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Case Series

Adalimumab in the Treatment of Complex Sarcoidosis-related Inflammatory Eye Disease: A Case Series

Mina Al-Awqati[1#], Supritha Prasad[2*#], Valeria Esparza[2#], Jacqueline Jansz[2#], Wuily Carpio[3], Christian Ascoli[4], Huan Chang[1], Pooja Bhat[3#], Ann-Marie Lobo-Chan[3#] and Nadera Sweiss[1]

[1]Division of Rheumatology, USA

[2]Department of Internal Medicine, USA

[3]Division of Ophthalmology, USA

[4]Division of Pulmonology, University of Illinois at Chicago, Chicago, Illinois, USA

[#]These authors contributed equally to the article

More Information

***Address for correspondence:** Supritha Prasad, Department of Internal Medicine, USA, Email: spprasa2@uic.edu

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Abstract

Background: Sarcoidosis is a systemic granulomatous inflammatory disease that is associated with inflammatory eye manifestations such as uveitis, cystoid macular edema, and retinal vasculitis. Although Corticosteroids (CS) have traditionally been the mainstay of treatment, there is a clinical need and growing interest in exploring alternative therapeutic options for patients who are refractory to or intolerant of CS or require long-term steroid-sparing agents.

Purpose: This case series aims to describe the effectiveness of adalimumab, an anti-tumor necrosis factor (TNF)-α monoclonal antibody, in the management of complex sarcoidosis-related inflammatory eye disease via reduction in CS dosage and ocular exam findings before and after initiation of adalimumab therapy.

Method: A retrospective chart review of patients between 2010 and 2023 seen at our academic center's rheumatology and eye clinics was conducted, with 5 patients meeting the inclusion criteria.

Results: Most patients were able to lower, discontinue, or remain off oral CS, while all 5 patients demonstrated a reduction in uveitis activity, Cystoid Macular Edema (CME), and/or retinal vasculitis.

Conclusion: These findings suggest a potential role for adalimumab as an effective and safe therapeutic option in the management of complex sarcoidosis-related inflammatory eye disease.

Introduction

Sarcoidosis is a systemic granulomatous inflammatory disease and is one of the leading causes of inflammatory eye disease. Ocular sarcoidosis can involve any part of the eye and its adnexal tissues. It can cause uveitis, episcleritis/scleritis, eyelid abnormalities, conjunctival granuloma, optic neuropathy, lacrimal gland enlargement, and orbital inflammation such as uveitis, cystoid macular edema, and retinal vasculitis. Glaucoma and cataracts are usually either due to the inflammation itself or adverse effects from therapy [1]. It is approximated that ocular inflammation occurs in ten to fifty-five percent of Caucasian patients with sarcoidosis, with higher prevalence suggested in the Asian population and limited data in the African American population [2]. The most common of these ocular manifestations is anterior uveitis, which is more common than intermediate, posterior, or pan-uveitis. Diagnosis may involve the presence of non-caseating epithelioid and giant cell granulomas however this is a non-specific finding given associations with tuberculosis and multiple sclerosis among other disease processes [2]. Intermediate uveitis can present with CME, or macular thickening, as well as vitreous inflammation, which can often lead to decreased vision [1]. Retinal vasculitis can occur due to a disrupted blood-retinal barrier and has been associated with sarcoidosis as well as other rheumatologic conditions like SLE and Behcet's disease [3].

Although Corticosteroids (CS) have traditionally been the mainstay of treatment, there is a clinical need and growing

interest in exploring alternative therapeutic options for patients who are refractory to or intolerant of CS or require long-term steroid-sparing agents. Additionally, elevated intraocular pressure is noted to be a consequence of CS usage. While adalimumab, an anti-Tumor Necrosis Factor (TNF)-α monoclonal antibody, has been extensively studied in other autoimmune inflammatory diseases such as Rheumatoid Arthritis (RA) and Inflammatory Bowel Disease (IBD), its use in ocular sarcoidosis remains relatively unexplored. This case series aims to describe the effectiveness of adalimumab in the management of complex sarcoidosis-related inflammatory eye disease based on CS dosage and ocular exam findings before and after initiation of adalimumab therapy.

Methods

A retrospective medical record review was performed between 2010 and 2023 in a single academic center. An initial database included approximately 1030 patients with a documented diagnosis of sarcoidosis based on a data exploration of the electronic medical record. From this point, four chart reviewers manually reviewed charts to determine patients who had been seen in our institution's eye clinic. The charts were further reviewed to obtain specific details and ultimately patients were only included if there was documentation of adalimumab initiation, pre- and post-initiation CS dose, as well as pre-and post-initiation ocular examination findings. A total of 5 patient charts had all the desired data. Ocular examination findings were interpreted from physician documentation with the guidance of a team of ophthalmologists at our institution. Response to adalimumab via a change in CS dosage and status of ocular inflammation were assessed at follow-up visits within a year of adalimumab initiation.

Findings

Five patients with ocular sarcoidosis (Table 1) had available data showing that they received adalimumab as an adjunct agent following corticosteroids and/or Disease-Modifying Anti-Sarcoid Drugs (DMASDs). Ocular manifestations included uveitis, cystoid macular edema, and/or retinal vasculitis. All patients were refractory to or intolerant of CS and required long-term immunosuppression. Four of 5 patients of interest had biopsy-proven sarcoidosis while 1 had highly probable sarcoidosis with difficulty obtaining a biopsy. The age range was 47 to 66 years old, thus with a mean age of 55.4. Sixty percent of our studied patients were female with fifty percent white and fifty percent black individuals based on those who self-reported. Most patients responded well to therapy and were able to lower, discontinue, or remain off oral corticosteroids, while all 5 patients demonstrated a reduction in uveitis activity, macular edema, and retinal vasculitis. These findings suggest a potential role for adalimumab as an effective and safe therapeutic option in the management of complex sarcoidosis-related inflammatory eye disease.

Discussion

This case series highlights several clinical outcomes of adalimumab therapy in sarcoid-related inflammatory ocular disease, thus providing valuable insight into its use in this application. Adalimumab demonstrated promising efficacy, with a reduction of steroid dosage in three of our four patients on steroids. This reduction can help mitigate many multiple unwanted adverse effects of corticosteroid treatment including elevated intraocular pressure leading to iatrogenic vision loss, weight gain, diabetes mellitus, and osteoporosis.

There is relatively limited data regarding the use of TNF-inhibitors (TNFi) in sarcoid-related eye disease compared to other autoimmune diseases, however, the literature review shows our results to be consistent with prior investigations demonstrating response or complete remission of sarcoid-associated ocular disease [4]. It is important to note, however, that in a trial of 25 patients on anti-TNF-α for ocular sarcoidosis, all patients were initially noted to have improvement in ocular disease, but only 10 patients were noted to have a sustained improvement [5]. Thus, it would be beneficial for subsequent studies to involve longer follow-up periods to better investigate sustained response to therapy.

Table 1: Complex sarcoidosis-related inflammatory eye disease patient data and outcome summary.

Data	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age, years	47	63	43	66	58
Sex	F	M	F	F	M
Self-Reported Race	Black	White	Not reported	Black	White
Ocular Sarcoidosis Manifestations	Anterior uveitis and retinal vasculitis	Intermediate uveitis, retinal vasculitis, and CME	Panuveitis, retinal vasculitis, and CME	Panuveitis and CME	Anterior and intermediate uveitis, CME
Extraocular Sarcoidosis Manifestations	Lung and skin	Lung	Lung	Lung	None
Adalimumab Dose, mg	40 every 14 days	40 every 14 days	40 every 14 days	40 every 7 days	40 every 7 days
Maximum Steroid Dose Before Adalimumab Initiation, mg	10	2.5	0	2.5	10
Steroid Dose After Adalimumab Initiation, mg	0	0	0	2.5	0
Second Line DMASD Used	Methotrexate and MMF	Methotrexate	Methotrexate and MMF	None	MMF
Ocular Exam Findings After Adalimumab Initiation	Resolved anterior chamber inflammation with no cells	Decreased inflammation in the vitreous chamber, improved retinal vasculitis, improvement in CME	Stable panuveitis, improved retinal vasculitis, resolved CME	Improved inflammation with trace cells, resolved CME	Resolved CME

DMASD: Disease-Modifying Anti-Sarcoid Drug; CME: Cystoid Macular Edema; MMF: Mycophenolate Mofetil.

A multicenter study from the French Uveitis Network aimed to investigate the impact of infliximab or adalimumab vs. IL-6 inhibitor tocilizumab on refractory uveitic macular edema, a proportion of which was noted to be secondary to sarcoidosis. Both groups showed promising complete and partial response rates. Although tocilizumab was associated with higher rates of complete response compared with the TNFi, there was no statistically significant difference in CS-sparing effect or relapse rate [6]. Further comparative studies between agents are needed.

Inhibition of TNF-α has shown benefit in several rheumatologic diseases via a decrease in inflammatory signaling. Nevertheless, its inhibition is not without potential for adverse effects. One meta-analysis investigated the adverse effects of TNFis in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. When compared with the absence of TNFi therapy or DMARD therapy alone, TNFi was associated with a statistically significant increase in overall adverse events, risk of serious infection, and cancer risk [7]. In contrast, other studies found no significant association between anti-TNF-α therapy and cancer development [8] and also suggested a dose-dependent relationship with increased risk of infection [9]. Studies with longer follow-up periods would help capture slower-developing adverse events such as cancer. Additionally, study designs allowing for subgroup analysis of drug doses and specific anti-TNF-α agents used would allow for a more nuanced understanding of therapeutic impact [7].

We acknowledge the limitations of our study rooted in our retrospective study design. Data acquisition occurred via chart review of available documentation in the electronic medical record, thus introducing expected differences in physician documentation. To increase accuracy and consistency in the interpretation of patients' ocular exam findings, the available documentation was reviewed with a team of ophthalmologists. Additionally, while chart review by four independent chart reviewers had the potential to cause variability in the collection of available data, this was mitigated via frequent discussions between reviewers to standardize terms and determine data parameters of interest. Lastly, the absence of desired data for many patients, including the initiation date of adalimumab, led to the exclusion of several patients for analysis, leading to a small sample size. Despite such limitations, we have laid a foundation for larger-scale, prospective, randomized controlled trials to assess the effectiveness, safety, and long-term outcomes of adalimumab and other TNF inhibitors in this complex subset of sarcoidosis patients.

Conclusion

Sarcoidosis-related inflammatory eye disease can affect more than half of patients with sarcoidosis. While CS is generally used in management, long-term steroid therapy is not without its consequences, thereby generating an interest in alternative therapies to manage sarcoidosis-associated ocular complications. Our retrospective review showed promising results for patients on adalimumab, with the benefit of reduced CS use and reduction in ocular inflammation. These findings suggest a potential role for adalimumab as an effective therapeutic option in the management of complex sarcoidosis-related inflammatory eye disease and aim to provide momentum for future studies to better elucidate safety and long-term tolerability.

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