Orbital Cellulitis following COVID-19 Vaccination

András Hári-Kovács Attila Vass Péter Lovas Viola Vince Mihály Végh Edit Tóth-Molnár

Department of Ophthalmology, Albert Szent-Györgyi Medical Faculty, University of Szeged, Szeged, Hungary

Keywords
Orbital cellulitis · Inactivated · COVID-19 vaccination · Adverse event

Abstract
A 72-year-old male patient was referred to our outpatient clinic with a painful left eye protrusion accompanied by marked conjunctival chemosis and external ophthalmoplegia being progressed despite topical and oral antibiotic therapy. He developed ocular symptoms 9 days after receiving his second SARS-CoV-2 vaccine (VeroCell). Of note, in previous history, 2 weeks after the first dose of the COVID-19 vaccine, he also developed a life-threatening laryngeal oedema treated at an emergency care unit. MRI of the orbit excluded pansinusitis as possible origin of the orbital cellulitis, and repeated COVID-19 antigen and antibody PCR tests were negative during his hospitalization. On the next day after his admittance, parenteral dexamethasone 250 mg/die treatment was commenced resulting in a quick and complete resolution of the symptoms. Due to the facts regarding this case, such as the temporal coincidence and the lack of respective comorbidity, there might be a causative relationship between the vaccination and the presented orbital cellulitis. To the best of our knowledge, this is the first report on orbital cellulitis as a possible ocular adverse event following COVID-19 vaccination.

Introduction

The COVID-19 pandemic has been presenting new challenges to the ophthalmologists. On one hand, in COVID-19 disease, a wide range of ocular manifestations from conjunctival hyperaemia [1] through the paresis of cranial nerves [2] up to orbital cellulitis with orbital
apex syndrome [3, 4] were encountered. On the other hand, there were also several COVID-19 vaccination-related ocular reactions documented. Most of the published cases presented after receiving mRNA vaccines and typically included eye diseases with presumed or confirmed autoimmune aetiology such as Vogt-Koyanagi-Harada disease [5], acute zonal occult outer retinopathy, arteritic anterior ischaemic neuropathy [6], and central serous chorioretinitis [7]. Recently, a case of acute macular neuroretinopathy following nCoV-19 adenoviral vector vaccine from AstraZeneca was also reported [8]. Beyond the well-known side effects, such as disorders of the oral mucosa [9], rheumatoid arthritis reactivation [10], subacute thyroiditis [11], acute motor sensory axonal neuropathy [12], etc., a most recent publication [13] also reported on various ocular adverse events including episcleritis, acute macular neuroretinopathy, paracentral acute middle maculopathy, and subretinal fluid accumulation in relationship with inactivated COVID-19 vaccine. We are first time reporting on a case of orbital cellulitis presented after the second dose of SARS-CoV-2 (VeroCell – China National Pharmaceutical Group Co. Ltd.) inactivated vaccine, which, considering the circumstances of the inflammation, deemed to be a probable side effect of the vaccination.

**Case Report**

In March 2021, a 72-year-old male patient was admitted to our department due to progressing left-eye proptosis. He presented 5 days before his admittance at an outpatient clinic with severe eyelid swelling and conjunctival chemosis, and in spite of topical and oral antibiotic therapy, symptoms further deteriorated, and progressing restriction in eye movements was developed. He suffered from headache but did not have fever, cough, or heavy breathing. Both COVID-19 antigen quick test and antibody PCR test were negative. As to the history, a probable late hypersensitivity reaction is to be mentioned which presented 2 weeks after receiving his first SARS-CoV-2 (VeroCell) vaccine and required intensive care due to the life-threatening lingual and laryngeal oedema. Of interest, the onset of his left eye swelling was 9 days following the second dose of the same vaccine (which, surprisingly, was not contraindicated due to the serious reactions being likely related to the first jab). According to the obtainable medical records, the patient never had been diagnosed with COVID-19 infection before, which was later confirmed by his wife, too. He had diabetes mellitus and systemic hypertension which were controlled by medication. Allergy to bee sting but not to any medication and decades ago, a blunt trauma of the left eye having resulted in mild ptosis were also registered.

On his admittance, 5-mm proptosis of the left eye with external ophthalmoplegia was noted (shown in Fig. 1), and mild left eye visual disturbance (BCVA RE 1,0; LE 0,7), normal IOP (8/11 mmHg), clear media, and fundi with no remarkable alterations were observed. The blood test revealed higher inflammatory parameters: We = 38 mm and CRP: 61 mg/L but no severe increase in white blood cell count. The urgent MRI showed higher contrast signal in the left retrobulbar space with widened soft tissues (shown in Fig. 2). In the paranasal sinuses, either inflammation or space occupying tissue could not be revealed. Having consulted with an ORL specialist, parenteral antibiotics and observation but no intervention was recommended.

Due to the lack of paranasal sinusitis and the history of presumed allergic complication following the first dose of COVID-19 vaccination, hypersensitivity as a possible cause of the cellulitis emerged, and beside the ongoing parenteral antibiotic treatment (amoxicillin 3 × 1 g/die, metronidazole 3 × 500 mg/die), 250 mg intravenous dexamethasone pro die was administered. The next day, the signs and symptoms started to improve, and 4 days later, completely resolved. On his emission, full visual acuity returned, the eyes moved freely in each gaze
position with no double vision noted, and 1-mm proptosis (Hertel: 19 mm/20 mm) was measured (shown in Fig. 3).

**Discussion**

The following circumstances of the above case strongly suggest a causative relationship between the vaccination and the presented orbital cellulitis. Although, COVID-19 disease can be complicated with orbital cellulitis it is always preceded by paranasal sinusitis [3, 4]. In our case, both the MRI of the orbit and the ORL consultation excluded sinusitis, furthermore, the repeated COVID-19 antigen and antibody tests remained negative during the follow-up period excluding COVID-19 infection.

Though, the discussion about the probable underlying immunological mechanism is out of scope of this report, considering the interval (14 and 9 days) between the vaccination and the onset of laryngeal and orbital oedema, respectively, as well as the quick and complete resolution of the symptoms following parenteral steroid treatment, a late hypersensitivity reaction to the SARS-CoV-2 vaccine cannot be excluded. There are a growing number of reports on adverse reactions of COVID-19 vaccination affecting the eye; however, to the best of our knowledge, this is the first report on orbital cellulitis as a possible side effect of a COVID-19 vaccine.
Fig. 3. Fully recovered versions of the eyes the day before the emission of the patient. Note that chemosis and proptosis also disappeared.

Statement of Ethics

The clinical examinations were conducted in accordance with the tenets of the Declaration of Helsinki. The investigation has been approved by the Regional and Institutional Review Board of Human Investigations in the University of Szeged (Approval No.: SZTERKEB-5079). The patient unfortunately passed away in September 2021. A written informed consent for publication of the details of medical case including clinical photos was obtained from his wife.

Conflict of Interest Statement

The authors have no conflict of interest to declare.

Funding Sources

This manuscript did not receive any funding.

Author Contribution

A. Hári-Kovács: editing and uploading the final version of the manuscript; A. Vass: collecting and constructing the images; P. Lovas: searching for and reviewing the literature; V. Vince: writing the main body of the manuscript; M. Végh: resources and keeping contact with the patient and his relative; and E. Tóth-Molnár: conceptualization and reviewing the final version.
Data Availability Statement

All data analysed during this study are included in this article. Further photos taken are not available publicly on ethical grounds; enquiries can be directed to the corresponding author.

References

1. Kumar KK, Sampritha UC, Prakash AA, Adappa K, Chandraprabha S, Neeraja TG, et al. Ophthalmic manifestations in the COVID-19 clinical spectrum. Indian J Ophthalmol. 2021;69:691–4.
2. Pérez-Bartolomé P, Sanchez-Quirós J. Ocular manifestations of SARS-CoV-2: literature review. Arch Soc Esp Oftalmol. 2021;96(1):32–40.
3. Turbin RE, Wawrzusin PJ, Sakla NM, Traba CM, Wong KG, Mirani N, et al. Orbital cellulitis, sinusitis and intracranial abnormalities in two adolescents with COVID-19. Orbit. 2020;39(4):305–10.
4. Bagheri M, Jafari A, Jafari S. Orbital apex syndrome in COVID-19 patient, a case report. Vis J Emerg Med. 2021;23:101006.
5. Koong LR, Chee WK, Toh ZH, Ng XL, Agarwal R, Ho SL. Vogt-Koyanagi-Harada disease associated with COVID-19 mRNA vaccine. Ocul Immunol Inflamm. 2021 Sep;10:1–4.
6. Maleki A, Look-Why S, Manhapra A, Foster CS. COVID-19 recombinant mRNA vaccines and serious ocular inflammatory side effects: real or coincidence? J Ophthalmic Vis Res. 2021 Jul–Sep;16(3):490–501.
7. Fowler N, Mendez Martinez NR, Pallares BV, Maldonado RS. Acute-onset central serous retinopathy after immunization with COVID-19 mRNA vaccine. Am J Ophthalmol Case Rep. 2021;23:101136.
8. Bohler AD, Strom ME, Sandvig KU, Moe MC, Jorstad OK. Acute macular neuroretinopathy following COVID-19 vaccination. Eye. 2021;1:1–2.
9. Riad A, Sagiroglu D, Üstün B, Polkorná A, Klugarová J, Attia S, et al. Prevalence and risk factors of CoronaVac side effects: an independent cross-sectional study among healthcare workers in Turkey. J Clin Med. 2021 Jun;10(12):2629–38.
10. An QJ, Qin DA, Pei JX. Reactive arthritis after COVID-19 vaccination. Hum Vaccin Immunother. 2021 Sep 2;17(9):2954–6.
11. Iremli BG, Sendur SN, Ünlütürk U. Three cases of subacute thyroiditis following SARS-CoV-2 vaccine: postvaccination ASIA syndrome. J Clin Endocrinol Metab. 2021 Aug 18;106(9):2600–5.
12. Tutar KN, Eyigürbüz T, Yıldırım Z, Kale N. A variant of Guillain Barre syndrome after SARS-CoV-2 vaccination: AMSAN. Clin Neurosci. 2021;74:7–8.
13. Pichi F, Aljneibi S, Neri P, Hay S, Dackw C, Ghazi NG. Association of ocul ar adverse events with inactivated COVID-19 vaccination in patients in Abu Dhabi. JAMA Ophthalmol. 2021;139(10):1131–5.