Optic neuropathy in a patient treated with adalimumab for hidradenitis suppurativa

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INTRODUCTION

Adalimumab (Humira AbbVie) is a fully human IgG1 monoclonal antibody specific for tumor necrosis factor α (TNF-α) that was recently approved by the United States Food and Drug Administration for treatment of mild-to-moderate hidradenitis suppurativa (HS).[1] Common adverse effects of adalimumab include headaches, upper respiratory tract infections, rash, abdominal pain, and infection.[1] Though uncommon, ocular complications involving the optic nerve have been associated with TNF inhibitors.[2] Herein, we report a case of non-arteritic anterior ischemic optic neuropathy (NAION) as an adverse reaction to adalimumab in the treatment of HS.

Abbreviations used:

AD:	atopic dermatitis
BCVA:	best-corrected visual acuity
HS:	hidradenitis suppurativa
NAION:	non-arteritic anterior ischemic
RAPD:	relative afferent pupillary defect
TNF-α:	tumor necrosis factor α

CASE REPORT

A 40-year-old Black woman with a history of severe childhood atopic dermatitis (AD), currently in remission, and Hurley stage II-III HS presented to the dermatology clinic with an acute onset of constant aching pain and worsening vision in her left eye. She had been receiving prolonged biologic treatment for HS with the following treatment course: 40 mg weekly adalimumab for 33 months, followed by infliximab-abda for 5 months, and then restarted on 40 mg adalimumab weekly for 15 months. Adalimumab was immediately discontinued due to a presumed association.

Upon an emergent same-day referral to an ophthalmologist, the best-corrected visual acuity (BCVA) in the right eye was found to be Snellen 20/25 and counting fingers to 1 foot in the left eye.

Due to pharmacologic dilation of her eyes, a thorough eye exam was resumed the next day, which showed the presence of relative afferent pupillary defect (RAPD). Further Humphrey visual field 24-2 testing demonstrated superior altitudinal defect in the affected eye (Fig 1).

A week later, BCVA in the left eye had progressively worsened to only detecting hand motion. Diagnostic laboratory tests for possible autoimmune etiologies were remarkable for elevated erythrocyte sedimentation rate and C-reactive protein, prompting treatment with oral prednisone 10 mg 4 times daily and biopsy of the temporal artery, which was negative for giant cell arteritis. After 1 week of treatment, her BCVA in the left eye had significantly improved (Snellen 20/60). MRI of the head and orbits showed abnormal mid to posterior intraconal portion of the optic nerve left side consistent with an ischemic optic neuropathy such as NAION (Fig 2, *A* and *B*), and there were no MRI findings consistent

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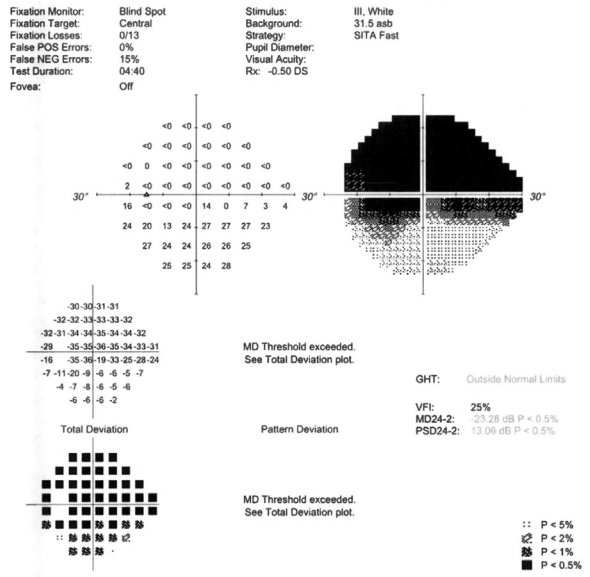

Fig 1. Non-arteritic anterior ischemic optic neuropathy (NAION). Humphrey Visual Field 24-2 of the *left eye* showing superior altitudinal defect at the patient's initial ophthalmology visit.

with multiple sclerosis (Fig 2, *C* and *D*). As the condition stabilized, the oral prednisone was gradually tapered down to 5 mg once daily until the following appointment.

Two months from the initial presentation, the ocular pain had completely resolved, her BCVA in the left eye had returned to baseline (Snellen 20/30), and the positive RAPD was less prominent. Since then, the patient has had no ocular complaints, and her condition has remained stable. In the meantime, her HS has been adequately treated with intralesional triamcinolone injections and oral antibiotics. Combination antibiotic therapy, spironolactone, and metformin were considered if her HS was refractory to current treatment.

DISCUSSION

HS is a chronic inflammatory dermatologic condition that causes lesions particularly in apocrine-rich areas and intertriginous areas.[3] The hypothesized pathogenesis of HS begins with hyperkeratinization of the follicular infundibulum occluding the follicular isthmus, thus leading to a pathologic cycle of inflammation, abscess formation, and resultant rupture which results in further disease progression and eventual sinus tract formation.[4] Skin biopsy of HS lesions have demonstrated significantly elevated cytokine secretions from dendritic cells, monocytes, and macrophages, which were reduced on repeat biopsy after 16 weeks of adalimumab treatment. Interestingly, the TNF receptors rather than TNF-α itself were reduced.[4]

NAION typically presents with acute unilateral loss of vision, optic disc edema, RAPD, and visual field defects.[5] Although adalimumab has been associated with retinal pathologies and optic neuritis as an early manifestation of multiple sclerosis in patients with pre-existing autoimmune conditions, NAION has rarely been reported with adalimumab use.[2,6] NAION has been documented in cases that used 40 mg adalimumab biweekly for HLA-B27-positive ankylosing spondylitis and rheumatoid arthritis for 17 and 6 months, respectively,[7,8] both of which are commonly linked to uveitis, a known risk factor for NAION.[2]

Our patient received adalimumab at higher frequency (40 mg weekly) and longer duration (48 months total) than is often used for other conditions. Furthermore, she did not develop ocular symptoms while on her initial 33-month course of adalimumab but rather after re-starting it after a 5-month hiatus. Additionally, our patient had an extensive history of severe AD, which has been associated with numerous ocular manifestations, including cataracts, keratoconus, retinal detachment, herpes infection, and glaucoma.[9] AD has not, however, been associated with ocular nerve defects such as NAION.

Several adverse events were documented during the 12-week study period and the subsequent 70-day observation period of the PIONEER I and II phase 3 clinical trials that led to the Food and Drug Administration approval; however, no ocular complications were noted.[1] A large retrospective review found that the incidence of HS among Black patients was 2.5 times higher than that of White patients.[10] This finding calls into question the generalizability of the findings of the PIONEER I and II phase 3 clinical trials, as the patient demographics were 80.1% White patients and 14.4% Black patients.[1] Future studies with higher external validity are necessary to better understand the association among adalimumab, HS, and ocular adverse events.

Overall, awareness of NAION as a possible consequence of adalimumab therapy should be brought to the attention of dermatologists, as this medication is used for numerous inflammatory and autoimmune disorders. Patients on adalimumab presenting with sudden-onset unilateral ocular pain and/or decreased vision should prompt concern for possible NAION. Immediate discontinuation of adalimumab treatment and urgent ophthalmologic consultation can aid in avoiding potential sight-threatening complications. Our patient's adalimumab-induced NAION was successfully managed using an oral prednisone taper, a

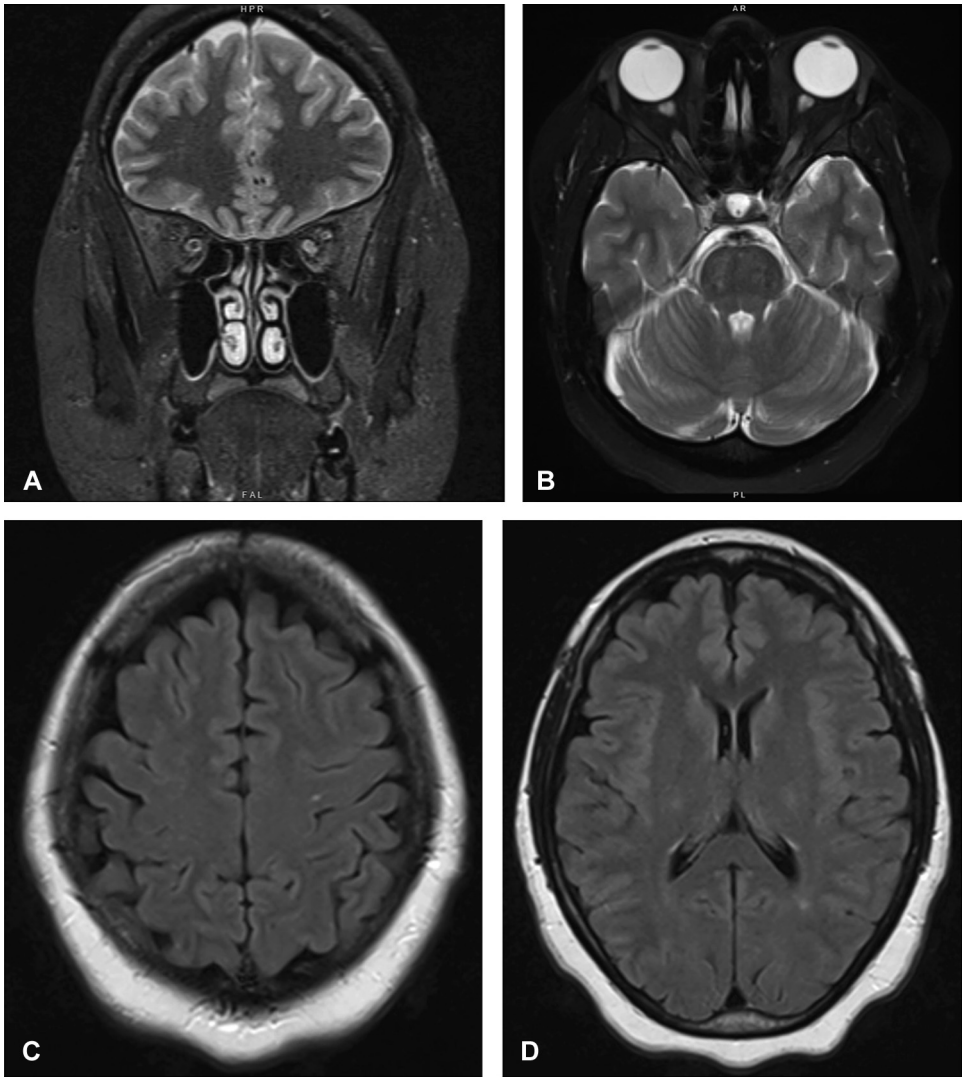

Fig 2. Non-arteritic anterior ischemic optic neuropathy (NAION). **A,** Orbital MRI Coronal T2 section showing increased signal in the mid to posterior aspect of the conal portion of the *left optic nerve*; (**B**) Orbital MRI Axial T2 section demonstrating asymmetry in the affected portion of the *left optic nerve*. Length of the involved area was estimated to be 15 mm. *Right optic nerve* chiasm appeared normal; Head MRI Axial Fluid-attenuated inversion recovery (FLAIR) with several small punctate areas of gliotic change identified in (**C**) *left frontal* region and (**D**) paraventricular region but deemed to be benign and nonspecific to the presenting symptoms. The remainder of MRI findings appeared normal.

treatment commonly used for NAION of other etiologies, until resolution of the ocular manifestations.

Conflicts of interest

None disclosed.

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