authors reported similar results in adult patients treated with infliximab for up to 2 years.[11,12]

3. Conclusions

To the best of our knowledge, our report is the longest reported clinical follow up of a pediatric VKH case supporting the use of infliximab and methotrexate without steroids treatment. Combined therapy of infliximab and methotrexate for up to 10 years was efficacious in this girl in controlling recurrent inflammation without associated side effects.

3.1. Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Acknowledgements and disclosures

Funding

No funding or grant support.

Conflicts of interest

The following authors have no financial disclosures: GB, LGF and AP.

Authorship

“All authors attest that they meet the current ICMJE criteria for Authorship.”

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