Anterior uveitis onset after bnt162b2 vaccination: is this just a coincidence?

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ABSTRACT

Background: Uveitis is a vision-threatening inflammation and is considered an ophthalmic emergency. It generally arises as a result of autoimmune conditions, infections, or ocular trauma, but it may also occur as an isolated disorder. Over the past decades, several cases of vaccine-associated uveitis have been described, with the hepatitis B virus vaccine being the leading cause.

Clinical case: A case of anterior uveitis in a 23-year-old male, with onset 14 days after the second dose of BNT162b2 COVID-19 vaccine, is reported here. Initial symptoms were pain, photophobia, and red eye. Ocular examination showed pericheratic and conjunctival hyperaemia, posterior synechiae, and anterior chamber cells ± keratic precipitates in the lower quadrants. The posterior segment did not show any alteration, and optical coherence tomography ruled out the presence of cystoid macular oedema. After a 10-day treatment course of topical steroids and cycloplegic eye drops, the ocular inflammatory signs disappeared and visual acuity was completely restored. Even if causality remains presumed, a warning should be given to physicians about the possibility of eye inflammation following SARS-CoV-2 vaccination.

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1. Introduction

Vaccine-related uveitis is a rare adverse event. However, several cases have been reported with almost all of the vaccines currently employed (Al-Dhibi et al., 2014, Benage and Fraunfelder, 2016, Moorthy et al., 2018, Holt et al., 2014, Fraunfelder et al., 2010, Escott et al., 2013). The mean age of these uveitis patients was 30 years (range 2 months to 86 years) and the median time from vaccination to uveitis onset was 16 days (range 1 day to 6 years).

Vaccine-related uveitis can manifest with a wide spectrum of ocular symptoms, ranging from eye redness, blurred vision, and light sensitivity to the presence of floaters. Clinical manifestations can also include eye pain and conjunctival hyperaemia. Common features are transience, involvement of the anterior eye segment, and a response to glucocorticoids and cycloplegic therapy.

The case of a 23-year-old male patient with acute uveitis, with onset 14 days after the administration of the second dose of BNT162b2 COVID-19 vaccine, is reported here.

2. Case report

A 23-year-old male, without significant medical history except for recurrent panic attacks treated with benzodiazepines, received the first dose of BNT162b2 vaccine as a health-worker on January 13, 2021, in accordance with the national system campaign. Five hours later he developed a unilateral periocular erythema, with involvement of the left eyelid, as shown in Figure 1A. He consulted the dermatology department and was prescribed a topical glucocorticoid treatment for 10 days. The symptoms resolved after 72 hours.

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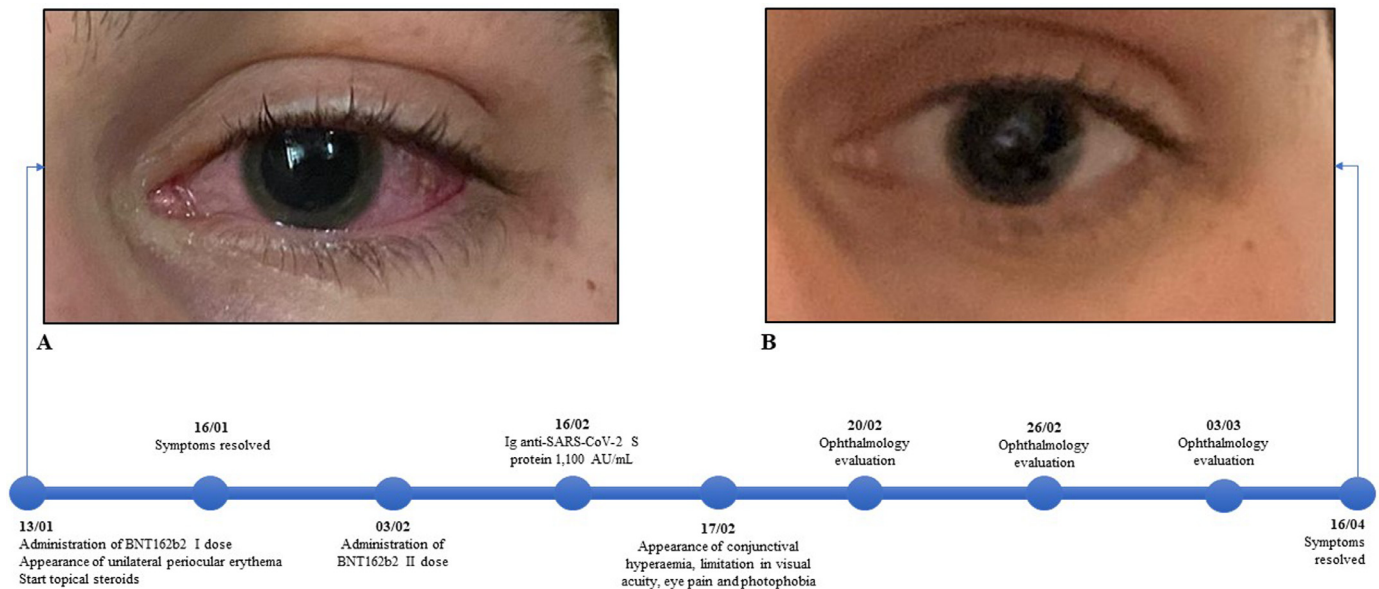*E-mail address:* andrea.lombardi@unimi.it (A. Lombardi).

Figure 1. Timeline of the case report with photographs of the affected eye (A) at the beginning of symptoms, and (B) after resolution.

On February 3, 2021, he was administered the second dose of BNT162b2 without any early reported adverse event. Fourteen days after the second BNT162b2 dose, the patient developed unilateral red eye on the left side, with conjunctival hyperaemia, associated with visual acuity reduction (0.3 logMAR), pain, and photophobia. He consulted the ophthalmology department 3 days after symptom onset. The slit lamp examination showed pericheratic and conjunctival hyperaemia, posterior synechiae, and anterior chamber cells ± keratic precipitates in the inferior quadrants. Funduscopic examination did not reveal any alteration, and optical coherence tomography (OCT) allowed the presence of cystoid macular oedema to be ruled out. The laboratory tests performed for the assessment of uveitis were unrevealing. Blood analysis including the white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) showed no alterations. Autoimmune screening was also requested; rheumatoid factor (RF) and antinuclear antibodies (ANA) were normal. Serology tests for toxoplasmosis, syphilis, herpes viruses, and cytomegalovirus were all negative. Serology for SARS-CoV-2 was performed and showed a positive antibody titre against spike protein, with a titre of 1100 U/ml, while anti-nucleocapsid antibodies were negative.

The patient was started on dexamethasone eye drops three times a day, as well as a cycloplegic agent (atropine 1%) twice daily. The follow-up appointment was held after 1 week, and evidence of resolution of the posterior synechiae was observed, while the pericheratic hyperaemia persisted. The glucocorticoid eye drops were increased to six times a day, and at the following evaluation, a minimal improvement of the eye inflammation was seen. Three weeks after symptom onset, his visual acuity had improved considerably (left eye 0.1 logMAR) and the inflammation had decreased further. Treatment was slowly tapered. Six weeks after the onset of the condition, the patient had no symptoms or signs of inflammation (Figure 1B), and his visual acuity was back to normal (left eye 0.0 logMAR).

3. Discussion

Several cases of vaccine-related uveitis have been reported, associated with almost all of the vaccines currently employed (Benage and Fraunfelder, 2016, Moorthy et al., 2018, Holt et al., 2014, Fraunfelder et al., 2010, Escott et al., 2013). However, it appears that the occurrence of uveitis associated with COVID-19 vaccines has not yet been described in the literature.

From data collected in a comprehensive review of 289 patients (Benage and Fraunfelder, 2016), vaccination against hepatitis B virus (HBV), either alone or in combination, appears to be the leading cause of vaccine-associated uveitis, followed by human papillomavirus (HPV, 15.6%), influenza virus (9.7%), bacille Calmette–Guérin (BCG, 7.3%), measles–mumps–rubella (MMR, 4.8%), varicella virus (alone or in combination, 4.8%), and hepatitis A virus (HAV, 2.4%) vaccination. The mean age of these uveitis patients was 30 years (range 2 months to 86 years) and the median time from vaccination to uveitis onset was 16 days (range 1 day to 6 years). The case reported here may represent a warning of an underreported ocular side effect from the BNT162b2 vaccine. The uveitis appeared 14 days after vaccination with the second dose in a young patient without other risk factors or disease that could cause uveitis. Moreover, in accordance with descriptions in the literature for other cases of vaccine-associated uveitis, the patient developed ocular inflammation, conjunctival hyperaemia, and eye pain (Benage and Fraunfelder, 2016); the uveitis was anterior, transient, and responsive to glucocorticoids and topical cycloplegic therapy.

Although the pathogenesis frequently remains unclear, different mechanisms have been hypothesized, including the following (Cunningham et al., 2019): molecular mimicry secondary to a close resemblance between the vaccine peptide fragments and uveal self-peptides, inflammatory damage induced by adjuvants such as aluminium salts, direct viral infection (applicable to live and attenuated vaccines), and delayed-type hypersensitivity with the deposition of immune complexes.

Ocular involvement during SARS-CoV-2 infection has been reported as conjunctivitis (Al-Dhibi et al., 2014, Lu et al., 2020). Similarly to severe acute respiratory syndrome coronavirus (SARS-CoV), the SARS-CoV-2 virus may infect ocular host cells via angiotensin-converting enzyme 2 (ACE2), which has been found in the aqueous humour (Seah and Agrawal, 2020). Regarding SARS-CoV-2 vaccinations, currently 12 cases of uveitis related to BNT162b2 administration have been reported according to the US Food and Drug Administration Vaccine Adverse Event Reporting System (FDA VAERS) (Van Assen et al., 2011), a safety surveillance system created by the FDA and US Centers for Disease Control and Prevention (CDC).

BNT162b2 is a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full length spike protein. In a multinational, placebo-controlled, observer-blinded trial, it demonstrated 95% efficacy against COVID-19 in persons 16 years of age or older. Its safety profile was found to be similar to that of other viral vaccines and was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache (Polack et al., 2020), while uveitis was not reported as an adverse event in registration studies. Differently from the HBV vaccine, which is one of the leading causes of post-vaccine uveitis, BNT162b2 does not contain aluminium salts as adjuvants in its formulation. However, both vaccines were developed by means of genetic engineering and express genes in microbial cells from pathogens that encode surface antigens capable of inducing neutralizing antibodies in the pathogen host. Cases of uveitis have also been reported after vaccination with the Moderna m-RNA-1273 vaccine (24 cases) and Janssen Ad26.CoV2.S vaccine (two cases). It may be speculated that mRNA vaccines induce strong activation of the cellular and humoral immune responses, which can result in a molecular mimicry that may lead to immune cross-reactivity, triggering an autoimmune disease like anterior uveitis. Many case reports have been published demonstrating flares of autoimmune inflammatory rheumatic diseases or new-onset autoimmune diseases following vaccination, but these adverse events remain rare, and a causal relationship has not been proved (Van Assen et al., 2011). Further research is needed to definitively understand the mechanism behind these adverse events.

In the case reported here, there was a clear temporal relationship between vaccination and the occurrence of uveitis, comparable to what has been described in the literature for other vaccines (Invernizzi et al., 2020); however, causality remains presumed (score 6 according to the Naranjo algorithm). It should be noted that the clinical presentation and response to glucocorticoids and cycloplegic therapy were similar to observations from other cases of vaccine-related uveitis.

In conclusion, a warning should be given to physicians about the possibility of eye inflammation following SARS-CoV-2 vaccination. Further data are needed to ascertain the precise occurrence of these events and assess their association with specific vaccines (mRNA vs viral vectors).

Conflict of interest

We declare that we have no conflicts of interest.

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