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A case of ustekinumab-induced sclerouveitis

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ABSTRACT

Purpose: Biologics have proven to be essential therapeutic agents in immune-mediated systemic diseases. Ophthalmologic adverse effects have been reported in the use of more traditional agents, such as TNF-α inhibitors, but there are limited data on ocular side effects associated with the newer generation of biologics.
Observations: In this report, we present a case of a suspected ustekinumab-associated recurrent sclerouveitis.
Conclusions: To the best of our knowledge, this is the first reported case of this type seen with ustekinumab injections. Our goal is to add to the existing literature in order to better understand the mechanism and management of this condition.

1. Introduction

Approximately 7.6–9.4% of the world's population is affected by autoimmune inflammatory diseases, many of whom are treated by drug therapies that target tumor necrosis factor (TNF).[1] With the introduction of newer biologics that target different mechanisms, there are side effect profiles that are not yet fully understood.[1] In this case report, we describe a patient with recurrent unilateral sclerouveitis presumed to be secondary to treatment of inflammatory bowel disease (IBD) with ustekinumab, an effect that has not previously been described in the ophthalmic literature.

2. Case report

A 64-year-old male with a past medical history of IBD managed with monthly ustekinumab injections and no known significant ocular history presented with complaints of blurry vision in his right eye for one month duration. Notably, the patient reported that one month ago was also his first treatment with ustekinumab, and that his blurry vision in the right eye occurred two days following that treatment. The patient's best corrected visual acuity (BCVA) was 20/25 in the right eye and 20/20 in the left eye. Anterior segment exam of the right eye showed posterior synechiae and pigment on the anterior capsule, suggesting that a more subacute or chronic inflammatory process had developed within this patient's eye, with a noninjected sclera and a quiet anterior chamber. The patient's left eye exam was within normal limits. Fundoscopic exam was notable for trace epiretinal membrane in both eyes. Lab testing was obtained including CBC, CMP, Lyme, Lipid panel, Quantiferon gold, A1C, Vitamin D, COVID, HLA-B27, CRP, RPR, and FTA-ABS, the results of all of which were unrevealing. The patient did not obtain a chest radiograph.

The patient returned five weeks later, shortly after his second dose of ustekinumab, reporting worsening pain in his right eye. His vision remained stable at 20/25, but his exam was now notable for 2–3+ scleritis with a quiet anterior chamber. The patient was treated initially with topical prednisolone acetate 1% ophthalmic drops twice daily and oral prednisone 40mg daily. Additional lab testing was ordered, including both p- and c-ANCA, urinalysis, anti-dsDNA antibodies, and anti-CCP antibodies, all of which returned normal results. Testing was not completed for anti-ustekinumab antibodies. Three weeks following this visit, the patient was symptomatically improved, and his exam showed suppressed scleritis and a quiet anterior chamber. He was noted at this time to have an elevated intraocular pressure (IOP), which was presumed to be a steroid related rise in IOP. The patient was started on an IOP lowering eye drop, the topical prednisolone acetate was discontinued, and his oral prednisone was tapered by 10mg weekly until he reached a dose of 10mg daily. On review of systems, there was no known history of herpes and on physical exam there were no findings to suggest herpetic eye disease including iris atrophy, granulomatous keratic precipitates, keratitis, or corneal scarring. The patient returned four weeks later with stable symptoms, continued suppression of his scleritis, a quiet anterior chamber, and well controlled IOP. He was instructed to decrease his oral prednisone dose to 7.5mg daily and to continue the IOP lowering medication. The patient reported that he would be receiving

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his next ustekinumab injection later that week.

Four days after his third ustekinumab injection, the patient represented with recurrence of his sclerouveitis despite having maintained a dose of 7.5mg of oral prednisone, with which the sclerouveitis had been previously suppressed. His anterior segment exam was significant for 2–3+ scleritis and 2+ anterior chamber cell, defined by the Standardization of the Uveitis Nomenclature (SUN) grading criteria as 16–25 cells in a field size of a 1mmx1mm slit beam.[2] At this time, the patient was given a diagnosis of presumed ustekinumab-induced recurrent sclerouveitis and he was instructed to increase his oral prednisone to 40mg daily. His symptoms resolved after 1 week on this therapy and on exam he was noted to have only trace scleritis and a quiet anterior chamber. At this time, he was again tapered to an oral prednisone dose of 10mg daily, which he has remained stable on since the time of this report.

When further history was obtained from the patient, it was noted that each episode of ocular inflammation correlated to occurring shortly after receiving his ustekinumab injections. To date, the patient has had three episodes of right eye inflammation, each one taking place two to four days following treatment with ustekinumab. There were no known predisposing factors that we could elucidate in the right eye that might have made it more prone to inflammation when compared to the left eye. The patient has since been transitioned to subcutaneous injections of adalimumab for the treatment of his IBD, and he has not experienced any additional flares of his ocular inflammatory disease. Of note, ustekinumab subcutaneous dosing is 45mg if the patient is less than or equal to 100kg and 90mg if the patient is greater than 100kg.[3] Our patient was experiencing sclerouveitis flares at a 45mg dose.

3. Discussion

Biologic agents are widely used in clinical practice for the treatment of systemic autoimmune conditions.[4] Paradoxical ophthalmologic reactions, including uveitis, sarcoid uveitis, scleritis, optic neuritis, diplopia, and visual field defects/scotomas have been reported in TNF-α inhibitors.[5] Ustekinumab (Stelara, Janssen Biotech Inc.) employs a different mechanism of action than the older anti-TNF agents.[6] It is an anti-p40 IL-12/IL-23 human immunoglobulin monoclonal antibody that reduces levels of IL-12/IL-23, which in turn downregulates multiple pro-inflammatory cytokines, such as TNF-α, IFN-γ, and IL-2.[3] In our literature review, we have not found a definitive mechanism of action that might explain why this paradoxical inflammatory effect may have occurred in this patient's eye. With other classes of drugs, such as tumor necrosis factor-α inhibitors, it is postulated that an upregulation in T-cell cytokines could be the risk factor that leads to a paradoxical inflammatory response in the eye.[7] As described above, ustekinumab reduces levels of specific interleukins (IL) and downregulates multiple pro-inflammatory cytokines, but in turn, assists in activating certain T-cells, which could be the catalyst that promotes a proinflammatory environment within the eye.[7] The patient's autoimmune disease could be playing a role in these acute inflammatory reactions, but since the patient had not experienced any episodes prior to his injections, we are led to believe that there was some correlation between the medication and his inflammatory disease.

4. Conclusions

We report the first known case report of presumed usetekinumab-associated sclerouveitis. With the growing market for new biologic agents, like ustekinumab, close patient monitoring will be important given the uncertainty of potential adverse side effects. Our patient's symptoms of presumed ustekinumab-induced recurrent sclerouveitis may be an early sign of ocular side effects that have yet to be described in the literature. Further case series and review should be done in conjunction with Rheumatology and Dermatology in order to effectively identify and manage patients who may be at risk for developing these conditions in the future.

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.

Conflicts of interest

No conflict of interest exists.

Funding

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Authorship

All listed authors meet the ICMJE criteria.
We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE.

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