

## Acute Bilateral Uveitis Following COVID-19 Vaccination: Case Reports

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### Abstract

**Introduction:** The development of the COVID-19 vaccines occurred promptly, and we are still learning about their side effects. Therefore, it is important to report possible medical associations to them.

**Case 1:** A 21-year-old female, with no significant medical history for this event, diagnosed with bilateral acute anterior uveitis three days after receiving the Pfizer-Biontech COVID-19 vaccine. An aggravation of the disease was observed after the administration of the second dose.

**Case 2:** A 70-year-old male, with no relevant medical history, presenting with a bilateral anterior uveitis after receiving the Pfizer-Biontech COVID-19 vaccine 3 to 4 weeks before. A macular edema of the right eye developed later in the course of the disease.

**Discussion:** Vaccines can induce uveitis and other ocular inflammatory conditions through different possible mechanisms. In both cases we reported here, the temporal relationship between the onset of the symptoms and the administration of the vaccines makes this medication a possible cause for the ocular manifestation.

**Keywords:** Uveitis; COVID-19; Vaccination; Adverse Drug Reaction; Ocular Inflammation

### Abbreviations

AAU: Anterior Acute Uveitis; IOP: Intraocular Pressure; LE: Left Eye; OCT: Optical Coherence Tomography; RE: Right Eye; VA: Visual Acuity

### Introduction

Throughout the years, there were many examples of vaccines that have been associated with adverse ocular manifestations, such as uveitis following the yellow fever vaccine, acute idiopathic maculopathy after H1N1 vaccine, Vogt-Koyanagi-Harada disease subsequent to hepatitis B vaccine or a white dot syndrome after influenza vaccination [1-6]. With the rapid emergence of

the vaccines against the SARS-CoV-2 there has also been some reports concerning possible secondary ocular effects to the administration of the different vaccines. Some examples are Bell's palsy, abducent nerve palsy, acute macular neuropathy, central serous chorioretinopathy, ophthalmic vein thrombosis, corneal graft rejection and new onset uveitis [7-13]. The development of these vaccines occurred in less than one year and long-term data of side effects are still developing thus the importance of reporting possible associations [10].

The purpose of this article is to report the cases of two patients with bilateral uveitis following the administration of Pfizer-Biontech COVID-19 vaccine that were observed in our Ophthalmology Department in August 2021.

### Case Report 1

A 21-year-old female, with a medical history of epilepsy and asthma, came to our emergency department with bilateral red eye, associated with photophobia and pain. She denied any reduction in her visual acuity, though she had a great difficulty at opening her eyes. The slit lamp examination showed ciliary conjunctival hyperemia and anterior chamber cells 2+ and flare 2+. The fundoscopic examination was unremarkable. Intraocular pressure (IOP) was 10 mmHg in both eyes. She referred having received the first dose of the Pfizer-Biontech COVID-19 vaccine three days before. She was diagnosed with a bilateral nongranulomatous anterior acute uveitis (AAU) and was medicated with dexamethasone hourly with night pause, prednisolone ointment at night and a cycloplegic agent (cyclopentolate twice daily). However, one week later little improve was observed since she maintained the same alterations at the slit lamp examination though feeling better. A subconjunctival injection of dexamethasone was administered, and she was referred to the ocular immunopathology specialist.

At the meantime, the patient received the second dose of the vaccine and perceived a worsening of the pain and photophobia after it. At the medical appointment eleven days after her last evaluation, she maintained the same clinical status, with maintenance of the visual acuity (VA) (0.8 at the right eye (RE) and 1.0 at the left (LE), with no correction), and no improvement at the slit lamp examination but still with no fundoscopic alteration (Figure 1). Blood workup including the hemogram, erythrocytes sedimentation rate, C-reaction protein, renal function, ionogram, immunoglobulins, protein electrophoresis, rheumatoid factor, interferon gamma release assay, antinuclear antibodies, HLA-B27, HLA-B51 and antineutrophil cytoplasmic antibodies, were all normal, and the serologies showed no relevant alterations or recent infection (anti-cytomegalovirus IgG positive and IgM negative, human immunodeficiency virus negative, anti-Ebstein-Barr virus EBNA and VCA IgG positive and VCA IgM negative, anti-toxoplasma IgG and IgM negative, anti-treponema pallidum IgG and IgM negative, anti-Borrelia burgdorferi IgG and IgM negative, anti-herpes simplex 1 IgG positive and IgM negative, anti-herpes simplex 2 IgG and IgM negative, anti-toxocara canis IgG negative). The anti-leptospira IgG and IgM showed a borderline value for positivity, but it was considered a false positive in this context. Urinary analysis was also normal.

**Figure 1:** OCT of the right and left eye (case 1).

She was started on oral prednisolone and continued with topical corticosteroid. The inflammatory activity observed at the anterior chamber diminished two months later (cells 1+ and flare 1+) and an extremely slow tapering of the oral and topical corticosteroids was tried. Only six months after her diagnosis was she inflammation-free and in her last appointment (eight months after the diagnosis) she was on none corticosteroid treatment with cells 0+ and flare 0+. During this period, she maintained without any lesion at the posterior pole.

### Case Report 2

A 70-year-old male, with a medical history of hypertension, dyslipidemia and rhinitis, attended our emergency department complaining of decreased visual acuity, redness and photophobia of both eyes with about 3 to 4 weeks of evolution, which started after receiving the second dose of the Pfizer-Biontech COVID-19 vaccine. He had a VA of 0.8 on the RE and 0.4 on the LE. Slit lamp examination showed ciliary conjunctival hyperemia, granulomatous keratic precipitates and cells at the anterior chamber (1+ on his RE and 2+ on his LE) and flare (1+ on his RE and 2+ on his LE). IOP was 14 mmHg at both eyes. No alteration was observed at the funduscopy. He was diagnosed with a granulomatous AAU was medicated the same way as the previous patient (dexamethasone, prednisolone ointment and a cycloplegic agent) and a systemic investigation similar to the previous case was also conducted with no relevant alterations.

A week later he returned for observation and had had an improvement of his clinical status with a decrease in the keratic precipitate and in the number of cells at the anterior chamber and no new findings. However, 21 days after, the patient sustained complaints of a decreased VA of the RE from 0.8 to 0.4 (VA of the LE improved to 0.8). A macular edema was observed at the fundoscopic evaluation and at the optical coherence tomography (OCT) (Figure 2). He was started on oral prednisolone and topical

nepafenac, with improvement observed a month later. A tapering of the oral corticosteroid was tried with a worsening of the macular edema, so the frequency of the topical corticosteroid was raised and so was the dose of the oral medication. Four months after the diagnosis he had cells 1+ and flare 1+ at both eye and a substantial improvement of the macular edema of the left eye. However, the oral corticosteroid had to be stop due to the diagnosis of a cancer and the need to start chemotherapy. Therefore, six months after the diagnosis (at his last follow-up appointment) an aggravation of the macular edema was observed.

**Figure 2:** OCT of the right eye (case 2).

## Discussion

Nearly one-half of all uveitis cases have no identifiable cause. Systemic, topical, and intravitreal medications as well as vaccines can induce uveitis and other ocular inflammatory conditions [14]. Some examples of vaccines that can cause this inflammatory pathology are described in the literature as referred before [1-6]. The mechanism of the disease in these cases is not fully understood and it can be caused by a direct insult from drug toxicity or an indirect process such as an immune-mediated vasculitis [14]. Some possible explanations for this reaction are the resemble between the vaccine peptide fragments and the uveal self-peptides (molecular mimicry); the damage caused by vaccine adjuvants; direct viral infection when vaccines are live or attenuated; and the deposition of immune complexes (delayed-type hypersensitivity) [15].

In a large review done in 2015, the median time from vaccination to onset of uveitis was 16 days and it reported the possibility of recurrence after redosing (this was verified, for example, with the Hepatitis B vaccine) [16]. In both cases we reported here, the temporal relationship between the onset of the symptoms and the administration of the vaccine makes this medication a possible cause for the ocular manifestation observed. Also, an aggravation was observed in the first case after the second dose of the vaccine

was administered, which corroborates this hypothesis. When applying the Naranjo Adverse Drug Reaction Probability Scale [17], we obtain a score of 5 for the first case (probable causality for the adverse drug reaction) and a score of 3 for the second case (possible causality for the adverse drug reaction).

It has been reported that the median duration of vaccine-associated uveitis is 346 days, thus it is expected that cases related to vaccines have a slow resolution, which is being observed in this two cases who aren't completely resolved yet [14]. These patients didn't have any prior history of uveitis or rheumatologic pathology and they had a severe presentation of the disease, both bilateral and the first one with a non granulomatous AAU difficult resolution and the second one with a macular edema later in the course of the disease. There are cases already reported that also show a severe presentation of uveitis after the Pfizer-Biontech and Oxford-AstraZeneca COVID-19 vaccines [13,18].

## Conclusion

Attention must be taken by the ophthalmologists to cases like these in order to report these situations to the competent entity of each country and allow a deeper knowledge about the ocular side effects of the COVID-19 vaccines. However, it is important to refer that so far, all vaccines have shown promising efficacy and a low incidence of adverse effects; the benefits outweigh potential risks, since these manifestations are rare [18].

## Declaration of Interest

The authors report no conflict of interests.

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