

**Title Page****COVID-19 Vaccine associated Optic Neuritis****Authors & Affiliations:**

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**Learning points for clinicians**

COVID-19 vaccines associated optic neuritis has been reported as a rare adverse effect for healthy people. Optic neuritis may be a prodromal disease for neuromyelitis optica spectrum disorder (NMOSD) or multiple sclerosis. Early identification and timely treatment may save the vision and prevent future demyelinating morbidities.

## Introduction

As the COVID-19 pandemic continues to rise, the development of effective vaccines is of crucial importance to prevent further morbidity and mortality. At the same time, the adverse effects induced by vaccine has been disclosed. However, the information of neuro-ophthalmic manifestations after COVID-19 vaccine is scarce. We reported a case who had unilateral optic neuritis after COVID-19 vaccination.

## Case

A 28-year-old woman presented at our department due to vision decline with extra-ocular movement pain in her right eye. On examination, her best-corrected visual acuity (BCVA) was 20/40 in her right eye, and 20/20 in her left eye. The anterior chamber was unremarkable. Her intraocular pressure of both eyes was normal. She had a positive relative afferent pupillary defect in her right eye by swinging light test. The subsequent color vision test revealed 14/15 OD and 15/15 OS by Ichihara test. The vitreous and retina was normal, and we did not observe disc edema in her right eye (**Figure 1A**).

Her recent medical history was significant for receiving her first Oxford-AstraZeneca (AZ, ChAdOx1 nCoV-19) COVID-19 vaccination two weeks prior to onset of symptoms. She soon had right eye pain with right-sided headache 2 days after the injection. Her eye pain was related to eye movements with blurry vision. At that time, she had blood tests, which revealed normal D-dimer (136.26 ng/mL), and

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4 high platelet counts (1024, 103/uL). Therefore, the physician told her that vaccine-  
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6 induced immune thrombotic thrombocytopenia (VITT) was less likely. Due to the  
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8 persistent headache that was not relieved by painkillers, a subsequent orbital MRI was  
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10 performed, which demonstrated no evidence of cavernous sinus thrombosis or other  
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12 intracranial vascular thromboses. Though VITT was excluded, she still had  
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14 thrombocytosis, and the physician checked JAK2 (V617F) but was negative, either.  
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22 One week later, the following platelet count returned to normal range (274, 103/uL),  
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25 but her right eye pain and vision became worse subjectively.  
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28 We soon arranged visual field examination (**Figure 1B**), FAG (**Figure 1C**), and  
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30 OCT, which confirmed the diagnosis of right eye optic neuritis clinically. She was  
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32 admitted for pulse corticosteroid therapy (methylprednisolone 1g/day, intravenously)  
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34 for 3 days with standard oral prednisolone tapering for 3 weeks. During admission,  
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37 we performed orbital MRI again, but there was no evidence of gadolinium  
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40 enhancement of the optic nerve on T1 images with fat suppression or high T2 signal.  
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46 Ten weeks later, her BCVA of the right eye improved to 20/20. The headache  
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48 improved a lot with no more extraocular movement pain. The timeline of her course  
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51 was illustrated in **Figure 2**.  
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## Discussion

As the world prepares for a massive rollout of newly approved COVID-19 vaccines, the safety issue of vaccines should be highly valued. Early in March 2021, some usual cases of thrombosis events with thrombocytopenia after AZ vaccination were reported in Europe[1]. Several countries, including Austria and Denmark suspended the use of AZ vaccines until further analysis of the reported cases were conducted by the drug regulatory authorities[2]. Luckily, with former experiences from European countries, we had some guidelines to follow to elucidate possible casual-relationship after AZ COVID-19 vaccination. However, the neuro-ophthalmic presentations after COVID-19 vaccines were rarely reported because this adverse effect was a rare presentation.

The existence of vaccine-associated optic neuritis is based on the temporal relationship between the administration of a vaccine and the development of optic neuritis in patients with no other known etiologies for infectious or non-infectious inflammation that could account for the optic neuritis. Optic neuritis post-vaccination was relatively rare compared to other well-known neurological adverse events, such as transverse myelitis or cardiovascular events, such as myocarditis. Optic neuritis after vaccination can only be diagnosed clinically because the symptoms (vision decline, eye pain, or visual field defect) were very subjective. Mild optic neuritis may recover gradually without treatment; therefore, the diagnostic rates might be underestimated. Previous reports of vaccine-related optic neuritis were related to influenza

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4 vaccines, anti-rabies vaccines, HPV vaccines, and others. Though there has been a research  
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7 reporting no increased risk of optic neuritis after vaccination[3], the other literature concluded  
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10 vaccine-induced optic neuritis is rare but existing[4]. A case series reported four cases of post-  
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13 vaccine optic neuritis, where three cases were unilateral and one case was bilateral[5]. Another  
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16 case report showed optic neuritis following the BNT162b2 mRNA COVID-19 vaccine. The other  
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19 case had optic neuritis after Ad26.COV2.S vaccine[6]. According to the above reports, we know  
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22 that any kind of COVID-19 vaccines may arouse immune reaction and lead to some neuro-  
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25 ophthalmic disorders, such as optic neuritis.

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28 Our patient received her second COVID-19 vaccine as mRNA-1273, but developed lower  
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31 limbs numbness after 2 weeks of inoculation. NMOSD was highly suspected despite no evidence  
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34 of transmyelitis on MRI. She had another corticosteroid pulse therapy, and kept regular checkups  
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37 in ophthalmic and neurologic department up to date.

#### 40 **Abbreviations:**

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43 COVID-19= coronavirus disease 2019; AZ= AstraZeneca; NMOSD= neuromyelitis optica  
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46 spectrum disorder; BCVA= best-corrected visual acuity; OD= right eye (oculus dexter); OS= left  
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49 eye (oculus sinister); VITT= vaccine-induced immune thrombotic thrombocytopenia; D-dimer=  
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52 Fibrin degradation product; JAK2V617F= Janus kinase 2, 617, Valine (V) → Phenylalanine (F),  
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55 test for myeloproliferative disorder (MPD); FAG= Fluorescein angiography; OCT= Optical  
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58 coherence tomography ; HPV= human papillomavirus  
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## References

1. Bano F, Badugama B, Chandra D: **Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination: a single UK centre experience.** *BMJ case reports* 2021, **14**(7).
2. Pottegård A, Lund LC, Karlstad Ø, Dahl J, Andersen M, Hallas J, Lidegaard Ø, Tapia G, Gulseth HL, Ruiz PL *et al*: **Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study.** *Bmj* 2021, **373**:n1114.
3. Baxter R, Lewis E, Fireman B, DeStefano F, Gee J, Klein NP: **Case-centered Analysis of Optic Neuritis After Vaccines.** *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2016, **63**(1):79-81.
4. Pillar G, Toubi E: **Vaccination-induced bilateral optic neuritis: rare but existing.** *The Israel Medical Association journal : IMAJ* 2012, **14**(11):690-691.
5. Roy M, Chandra A, Roy S, Shrotriya C: **Optic neuritis following COVID-19 vaccination: Coincidence or side-effect? - A case series.** *Indian journal of ophthalmology* 2022, **70**(2):679-683.
6. García-Estrada C, Gómez-Figueroa E, Alban L, Arias-Cárdenas A: **Optic neuritis after COVID-19 vaccine application.** *Clin Exp Neuroimmunol* 2022, **13**(2):72-74.

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4 **Figure Legends:**  
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7 **Figure 1**  
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10 (A) Fundus color photography revealed clear margin of bilateral discs and no obvious  
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13 retinal vessels abnormalities.  
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16 (B) Visual field examination revealed peripheral visual field defect of the right eye.  
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19 (C) Fluorescein angiography of both eyes had no evidence of retinal vessels thrombus  
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22 or occlusions.  
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25 **Figure 2** The timeline of the patient's clinical findings and disease course.  
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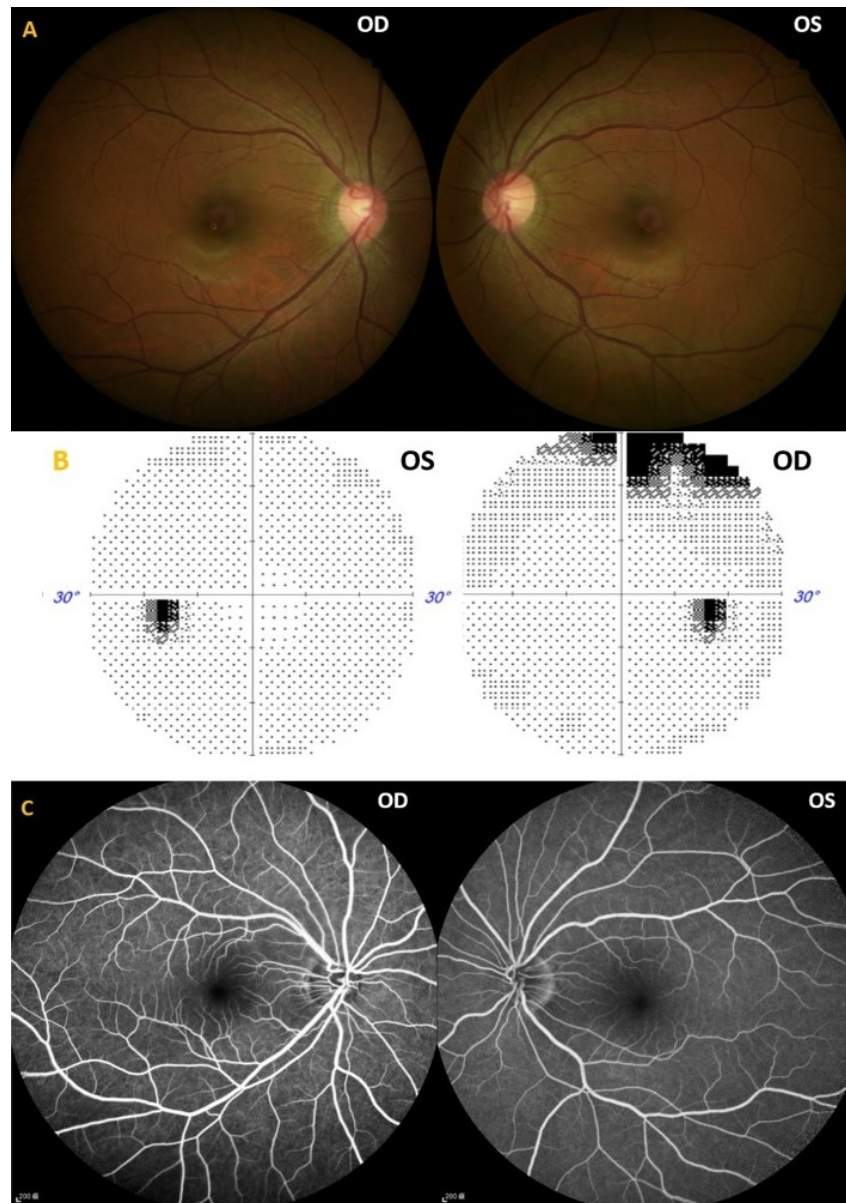


Figure 1

(A) Fundus color photography revealed clear margin of bilateral discs and no obvious retinal vessels abnormalities.

(B) Visual field examination revealed peripheral visual field defect of the right eye.

(C) Fluorescein angiography of both eyes had no evidence of retinal vessels thrombus or occlusions.

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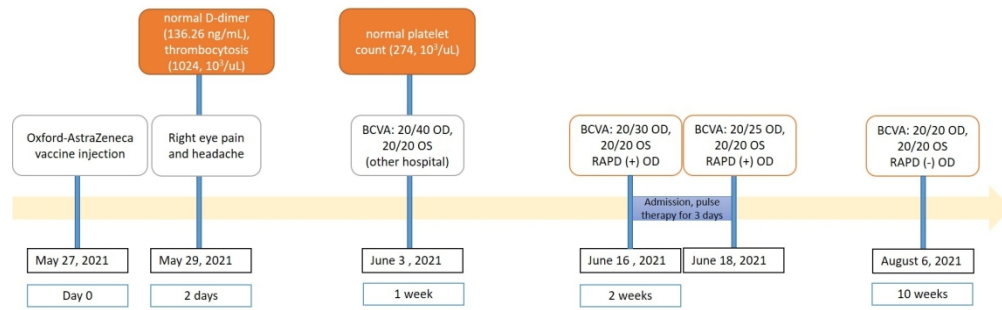


Figure 2 The timeline of the patient’s clinical findings and disease course.

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