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CASE REPORT

Anterior Uveitis in an HLA-B27 Positive Patient Following Influenza Vaccination

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Purpose: To report a case of acute anterior uveitis occurring shortly after influenza vaccination in a patient with HLA-B27 positivity, highlighting the potential role of genetic susceptibility in vaccine-related ocular inflammation.

Case Summary: A 35-year-old Asian male experienced progressive unilateral ocular redness, pain, and blurred vision starting from three days after receiving the trivalent influenza vaccine. Ophthalmic examination afterwards demonstrated conjunctival injection, fine keratic precipitates, anterior chamber flare and cells, and posterior synechiae with normal intraocular pressure. Diagnostic workup was unremarkable except for HLA-B27 positivity. The patient was diagnosed with unilateral acute non-granulomatous anterior uveitis and successfully treated with topical corticosteroids and cycloplegics, with resolution of inflammation and no recurrence over six months of follow-up.

Conclusions and Importance: The index report highlights that HLA-B27 positive individuals may be particularly vulnerable to diverse systemic triggers, including vaccines.

Keywords: uveitis, influenza vaccination, autoimmune disease, HLA-B27

Introduction

Uveitis refers to inflammation of the uveal tissues of the eye, including the iris, ciliary body, and choroid. Uveitis accounts for 10–20% of blindness in the United States and Europe and can be associated with significant visual morbidity.[1] The etiology of uveitis may be infectious, non-infectious, or idiopathic when no specific underlying condition can be identified.[2,3] Among all forms of uveitis, Human Leukocyte Antigen B27 (HLA-B27)-associated acute anterior uveitis is a most common clinical entity that mainly affects young patients.[4]

Influenza vaccines have been widely utilized to prevent influenza, with 170 million doses distributed in the United States in 2023. Although it is generally considered safe across populations, numerous adverse events, including anaphylaxis, Guillain-Barré syndrome and various forms of uveitis, have been documented following vaccination.[5] While anterior uveitis is the most common ocular manifestation, other conditions such as multifocal choroiditis, APMPPE, and MEWDS have also been reported in clinical literature.[6]

Herein we present a case of acute non-infectious HLA-B27-associated anterior uveitis (AU) that developed shortly after the administration of the influenza vaccine.

Case Presentation

A 35-year-old Asian male with no known systemic or ocular health conditions received Afluria Trivalent (IIV3) influenza vaccine, an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza

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A subtype viruses and type B viruses contained in the vaccine. No relevant medical or surgical history. Ocular history was unremarkable except for high myopia.

Three days post-vaccination (Day 3), he experienced redness and pain in his right eye (OD), and given the persistence of symptoms, the patient sought medical attention from a non-ophthalmology physician at an Express Care Clinic on Day 5. Ocular examination revealed conjunctival hyperemia with no other significant findings noted. He was diagnosed with acute bacterial conjunctivitis with prescription of topical ciprofloxacin and olopatadine.

On Day 6, his ocular pain worsened with the development of photophobia and blurry vision. Therefore, the patient visited an Emergency Department (ED) where he was examined by an ophthalmologist. His best-corrected visual acuity (BCVA) was 20/25 in both eyes (OU). The intraocular pressure (IOP) was 10 mmHg OD and 13 mmHg in his left eye (OS). No flare or cells were observed in the anterior chamber (AC) OU, and the conjunctival injection OD was significantly blanched with 2.5% phenylephrine eyedrop. The findings were in line with the diagnosis of episcleritis and oral indomethacin 50 mg, three times daily, was prescribed.

Four days following the NSAID treatment (Day 10), there was a mild decrease in the ocular pain with persistent photophobia OD. Therefore, the patient revisited the ED to follow up with ophthalmology. BCVA was 20/20 OU and slit-lamp examination revealed fine keratic precipitates (KPs) with 3+ AC cells and flare and posterior synechia OD. IOP was 8 mmHg OD and 14 mmHg OS. Fundus examination OU revealed tigroid appearance, tilted optic disc with peripapillary atrophy. Moreover, no lesions were observed on the macula, optic nerve or retinal vessels OU. Peripheral myopic chorioretinal degeneration with pigmentation was noted inferiorly and temporally OU (Figure 1). Spectral-domain optical coherence tomography (SD-OCT) showed partial posterior vitreous detachment, myopic foveal contour with no macular edema OU. Extensive laboratory tests, including *Bartonella* DNA, *Toxoplasma* DNA, Lyme disease antibody, *Treponema* screen, rapid plasma reagin (RPR), QuantiFERON test, angiotensin converting enzyme (ACE), human leukocyte antigen (HLA), HSV1-DNA, HSV2-DNA, CMV IgG, CMV IgM, lysozyme, chest X-Ray, and urinalysis screen, were performed. All results were unremarkable except for a positive HLA-B27 and mildly elevated ACE level (90 U/L, normal range: 16–85 U/L). CMV IgG was positive with negative IgM. A chest CT scan showed no signs of sarcoidosis. The diagnosis of acute unilateral non-granulomatous HLA-B27-associated AU was made and the treatment was changed to topical prednisolone acetate 1% one drop every two hours and cyclopentolate 1%, three times daily with a referral to a uveitis specialist.

On the patient's visit to the Uveitis Service on Day 20, symptoms had markedly improved with decreased photophobia. Slit lamp examination was unremarkable in OS and revealed 1+ AC cells and flare with no KPs or posterior synechia OD. Posterior segment evaluation demonstrated no evidence of inflammation. Fundus fluorescein angiography (FFA) was performed and showed clear view with no evident macular, perivascular or optic nerve leakage OU. Peripheral staining corresponding to the myopic chorioretinal degeneration was noted inferiorly and temporally (Figure 2). The patient was reassured that the inflammation is resolving with a recommendation of slow tapering of topical steroids over 12 weeks and monitoring of any signs of deterioration such as pain, photophobia, blurry vision or floaters. A further

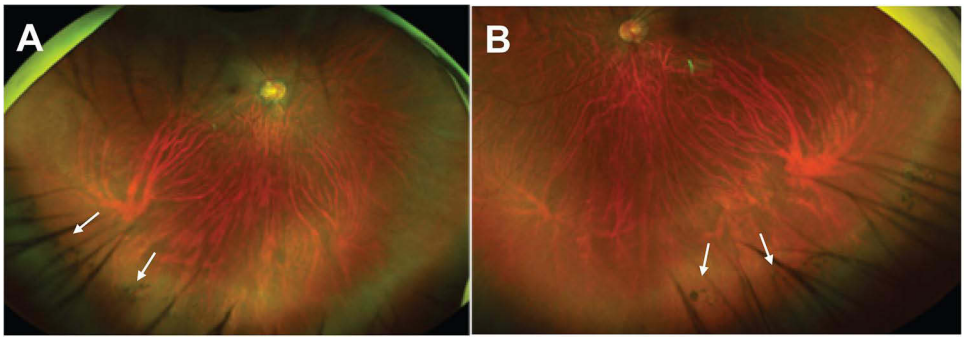

Figure 1 Fundus photos of right (**A**) and left (**B**) eye show clear view, tigroid appearance, tilted optic disc with peripapillary atrophy. No lesions were observed on macula, optic nerve or retinal vessels. Peripheral myopic chorioretinal degeneration with pigmentation noted inferiorly and temporally (white arrow).

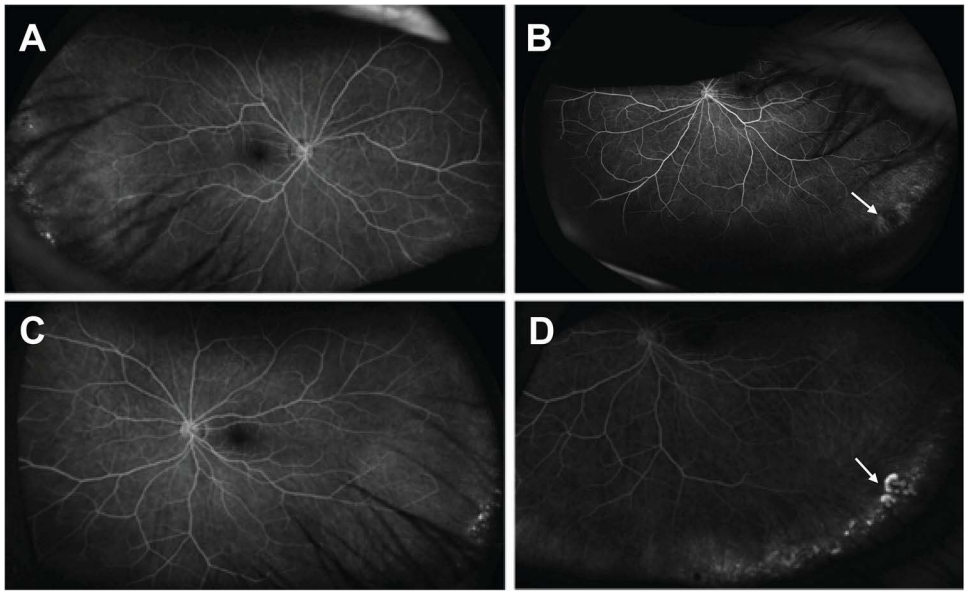

Figure 2 Fundus fluorescein angiography (late phase) of right (**A** and **B**) and left (**C** and **D**) eye reveal clear view with no evidence of macular, perivascular or optic nerve leakage. Peripheral staining corresponding to the myopic chorioretinal degeneration is noted inferiorly and temporally (white arrows).

evaluation with a rheumatologist confirmed erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are within normal value. There is no evidence of systemic involvement related to HLA-B27 positivity.

By week four, the patient demonstrated resolution of symptoms with AC cell reduced to a 0.5+ level. Topical steroid tapering continued, with no recurrence noted at a six-month follow-up.

Discussion

Generating a Diagnosis

The index case represents a rare instance of unilateral HLA-B27-associated acute anterior non-granulomatous uveitis following influenza vaccination. The patient had no previous history of systemic or ocular disease. The disease onset occurred three days following the vaccination which suggest that the influenza vaccine could be a plausible trigger for the immune system with subsequent occurrence of HLA-B27 associated AU, although causality cannot be definitively proven.

On Day 6, the patient's clinical status progressed, characterized by intensified ocular pain, new-onset photophobia, and blurred vision. Despite these classic indicators of intraocular inflammation, the initial diagnosis of episcleritis was maintained. The transition to a diagnosis of uveitis was not formally recognized until Day 10. Retrospectively, earlier awareness of the patient's recent vaccination history—a known systemic immune trigger—might have increased the index of suspicion for an autoimmune etiology, potentially facilitating an earlier diagnosis and mitigating the observed four-day diagnostic delay.

Uveitis following influenza vaccination, though rare, has been documented in the literature.[6–9] Therefore, vaccination history should be routinely explored during evaluations of ocular inflammation.

Proposed Immunological Mechanisms: HLA-B27 is Prone to Be Activated in Response to Certain Vaccine Antigens

Several immunological mechanisms have been reported to contribute to vaccination-induced autoimmune responses, including molecular mimicry[10] and bystander activation.[11] It is possible that molecular mimicry occurs when influenza vaccine antigens resemble ocular self-antigens, causing HLA-B27 to present these peptides to CD8+ T-cells, potentially activating autoreactive T-cells and inducing ocular inflammation.[12] As the primary site for antigen presentation, the tissue-draining lymph node likely plays a critical role in the initial activation and expansion of specific autoreactive T cell

clones.[13] However, it remains unclear whether the patients' regulatory T cells (Tregs) fail to suppress the dysregulation of these autoreactive T cell clones in this context because of vaccination or the patient's HLA typing and immune alteration. Additionally, general immune activation triggered by the vaccine can cause systemic inflammation through the release of cytokines and chemokines, potentially leading to bystander activation of immune cells that inadvertently target ocular tissues.[14] Certain adjuvanted influenza vaccines designed to enhance immune responses have been proposed to contribute to autoimmune activation through mechanisms associated with Autoimmune/Inflammatory Syndrome Induced by Adjuvants (ASIA).[15]

Why Was the Inflammation Unilateral?

The patient in the current case developed uveitis only in the right eye. Upon reviewing the literature, we found that both unilateral[16] and bilateral uveitis[8,9,17,18] have been reported after influenza vaccination. One possibility is that the right eye had pre-existing conditions, such as ocular surface inflammation, which can alter chemokine expression in the local tissue and attract activated immune cell infiltration, such as T cells, making it more susceptible to developing an autoimmune response following vaccination compared to the other eye.[19] Another explanation is that the immune system can sometimes mount a localized response rather than a systemic one. Such scenario could occur if the immune activation following the vaccine inadvertently targets one eye due to minor variations in local immune surveillance or tissue markers.[20] Indeed, influenza vaccines have also been reported to trigger unilateral symptoms in Guillain-Barré Syndrome[21] and juvenile rheumatoid arthritis.[22]

In addition to vaccines, other potential triggers have been implicated in the development of unilateral ocular inflammation in HLA-B27 positive individuals. For instance, Regenold et al described a similar case of acute anterior uveitis with macular edema triggered by sildenafil citrate in an HLA-B27 positive patient.[23] Similar to our case, there was a close temporal association between the vaccination and the onset of ocular inflammation.

Further research is needed to provide a better understanding of the immunological mechanisms underlying vaccine-associated uveitis and to establish guidelines for managing such cases in susceptible populations.

Conclusion

This case highlights a potential increased susceptibility to immune-mediated ocular inflammation in HLA-B27–positive individuals following systemic triggers such as vaccination. Although rare and manageable, clinicians should remain vigilant for post-vaccination ocular symptoms in predisposed patients. Vaccination should not be discouraged; rather, emphasis should be placed on early symptom recognition and prompt management.

Declaration of Generative AI and AI-Assisted Technologies in the Manuscript Preparation Process

During the preparation of this work the authors used ChatGPT4o to assist language polishing. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Patient Consent

A written informed consent has been provided by the patient to have the case details and any accompanying images published. Institutional approval was not required for the publication of this individual case report.

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Disclosure

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