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Case Report

Ocular Presentation of Behcet's Syndrome Associated with Covid-19 Vaccination

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Abstract

Purpose: To shed some light on the long debate as to whether autoimmune diseases might also be triggered by vaccines, through the immune cross-reactivity mechanism.

Observations: We report a case of bilateral pan uveitis and vasculitis, being a first presentation of Behcet syndrome in a young healthy patient who received COVID-19 vaccine. The vaccine might have triggered de novo ocular inflammatory process or ocular exacerbation of an impending Behcet disease, through the immune cross-reactivity mechanism. The patient was treated with oral prednisone and azathioprine with good response. Conclusions and Importance: In our case it might be due to de novo ocular inflammatory process or due to ocular exacerbation of an impending Behcet disease, both might have been triggered by the COVID-19 vaccine the patient received It is important for clinicians to be aware of the association we encountered, and for future post-marketing studies of COVID-19 vaccine to address it.

Conclusions and Importance: In our case it might be due to de novo ocular inflammatory process or due to ocular exacerbation of an impending Behcet disease, both might have been triggered by the COVID-19 vaccine the patient received It is important for clinicians to be aware of the association we encountered, and for future post-marketing studies of COVID-19 vaccine to address it.

Keywords: Behcet's Syndrome; COVID-19 Vaccination

Introduction

The incidence of uveitis after vaccination is reported to range from 8 to 13 in 100000 persons/year [1]. Several vaccines have been implied to cause uveitis including those against influenza, varicella zoster, diphtheria-tetanus-pertussis, Bacillus Calmette-Guérin (BCG), hepatitis B, hepatitis A, brucella, Human Papilloma Virus (HPV), pneumococcus, and Measles-Mumps-Rubella (MMR) [2]. Vaccination can induce all types of uveitis including specific ocular syndromes such as Multiple Evanescent White Dot Syndrome (MEWDS), Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE), or Vogt-Koyanagi-Harada (VKH), vasculitis, and pan uveitis [3-9]. Three mechanisms have been proposed for vaccine-induced uveitis, by perpetuation of the immune system [10]. Recrudescence of a previously quiet inflammation was reported in after some immunizations, suggesting that a vaccine might not only trigger de novo inflammatory processes but also exacerbate pre-existing inflammation [11]. The COVID-19 has spread worldwide, leading to an ongoing pandemic, necessitating global vaccination programs on the rapid timeline and scale of COVID 19 infections during 2020. Israel leads the world in COVID-19 vaccinations and has vaccinated nearly 40% of its population in just over two months. It has almost exclusively been using the two-

shot COVID-19 vaccine developed by Pfizer and BioNTech, which is composed of nucleoside-modified Messenger Ribonucleic Acid (mRNA) (modRNA) encoding a mutated form of the spike protein of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The COVID-19 vaccines have not so far caused worrisome side effects related to vision and have not so far been implicated.

Case Report

We report on a healthy 20-year-old male who developed photophobia and visual disturbances 10 days after receiving the first dose of Coronavirus disease 2019 (COVID-19) vaccine injection. In addition, he developed a few aphthous ulcers, and a pseudo folliculitic rash appeared on his back with acneiform nodules. Upon presentation, ophthalmic examination revealed bilateral corneal Keratic Precipitates (KPS), cells and flare in anterior chamber. Fundoscopy showed bilateral vitritis, bilateral mild retinitis and mild signs of vasculitis in both eyes, including focal perivascular sheathing and intraretinal infiltrates (Figure 1). Fluoresceine Angiography (FA) demonstrated bilateral temporal peripheral vascular wall attenuation and perivascular hyper fluorescence, suggesting capillary leakages. There was also a small peripheral temporal area of capillary non-perfusion, with no signs of retinal neovascularization (Figure 2). Work up for infectious and inflammatory diseases was inconclusive. Skin pathergy test was negative. The patient was found positive to Human Leukocyte Antigen B51 (HLA-B51). There were no other organ systems involved in the disease. Our patient had bilateral pan uveitis with signs of vasculitis upon presentation. He was diagnosed with Behcet disease based on the International Study Group Criteria (1990) due to his ocular presentation, oral ulcers, and pathognomonic skin lesions. No other underlying disease had been found. He was treated with oral prednisone. A follow up over 3 weeks showed significant clinical improvement with resolution of inflammatory signs in the anterior chamber and vitreous, and improvement of vasculitis signs in both eyes. Prednisone was tapered to a lower dose, and azathioprine treatment was initiated for a long-term effect. A follow-up over 6 months was uneventful.

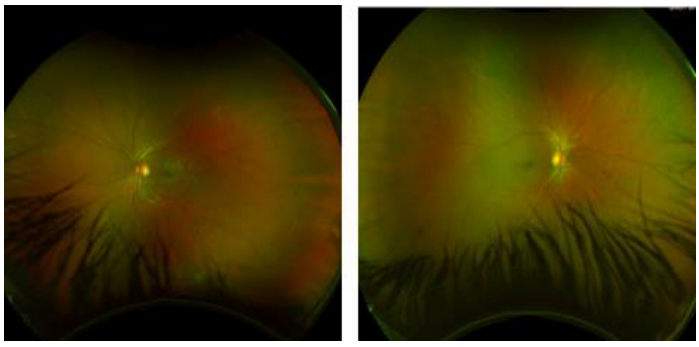

Figure 1: Optos wide-field fundus examination showing bilateral peri-vascular sheathing, vasculitis, and retinitis.

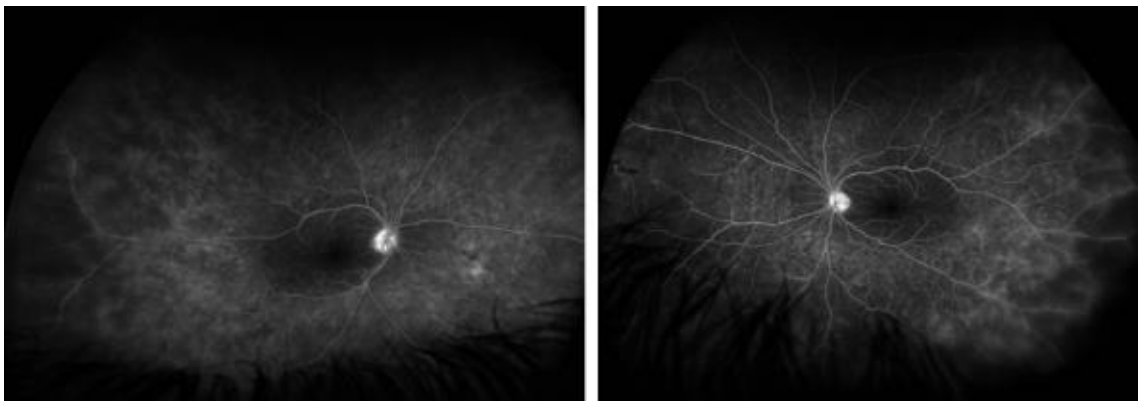

Figure 2: Optos Wide Field Fluorescein Angiography late phase demonstrating bilateral temporal vascular wall attenuation and perivascular hyper fluorescence, suggesting leakages.

Discussion

Behcet disease is a systemic vascular disease that can affects a variety of organ systems. Ocular manifestations carry the most serious implications, affecting roughly 70% of patients [12]. The severity is due to recurrent nature of the uveitis, which can lead to permanent, often irreversible, ocular tissue damage. The most significant damage is due to retinal vasculitis, which can cause vascular occlusions, hemorrhages, and macular edema, with significant visual loss [13]. There were previous reports of Behcet disease exacerbation following other vaccinations, like Typhoid [14] and Pneumococcal polysaccharide [15]. Our patient is a previously healthy young individual, who presented with a new onset of bilateral pan uveitis and vasculitis, combined with a previous history of oral ulcers, and late appearance of skin lesions. Ocular disease is the first presentation in only 10-20% of Behcet cases [16]. In our case it might be due to de novo ocular inflammatory process or due to ocular exacerbation of an impending Behcet disease, both might have been triggered by the COVID-19 vaccine he received. In our case, the diagnosis and treatment prevented further development of Behcet extra ocular manifestations. The association between infection and autoimmune disease has stimulated a long debate as to whether such diseases might also be triggered by vaccines, through the immune cross-reactivity mechanism [17].

Conclusion

Several cases associating uveitis with vaccination have been published in the past, but no association has yet been suggested considering the newly authorized COVID-19 vaccine. With ongoing vaccination efforts worldwide, it is important for clinicians to be aware of the association we encountered, and for future post-marketing studies of COVID-19 vaccine to address it.

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.

Declarations

a. Ethics approval and consent to participate- Not applicable.

b. Consent for publication- Not applicable.

c. Availability of data and material- Not applicable (patient's anonymity is protected, patient presented is unidentifiable).

d. Competing interests - The authors declare that they have no competing interests.

e. Funding - None.

f. Author's contributions - SV was first to examine the patient and suggesting diagnosis, analyzed and interpreted the patient data, and wrote the manuscript. BS followed and treated the patient and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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b. Competing interests - The authors declare that they have no competing interests.

c. Conflicts of interest - The following authors have no financial disclosures: SV, BS

d. Authorship: All authors attest that they meet the current ICMJE criteria for Authorship.

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