EJCRIM
European Journal
of Case Reports
in Internal Medicine

ADALIMUMAB-INDUCED OPTIC NEUROPATHY IN A PATIENT WITH BEHÇET'S SYNDROME

Sofia Miranda[1], Daniel Calado[1], Joana Rua[2], Fernando Salvador[2]

[1] Internal Medicine Department, Hospital do Divino Espírito Santo, Ponta Delgada, Portugal
[2] Internal Medicine Department, Unidade Local de Saúde de Trás-os-Montes e Alto Douro, Vila Real, Portugal

Corresponding author's e-mail: sofiairmiranda@gmail.com

Received: 23/12/2024
Accepted: 30/12/2024
Published: 13/01/2025

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Informed consent was obtained from the patient and can be provided upon request.
This article is licensed under a Commons Attribution Non-Commercial 4.0 License

How to cite this article: Miranda S, Calado D, Rua J, Salvador F. Adalimumab-induced optic neuropathy in a patient with Behçet's syndrome. *EJCRIM* 2025;**12**:doi:10.12890/2025_005112

ABSTRACT

A 37-year-old woman with a diagnosis of Behçet's syndrome, treated with colchicine and prednisolone, maintained low disease activity for a period of 10 years, after which, she developed a new episode of anterior uveitis. A cycle of high dose systemic corticosteroids was required but the patient presented with a new flare during dose tapering. A decision to initiate a corticosteroid-sparing agent was then made, with an initially satisfactory response. However, 3 months later the ocular symptoms recurred, and a new bout of oral ulceration appeared concurrently. As a result, adalimumab was then started, but the patient presented with a sudden and severe decrease of visual acuity in her right eye 4 months later. The initial bloodwork showed no elevated inflammatory markers. A lumbar puncture showed a normal cerebrospinal fluid composition. Although these findings made it less probable that the patient's symptoms were caused by infectious or autoimmune disease, extensive investigations directed at these possible causes were performed, with negative results. Several imaging tests were also performed, which showed no alterations. However, a sensory evoked potentials test revealed a functional compromise at the pre-chiasmatic level. An iatrogenic optic neuropathy induced by adalimumab seemed the most probable cause and a decision to suspend the treatment was made. A new cycle of high dose systemic corticosteroids consisting of three pulses of methylprednisolone followed by pred-nisolone with a quick tapering over 4 weeks was also started, with gradual improvement of visual acuity.

KEYWORDS

Adalimumab, optic neuropathy

LEARNING POINTS

- Albeit used for the management of ocular manifestations of systemic diseases like Behçet's syndrome, anti-tumour necrosis factor (TNF)-alpha inhibitors can paradoxically be associated with ocular adverse effects.
- Optic neuritis is one of the possible ocular adverse effects although rarer than anterior uveitis.
- Iatrogenic optic neuritis due to anti-TNFα inhibitors remains a diagnosis of exclusion but should be kept in mind.

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

© EFIM 2025 - European Journal of Case Reports in Internal Medicine - Doi: 10.12890/2025_005112

INTRODUCTION

Uveitis refers to inflammation of the uvea. However, the term has also been used to refer more broadly to inflammation within the eye and, therefore, to adjacent structures such as the retina.

Regarding its etiology, uveitis can be categorized as infectious or non-infectious. Amongst the known causes of non-infectious uveitis are systemic immune mediated diseases like Behçet's syndrome (BS) that when difficult to treat require the administration of immunosupressive drugs, like anti-TNFα inhibitors.

CASE DESCRIPTION

A 37-year-old woman presented with recurrent oral and genital ulceration, inflammatory polyarthritis, and a previous episode of anterior uveitis requiring a cycle of systemic corticosteroids over several years before being referred to the Autoimmune Diseases Outpatient Unit, where she was diagnosed with BS and treated with colchicine and prednisolone.

The patient maintained low disease activity for a period of 10 years, after which, she developed a new episode of anterior uveitis. A cycle of high dose systemic corticosteroids was again required but this time the patient presented with a new flare during dose tapering. A decision to initiate a corticosteroid-sparing agent was then made, with azathioprine being the chosen agent. However, an early switch to methotrexate was needed due to intolerance of azathioprine. The clinical response was initially satisfactory, but 3 months later the ocular symptoms recurred, and a new bout of oral ulceration appeared concurrently (Behçet's Disease Activity Index 3). Adalimumab (ADA) 40 mg every 2 weeks was then started, with a good initial clinical response. However, 4 months later, the patient presented with a sudden and severe decrease of visual acuity in her right eye (2/10), without ocular pain, photophobia, eye floaters or dysphotopsias. No other systemic symptoms were noted. On examination, neither eye redness, synechiae or changes in ocular motility and or in the fundus were apparent. A graphic representation of this case timeline can be found in *Figure 1*.

The initial bloodwork showed no elevated inflammatory markers; therefore, a flare of BS was unlikely. A lumbar puncture was then performed, showing a normal cerebrospinal fluid (CSF) composition: 4 cells/µl, proteins 0.33 g/l and glucose 57 mg/dl (serum level of 100 mg/dl). Although this finding rendered both infectious and autoimmune causes less probable, extensive testing for both was the next step.

Concerning the former, no bacterial or fungal growth was detected on cultural exams and India ink preparation for Cryptococcus, VDRL and TTPA for syphilis, acid-fast stain, culture, and polymerase chain reaction of CSF for *Mycobacterium tuberculosis* and viral serologies for cytomegalovirus, Epstein-Barr virus, herpes simplex and zoster were all negative. Serologies for human immunodeficiency virus, hepatitis B and C and a blood panel for the detection of zoonotic diseases (included *Anaplasma*, *Ehrlichia*, *Borrelia*, *Coxiella*, *Babesia* and *Rickettsia*) on blood were all negative. Concerning the latter, both the IgG index and angiotensin-converting enzyme level were lower than their respective cut-off values and no oligoclonal bands were detected in CSF. Anti-neuronal, NMDAR, VGKC, MOG and aquaporin-4 antibodies were also negative.

The last step consisted of several imaging tests, which included an orbit and brain computerized tomography scan, intracranial vessel wall and spinal magnetic resonance imaging, a transthoracic echocardiogram and a carotid doppler, which showed no alterations. However, a sensory evoked potentials test revealed a functional compromise at the pre-chiasmatic level.

Considering the aforementioned investigation, iatrogenic optic neuropathy induced by ADA seemed the most probable cause and, a decision to suspend the treatment was made. A new cycle of high dose systemic corticosteroids consisting of three pulses of methylprednisolone 750 mg followed by prednisolone 1 mg/kg/day with a quick tapering over 4 weeks was also started, with gradual improvement on visual acuity (6/10 at the time of writing).

DISCUSSION

The wide variety of ocular manifestations associated with autoimmune diseases range from minor disturbances to sight-threatening conditions that require immediate medical intervention. In some cases, anti-TNF inhibitors will be needed to stop further progression. However, anti-TNFα inhibitors have been associated with paradoxical

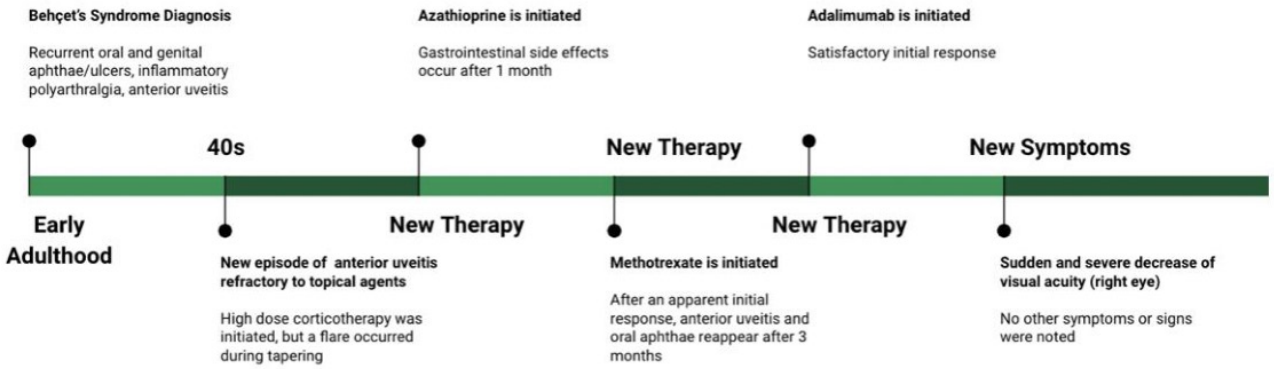


Figure 1. Disease timeline.

reactions including ocular adverse effects, mainly anterior uveitis[1]. Optic neuritis has also been reported as a potential manifestation, albeit much rarer. The SABER study, the first large cohort study examining optic neuritis incidence in patients treated with these agents, estimated an incidence of 5-10 cases per 100.000 patient-years, a rate similar to that in patients who started non-biologic immunosuppressive therapies[2]. Moreover, it seemed that its development was highly dependent on a previous history of neuritis or demyelinating diseases. In all the cases collected patients had rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis or inflammatory bowel disease. Since then, other case reports and retrospective studies identified new optic neuritis cases related to anti-TNFα agents, but always in patients with autoimmune diseases more associated with musculoskeletal manifestations, inflammatory bowel disease or uveitis[3-5].

In our case, a Naranjo score of 6 suggested a probable adverse drug reaction and made this diagnosis more robust. To our knowledge, this is the first case of optic neuritis in a patient with BS, and it not only strengthens the evidence regarding a relationship between optic neuritis and anti-TNFα therapy, but also suggests that this association is independent from the type of rheumatic disease for which the patient received treatment, whether it was vasculitis or an autoimmune disease with preferential gastrointestinal or musculoskeletal manifestations.

REFERENCES

1. Susanna FN, Pavesio C. A Review of Ocular Adverse Events of Biological Anti-TNF Drugs. *J Oph-thalmic Inflamm Infect* 2020;**10**:11.
2. Winthrop KL, Chen L, Fraunfelder FW, Ku J, Varley C, Suhler E et al. Initiation of Anti-TNF Therapy and the Risk of Optic Neuritis; From the Safety Assessment of Biologic ThERapy (SABER) Study. *Am J Ophthalmol* 2013;**155**:183–189.
3. Komandur A, MacIntosh P, Moss H. Acute Inflammatory Optic Neuritis Associated with a Self-Taper of Oral Prednisone in a Patient Taking Adalimumab. *Neuroophthalmology* 2019;**44**:186-189.
4. Alexandre B, Vandermeeren Y, Dewit O, Moreels T, de Boer N, Daar A et al. Optic Neuritis Associated or Not with TNF Antagonists in Patients with Inflammatory Bowel Disease. *J Crohns Colitis* 2016;**10**:541–548.
5. Becerra CM, Ding Y, Kenol B, Hendershot A, Meara AS. Ocular Side Effects of Antirheumatic Medications: A Qualitative Review. *BMJ Open Ophtalmol* 2020;**5**:e000331.