

# UVEITIS FOLLOWING COVID-19 VACCINATION: A CASE REPORT AND A LITERATURE REVIEW

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**ABSTRACT – Objective:** This case-based review aims to list all the cases previously published in the literature about COVID-19 related to uveitis and to add a new case.

**Materials and Methods:** We searched articles about COVID-19 and uveitis.

**Case presentation:** A 51-year-old male patient with no previous chronic diseases received a diagnosis of AS in 2012 due to low back pain and recurrent uveitis. After he received his first dosage of the COVID-19 vaccine (Oxford-Astra-Zeneca, Fiocruz, Rio de Janeiro, Brazil) on Jun 17th, 2021 he experienced a new uveitis crisis (after 17 days) on his right eye, diagnosed by the ophthalmologist, which was characterized by a mild picture of light pain eyes, red eyes, and light sensation of a foreign body in the eye.

**Results:** A total of 86 patients are described, with the majority affected being male (52/86) and with a mean time to onset of uveitis symptoms after vaccination of 9.95 days. Patients with a history of uveitis accounted for 45% of the cases, while 18% had other previous diseases. The rate of patients who received drug treatment was 80%, while 89% corresponded to the patients who had a complete recovery.

**Conclusions:** This study reviewed all cases and adds one more case for uveitis after COVID-19 vaccine.

**KEYWORDS:** Vaccine, Vaccination, Uveitis, Immunization, COVID-19, Coronavirus disease 2019.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a pandemic infection initiated in 2019 in Wuhan (China) and spread out worldwide. Nowadays, about 5 million deaths occurred after COVID-19, and the most important weapon against this disease is the vaccination process. In November 2021, there were 247.968.227 cases confirmed, 5.020.204 deaths, and 7.027.377.238 vaccine doses as registered by the World Health Organization<sup>1</sup>.

There are presently four types of COVID-19 vaccines, and they are: (1) mRNA vaccines (BNT162b2, Pfizer-BioNTech; mRNA-1273, Moderna), (2) protein subunit vaccines (NVX-CoV2373, Novavax), (3) vector vaccines (Ad26.COVS2, Janssen Johnson & Johnson; and ChAdOx1 nCoV-19/ AZD1222, Oxford- AstraZeneca), and (4) whole virus vaccines (PiCoVacc, Sinovac; BBIBP-CorV, Sinop harm)<sup>2</sup>. The vaccine is efficacious and safe. Although there are reports on the side effects of the COVID-19 vaccine, a few cases of uveitis have been described. About 7 case reports and three case series with 86 cases of uveitis following the COVID-19 vaccine are described in the literature<sup>3-12</sup>. Herein, we added a new case of uveitis following the COVID-19 vaccine in a patient with ankylosing spondylitis (AS).

This article aims to add one more case relating to uveitis and the COVID-19 vaccine and to list the cases already reported in the literature on this topic.



## MATERIALS AND METHODS

This article presents a descriptive and transversal study performed through the retrospective analysis of the chart of one patient diagnosed with AS according to the modified New York criteria<sup>13</sup> and uveitis after the COVID-19 vaccine.

### Bibliographic Review

We searched articles related to COVID-19 and uveitis involving the following keywords: “uveitis”, “vaccination”, and “COVID-19”. The articles found were reviewed about demographic characteristics (gender, age), clinical characteristics (previous disease, types of uveitis), vaccine type, complication uveitis following the first and second dose of vaccine, the time between vaccine and uveitis, treatment and outcomes. The literature search found 10 articles (3 case series and 7 case-related) on the field of coveting and uveitis-related disorder and added one new case (Table 1).

### Case Report

A 51-year-old male patient with no previous chronic diseases received a diagnosis of AS in 2012 due to low back pain and recurrent uveitis. Blood analysis, including the white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), showed no alterations, and HLA-B27 was positive. It was evidenced sacroiliitis bilateral on magnetic resonance imaging. The patient was treated with methotrexate 25 mg/week, glucocorticoid eye drops, and cycloplegic agent (atropine 1%) twice daily, besides a gluten-free diet and physical exercises, with reasonable disease control. He was stable when on Jun 17th, 2021, he received his first dosage of the COVID-19 vaccine (Oxford-Astra-Zeneca, Fiocruz, Rio de Janeiro, Brazil). On July 3rd, 2021 (after 17 days), he experienced a new uveitis crisis on his right eye, diagnosed by the ophthalmologist, which was characterized by a mild picture of light pain eyes, red eyes, and light sensation of a foreign body in the eye. Ocular examination showed pericheratic and conjunctival hyperemia. The posterior segment did not show any alteration. He was treated with dexamethasone eye drops every 6 hours with a quick clinical response after 2 days, tapering in the glucocorticoid in 7 days. AS remained stable, with no other sign of disease activity. After 6 months of the uveitis, the patient continued to receive one additional dose of vaccination, and he did not have a uveitis flare.

## RESULTS

A total of 86 patients are described, with the majority affected being male (52/86) and with a mean time to onset of uveitis symptoms after vaccination of 9.95 days (1–30 days). Patients with a history of uveitis accounted for 45% (39/86) of the cases, while 18% (16/86) had other previous diseases, as mentioned in Table 1. The rate of patients who received drug treatment was 80% (69/86), while 89% (77/86) correspond to the patients who had complete recovery.

## DISCUSSION

This study adds a new case among those reported in the literature in which the patient with a previous history of AS had uveitis following the COVID-19 vaccine. Additionally, we reviewed all the cases previously published in the literature about uveitis after the COVID-19 vaccine.

There is an extraordinary amount of data regarding uveitis following different vaccines<sup>14,15</sup>. For example, a recent review including 289 patients revealed that against hepatitis B virus vaccine appeared to be the most crucial cause of vaccine-associated uveitis, followed by human papillomavirus (15.6%), influenza virus (9.7%), bacilli Calmette–Guérin (7.3%), measles–mumps–rubella (4.8%), varicella virus (4.8%), and hepatitis A virus (2.4%) vaccination<sup>15</sup>. Regarding COVID-19, the number of cases has increased since the Renisi et al<sup>8</sup> publication. About seven cases and three multicenter studies have been reported in the scientific literature. By investigating all the cases of our knowledge reported in the literature, it is possible to describe that most cases of uveitis after vaccination are related to the first dose of the COVID-19 vaccine. Moreover, it is not yet known if there is an established association between these two events, but it is known that the COVID-19 vaccine promotes an increase in type I interferon (IFN-I), which could contribute to the manifestation of autoimmune events or be a trigger in genetically susceptible individuals<sup>3,8</sup>.

Table 1. Summary of the all-previous published cases of uveitis following COVID-19 vaccination.

Author, year	Number of patients, age or mean age and gender	Previous disease	Type of uveitis	Vaccine type	Complication Uveitis Following 1 <sup>st</sup> or 2 <sup>nd</sup> dose of vaccine	Time between vaccine/ uveitis	Treatment for Uveitis	Outcome
Rabinovitch et al <sup>3</sup>	21, 51.3 (23-78) years, 9 female and 12 males	AS – 3 cases Herpeszoster Ophthalmics – 1 case Mild psoriasis – 1 case CD – 1 case ND – 15 cases	21 anterior uveitis cases, two with bilateral inflammation	BNT162b2 mRNA	1 <sup>st</sup> dose: 8 patients 2 <sup>nd</sup> dose: 13 patients	7.5 ± 7.3 days (1-30 days)	Topical corticosteroids (DEX-SP) and cycloplegic eye drops	Complete recovery in all but two eyes, which improvement significantly
Goyal et al <sup>4</sup>	1, 34, male	ND	Bilateral multifocal choroiditis	Covishield (Oxford/AstraZeneca, India)	2 <sup>nd</sup> dose	9 days	Prednisolone 100 mg/day	Complete recovery
Mambretti et al <sup>5</sup>	2, 22 and 28, 2 females	ND	Acute macular neuroretinopathy	Vaxzevria (ChAdOx1 nCoV-19, by Oxford/AstraZeneca)	1 <sup>st</sup> dose: 2 patients	2 days	ND	ND
Pan et al <sup>6</sup>	1, 50, female	ND	Bilateral posterior uveitis	ND (only written inactivated vaccine)	ND (only written about the disease after vaccination)	5 days	Triamcinolone (40 mg, pericocular injection) and prednisone (20 mg/day)	Complete recovery
Mudie et al <sup>7</sup>	1, 43, female	ND	Panuveitis	Pfizer-Biontech mRNA vaccine	2 <sup>nd</sup> dose	3 days	Oral and topical prednisone 50mg/day	Mild recurrence after an attempt of therapy tapering
Renisi et al <sup>8</sup>	1, 23, male	ND	Anterior left uveitis	BNT162b2	2 <sup>nd</sup> dose	14 days	Topical dexamethasone and atropine 1% t	Complete recovery
EISheikh et al <sup>9</sup>	1, 18, female	JIA	Anterior uveitis	Sinopharm	2 <sup>nd</sup> dose	5 days	ND	ND
Bolletta et al <sup>10</sup>	34, but uveitis 6, 49, 8 (18- 83), 20 females and 14 males	SAH: 2 cases PsA: 1 case SpA: 1 case VKH: 2 cases DM: 1 case	Keratouveitis: 2 cases NGAU: 3 cases Bilateral Panuveitis: 1 case	ChAdOx1 nCoV-19 (2 patients); BNT162b2 (10 patients); mRNA-1273 (1 patient); Ad26.COV2 (1 patient).	1 <sup>st</sup> dose: 2 patients 2 <sup>nd</sup> dose: 4 patients	7,5 days	Oral valaciclovir (2); MMF 2g (2);	Complete Recovery
Jain and Kalamkar <sup>11</sup>	1, 27, male	JIA	Bilateral Uveitis.	Covishield - Serum Institute of India	1 <sup>st</sup> dose	2 days	Cyclo + Topical Steroids	Complete Recovery
Testi et al <sup>12</sup>	70, but uveitis 50, 51 (19-84), 35 females and 27 males.	ND	Anterior Uveitis 41 cases, Posterior Uveitis 9 cases.	ND (Not specified in the multi-center study)	1 <sup>st</sup> dose: 28 patients 2 <sup>nd</sup> dose: 22 patients	14 days	Systemic Anti-inflammatory (7); Topical Anti-inflammatory (1).	Complete Recovery
Carvalho (present case)	1, 51, male	AS	Anterior uveitis	Oxford/Astra-Zeneca	1 <sup>st</sup> dose	17 days	Topical dexamethasone	Complete recovery

Legend. AS: ankylosing spondylitis; ND: not described; CD: Crohn Diseases; HzO: Herpeszoster Ophthalmics; SAH: Systemic Arterial; Hypertension; DM: Diabetes Mellitus; JIA: Juvenile Idiopathic Arthritis; NGAU: Non-granulomatous Anterior Uveitis; SpA: spondyloarthritis; PsA: psoriatic arthritis; VKH: Vogt-Koyanagi-Harada disease; SAH: systemic arterial hypertension; MMF: mycophenolate mofetil; DEX-SP: Dexamethasone Sodium Phosphate 0,1%; DEX-oint: Ointment Containing Dexamethasone 1 mg; Cyclo: Cyclopentolate 1%; Tropi: Tropicamide 0,1%.

Interestingly, AU was reported in patients with or without a history of previous uveitis and/or uveitis-related systemic disease<sup>3,8</sup>. The vaccine-induced increase in IFN-I secretion could drive autoimmunity in subjects with a history of autoimmune disorders with yet unknown susceptibility to develop one<sup>3,16</sup>. The following processes are proposed: molecular mimicry, inflammatory damage induced by adjuvants (e.g., aluminium salts), direct viral infection, and immune complex deposition and IFN-I secretion<sup>11</sup>.

Several ocular complications were reported following COVID-19 vaccination including facial nerve palsy/Bell's palsy, abducens nerve palsy, AMN, superior ophthalmic vein thrombosis, corneal graft rejection, uveitis, optic neuritis, myasthenia gravis, central serous chorioretinopathy, VKH reactivation, and onset of Graves' disease<sup>17-19</sup>. The causal relationship between COVID-19 vaccines and ocular inflammation, including uveitis, is unclear. Commonly proposed mechanisms of vaccine-associated uveitis include molecular mimicry and antigen-specific cells, as well as antibody-mediated hypersensitivity reactions. Since inert spike antigen proteins are produced by mRNA vaccines for COVID-19, which affect coded protein production, SARS-CoV-2 mRNA vaccine administration could trigger antibody-mediated acquired immunity. Thus, COVID-19 vaccines might accelerate an abnormal immunological responses<sup>20</sup>.

In patients with AS, it can be noted that uveitis is the most common extra-articular manifestation, especially anterior uveitis<sup>21</sup>. Among the clinical manifestations of uveitis, one should be aware of red-eye, blurred vision, photosensitivity, foreign body sensation in the eye, and pain. In this way, it can be inferred that patients with a history of autoimmune diseases have a greater predisposition to develop uveitis<sup>22</sup>. However, when uveitis post COVID-19 vaccine management is done correctly, there is an excellent chance of complete recovery, as seen in our review. Reinforcing these findings, Rabinovitch et al<sup>3</sup> reported twenty-one cases of uveitis after COVID-19 vaccination, 3 patients with AS, of which nineteen were diagnosed with anterior uveitis, and two developed multiple evanescent white dot syndrome (MEWDS). All but three presented as mild to moderate disease. At the final follow-up, complete resolution was achieved in all cases.

## Conclusions

This study demonstrates the case of a patient with a history of AS who developed uveitis after the second dose of the COVID-19 vaccine. Performing several literature reviews, it is possible to deduce a possible association between the COVID-19 vaccine and the development of uveitis, even though there is not yet a well-defined pattern. However, most cases presented as mild to moderate disease, and almost all achieved complete resolution. In this way, physicians need to be aware of this possible reaction that patients manifest after vaccination and the appropriate management of uveitis since its complications can cause severe damage to the patient's vision, such as cataracts, synechiae, and glaucoma.

## CONFLICT OF INTEREST:

The authors have no conflict of interest to declare

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