

# Eyelid edema following the first Pfizer-BioNTech COVID-19 vaccination: is it a coincidence?

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**Abstract. – OBJECTIVE:** This report describes an ocular allergic reaction manifested as eyelid edema after Pfizer-BioNTech COVID-19 vaccination.

**CASE DESCRIPTION:** A 28-year-old female had the first Pfizer-BioNTech COVID-19 vaccine dose and was discharged following a 20-minute post-vaccination observation for potential adverse complications. She came to the emergency department after her left eyelid swelled unexpectedly two hours later, accompanied by itching and redness. Aside from left eyelid edema and redness, there were no other remarkable bilateral ocular findings. The lack of recent history of any cause of eyelid edema suggested a vaccine-induced ocular allergy. Immediate administration of systemic and topical anti-allergic medications resulted in a significant clinical improvement within 4-6 hours.

**CONCLUSIONS:** Reporting any adverse reactions to vaccines, especially recently approved ones, is extremely critical. Local ocular allergy, as opposed to systemic allergy, could be considered one of the COVID 19 vaccine's rare and mild side effects.

*Key Words:*

Allergy, COVID 19, Eyelid edema, Hyperemia, Pfizer-BioNTech COVID-19 vaccine.

## Introduction

Several techniques have been used to develop vaccines against the Coronavirus disease of 2019 (COVID-19)<sup>1</sup>, which has affected over 170 million people globally. Devastating effects of this disease prompted the FDA to quickly approve two vaccines against a novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV2), including Pfizer-BioNTech COVID-19 (12/11/2020) and Moderna COVID-19 (18/12/2020) vaccines<sup>2,3</sup>. The SARS-CoV-2 spike protein is encased in lipid nanoparticles and encoded using mRNA in both vaccines. This protein binds to a cell membrane and enters the cell, producing spike protein for

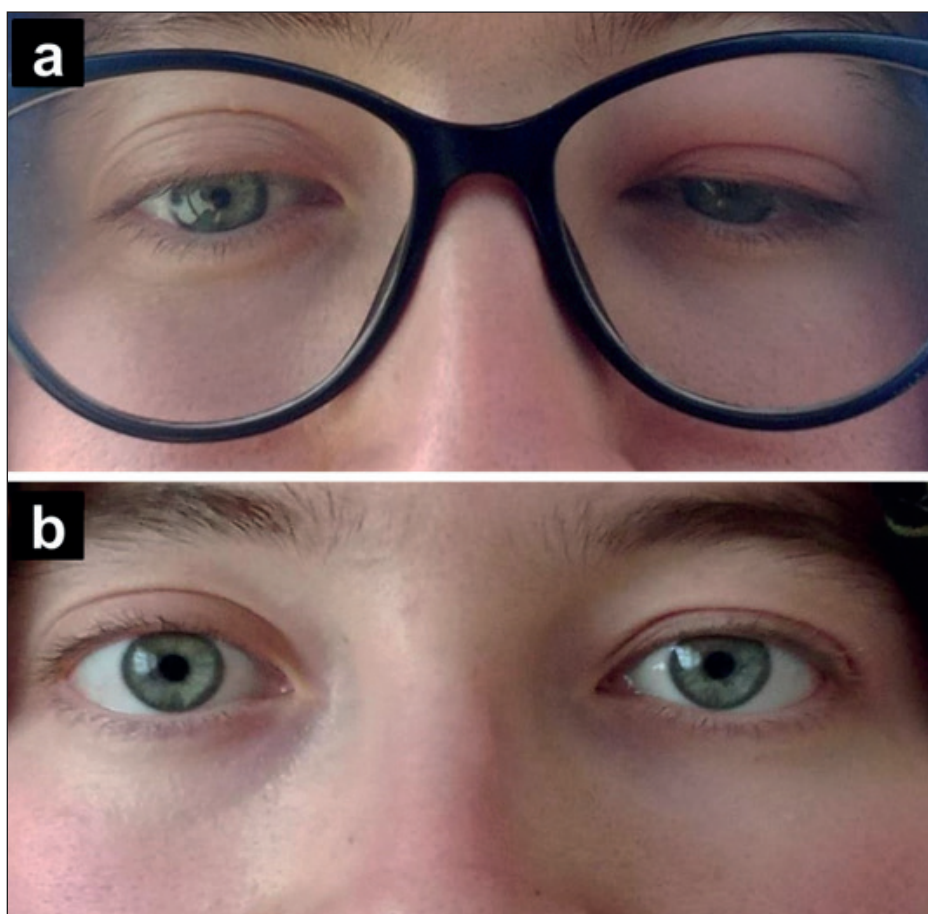
antigen presentation and immune system activation<sup>1-3</sup>. Although the novel vaccine technology is thought to be safe, the adverse effects of mRNA vaccines are poorly defined and understudied.

This report describes an ocular allergic reaction manifested as eyelid edema two hours after receiving the first dose of Pfizer-BioNTech COVID-19 vaccine.

## Case Description

A 28-year-old Caucasian female patient without history of any disease or medication received the first dose of Pfizer-BioNTech COVID-19 vaccine at Batman Educational and Research Hospital. She was then discharged after a 20-minute post-vaccination observation for potential immunization adverse complication. She came to the emergency department two hours later as her left eyelid swelled unexpectedly, accompanied by itching and periocular hyperemia. No recent history of any cause that could lead to eyelid edema was reported, including insect bite and/or suspicious food ingestion. There was no history of trauma and pregnancy, too. Thus, a vaccine-related ocular allergy was suspected. Corticosteroid (Prednol-L<sup>®</sup> 40 mg methylprednisolone) and anti-allergic (Avil<sup>®</sup> 45.5 mg /2 ml pheniramine hydrogen maleate) medications were given intravenously right away. An ophthalmologist was also consulted.

Ocular examination revealed bilateral 20/20 Snellen visual acuity and an intraocular pressure of 13 mmHg (Goldmann; Haag-Streit AG, Köniz, Switzerland). The patient had no history of diplopia, and diplopia tests were negative. Also, ocular movements were normal in all gazes, as were pupillary responses in dim or bright light conditions. Biomicroscopy revealed that the right eye's anterior segment was unremarkably normal, whereas the left eye had severe eye-



**Figure 1.** A 28-year-old female patient presented with non-globe-involved apparent eyelid edema and hyperemia in the left eye but not in the right (a). Both eyelid edema and periocular hyperemia appeared to have significantly resolved following topical and systemic therapies (b).

lid edema and appeared hyperemic (Figure 1a). Bilateral funduscopy revealed nothing clinically noteworthy. Following that, a topical anti-allergic drop, Oladin® (0.1% olopatadine) 2x1, an artificial tear, Systane® (propylene glycol) 4x1, and a topical corticosteroid, Lotemax® (0.5% loteprednol) 3x1 were prescribed. This was quickly followed by a significant clinical improvement in left eyelid edema within 4-6 hours of both topical and systemic therapy on the same day (Figure 1b).

## Discussion

Vaccines have long been used to develop immunity against pathogens. Vaccine-related ocular complications, though rare, may appear in various manifestations<sup>4</sup>. Periorbital edema with ocular vaccinia is a well-known adverse effect of the

smallpox vaccine<sup>5</sup>. Influenza vaccine-induced complications, including transient eyelid edema as a symptom of ocular respiratory syndrome<sup>6</sup>, as well as uveitis, multiple white-dot syndrome, and acute macular neuroretinopathy<sup>7-9</sup>, have also been reported. Besides, uveitis after hepatitis B vaccination<sup>10</sup>, posterior uveitis<sup>11</sup>, and pan-uveitis with posterior retinal detachment<sup>12</sup> after HPV vaccination are among the other vaccine-related ocular adverse effects described in the literature.

The Pfizer-BioNTech COVID-19 vaccine (BNT162b2), which encodes the entire SARS-CoV-2 spike protein, was the first to be approved by the FDA and distributed in the USA<sup>13</sup>. Its second dose revealed 95% efficacy<sup>14</sup>. Despite this, many adverse effects have been documented, including mild to moderate pain at the injection site, swelling and redness, chills, fatigue, and headache. There have also been reports of diarrhea, nausea, vomiting, dermatitis, and extreme

fatigue. Unlikely, in this report, these symptoms have been reported to appear 1-2 days after the second dose and to last for a few days<sup>3,15</sup>.

The vaccine-related isolated ocular reactions have been revealed to be rare<sup>4</sup>. A recent study<sup>16</sup> described three female patients (mean age: 39.3 years) who developed spontaneous unilateral eyelid edema and erythema on the first or second day after receiving their first or second dose of the Pfizer-BioNTech COVID-19 vaccine. An acute visual disturbance and visual field loss have been reported after the same vaccine<sup>13</sup>. The precise evidence is inconclusive and cannot be linked to the vaccine definitively. Nonetheless, the exact pathophysiology of spontaneous eyelid edema in our case could be due to a vaccine dissolution medium or a primarily idiosyncratic drug interaction.

Moreover, the complement system activation, which is important in the COVID-19 pathogenicity<sup>17</sup>, and molecular mimicry are two immunologic mechanisms proposed to explain adverse vaccine-induced effects. In normal immunology, the complement system within the tear film is essential in the immune defense of the closed eye. Following activation, there is an increase in cytokine inflammatory mediators<sup>18</sup>. This could also be the case in our report, where the vaccine induced complement activation, resulting in increased inflammatory mediators in the plasma and tear film and, eventually, eyelid edema. Many SARS-CoV-2 proteins are cross-reactive with human proteins, potentially resulting in autoimmunity. Antibodies against the spike glycoprotein in mRNA vaccines can also trigger an acute autoimmune response<sup>17</sup>. Consequently, the eyelid edema described in this case report could be the result of the mRNA vaccine reactivating an autoimmune response.

Although there have been few studies<sup>16</sup> on the subject, this could be a case report of a rare Pfizer-BioNTech COVID-19 vaccine-related reaction that was treated minimally. Similar incidents should be investigated to rule out the presence of masked entities. This could aid physicians in recognizing this potentially vaccine-related condition in the proper perspective. We fervently believe, as do other researchers, that it is critical to report any adverse reactions to vaccines after they have been administered, particularly for newly approved vaccines. This could be due to fatal systemic conditions caused by not only the COVID-19, but also the vaccine, or their combined effects.

## Conclusions

A local ocular allergy alone could be regarded as a rare and mild adverse effect of the COVID-19 vaccine when compared to a systemic allergic reaction. Prospective studies with an adequate data could help characterize and fully comprehend this vaccine-related immunological adverse process.

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## Informed Consent

Written informed consent was obtained from the patient for the publication of this report and the accompanying images.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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