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Unilateral idiopathic neuroretinitis following Pfizer-BioNTech COVID-19 vaccine: a case report

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ABSTRACT

This case report describes a temporal relationship of unilateral neuroretinitis following the second Pfizer-BioNTech COVID-19 (Pfizer) vaccine. A 16-year-old male of mixed ethnicity presented with gradual loss of vision and pain on eye movement in his left eye 12 days after his second Pfizer vaccine. His visual acuity in the left eye was counting fingers at half a meter. There was optic nerve head swelling and macular exudates in a star-shaped pattern with peripapillary and foveal subretinal fluid consistent with left neuroretinitis. His serological and radiologic investigations were negative for any alternative aetiology. He was commenced on doxycycline, rifampicin, and oral prednisone on a tapering dose. Four months after presentation, his left eye vision improved to 6/24-2; limited by loss to the outer retinal layers over the fovea. The close proximity of the second Pfizer vaccine dose poses a temporal association with plausible causation.

KEY WORDS: neuroretinitis; COVID-19; SARS-CoV-2; Pfizer; New Zealand

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INTRODUCTION

Successive vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was a primary public health strategy during the COVID-19 pandemic. Pfizer-BioNTech COVID-19 (Pfizer), is the nationally approved and disseminated vaccine in New Zealand (NZ) [1]. This mRNA vaccine is provided as an intramuscular injection with two sequential doses required at a 3–4 week interval to achieve satisfactory immunogenicity [2]. Due to the relative infancy of Pfizer's commercial use, its ocular side effect profile is continuing to emerge, particularly from anecdotal accounts. This case report describes a temporal relationship of unilateral neuroretinitis following the second Pfizer vaccine, providing evidence for a potentially rare vaccine-related side effect.

CASE PRESENTATION

A 16-year-old male of Maori, Pacific Islander, and NZ European background presented to a regional ophthalmology service with a 12-day history of gradual vision loss in his left eye and pain on eye movement. A review of the systems was negative, with no constitutional symptoms. He had

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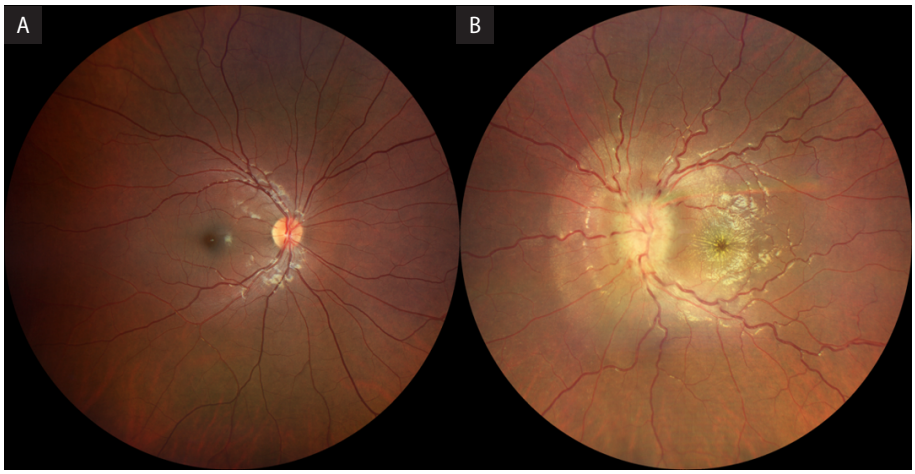

FIGURE 1. Fundus photography of right eye (**A**) and left eye (**B**). The left eye demonstrates diffuse optic nerve head swelling with macular hard exudates in a star pattern characteristic of left neuroretinitis

limited exposure to farm animals with no direct exposure to domestic animals such as cats. He was not sexually active, denied intravenous drug use, and had no history of overseas travel. However, he recently had two successive doses of the Pfizer-BioNTech COVID-19, with his second vaccination 24 days before presentation and 12 days before symptom onset.

On examination, his visual acuity in the right eye was 6/4.5, while his left eye was counting fingers. His intraocular pressures were 16 mm Hg and 10 mm Hg in his right and left eye, respectively. He had a grade III left relative afferent pupillary defect (RAPD). While he had a full range of eye movement, there was a pain in moving his left eye. His left optic nerve was grossly swollen with a macular star (Fig. 1). There was no anterior chamber inflammation or vitritis. Optical coherence tomography of the retinal nerve fibre layer (OCT RNFL) assessment showed an average RNFL thickness of 481µm, with peripapillary subretinal fluid extending to the fovea (Fig. 2). Automated perimetry demonstrated an early central scotoma in the left visual field with a mean deviation (MD) of –4.35 dB. He had a normal right ocular examination and ancillary investigations. Clinical examination and investigations were consistent with left neuroretinitis.

The patient's infectious screen was negative. The screen included the following tests: Quantiferon-TB Gold, syphilis, *Bartonella henselae* immunoglobulin G (IgG)/immunoglobulin M (IgM), human immunodeficiency virus (HIV) antigen and antibody (Ag/Ab), cytomegalovirus (CMV) IgG/IgM, toxoplasma IgG/IgM and leptospiral IgM enzyme-linked immunosorbent assay (ELA). Serum angiotensin-converting enzyme (ACE) and chest X-ray were normal. Lyme disease serology (*Borrelia burgdorferi*) was not tested as he had not travelled outside of NZ. *Bartonella henselae* serology was negative when sequentially tested on initial presentation as well as 4 and 8 weeks later. He had a normal full blood count, liver function, renal function, serum folate, and B12. His antinuclear antibodies (ANA) were weakly positive and inconclusive with negative extractable nuclear antigen (ENA), antineutrophil cytoplasmic antibodies (ANCA), and double-stranded deoxyribonucleic acid (dsDNA). Neuromyelitis optica (NMO) IgG antibodies were initially positive however negative on repeat testing 4 weeks later, including negative myelin oligodendrocyte glycoprotein (MOG) antibodies. Magnetic resonance imaging (MRI) of the head, orbits, and spine with gadovist contrast were consistent with left retrobulbar optic neuritis without intracranial or spinal involvement (Fig. 3).

The patient was discussed with infectious disease and neurology subspecialties and subsequently commenced on doxycycline 100 mg twice a day, rifampicin 300 mg twice a day, and oral prednisone 60 mg daily tapered by 10 mg per week over for a total of six weeks. He was also supplemented with vitamin D3. The patient's retrobulbar pain improved within a week of treatment commencement. His best-corrected vision improved to 6/24-2 four months after presentation. His RAPD resolved entirely; however, he continued to demonstrate reduced vision due to subfoveal outer

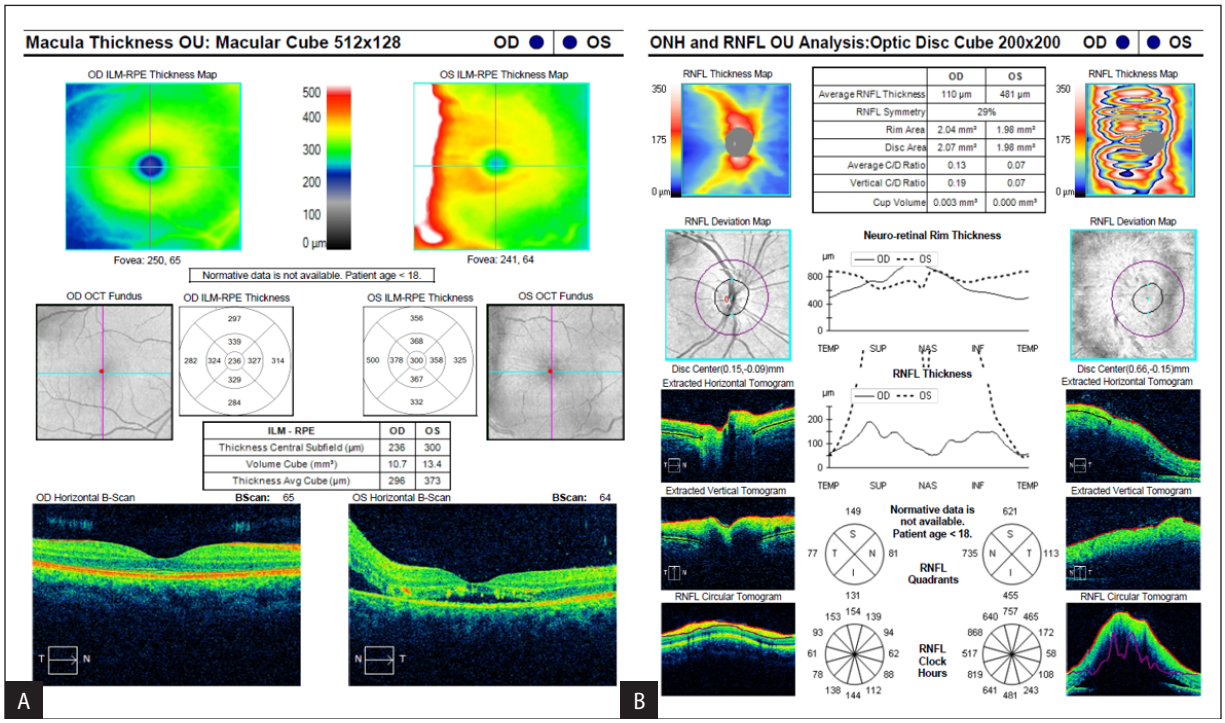

FIGURE 2. Zeiss optical coherence tomography (OCT) macular 512 × 128 cube (**A**) and disc retinal nerve fibre layer (RNFL) 200 × 200 cube (**B**) of both eyes. The left eye demonstrates optic nerve head oedema (**B**) with peripapillary and foveal subretinal fluid (**A**)

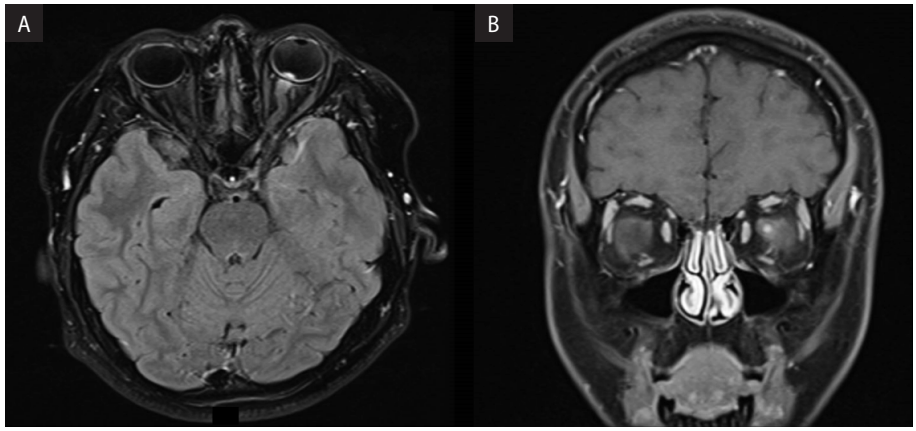

FIGURE 3. Magnetic resonance imaging (MRI) of head and orbits with T2 axial turbo T2 weighted spin echo (TSE) fluid attenuated inversion recovery (FLAIR) sequence (A) and T1 coronal TSE Dixon sequence with contrast (**B**). Focal enhancement of the anterior margin of the left optic nerve at its junction with the globe is demonstrated without other demyelination or parenchymal intracranial pathology

retinal disruption. The optic nerve head swelling improved with peripapillary and foveal subretinal fluid resolution (Fig. 4). His macular hard exudates, previously in a star-shaped pattern, also improved, as did his early visual field defect on automated perimetry. The patient remains under the care of ophthalmology and neurology outpatient departments with ongoing follow-up at the time of publishing.

DISCUSSION

An increasing number of case reports and retrospective case studies have emerged detailing possible adverse effects of vaccination against COVID-19 [3, 4]. These appear to encompass a wide variety of ophthalmic manifestations, including orbital, corneal, uveitic, retinal, and neurological disorders [3]. Given the strong association between uveitis and immunologic phenomena,

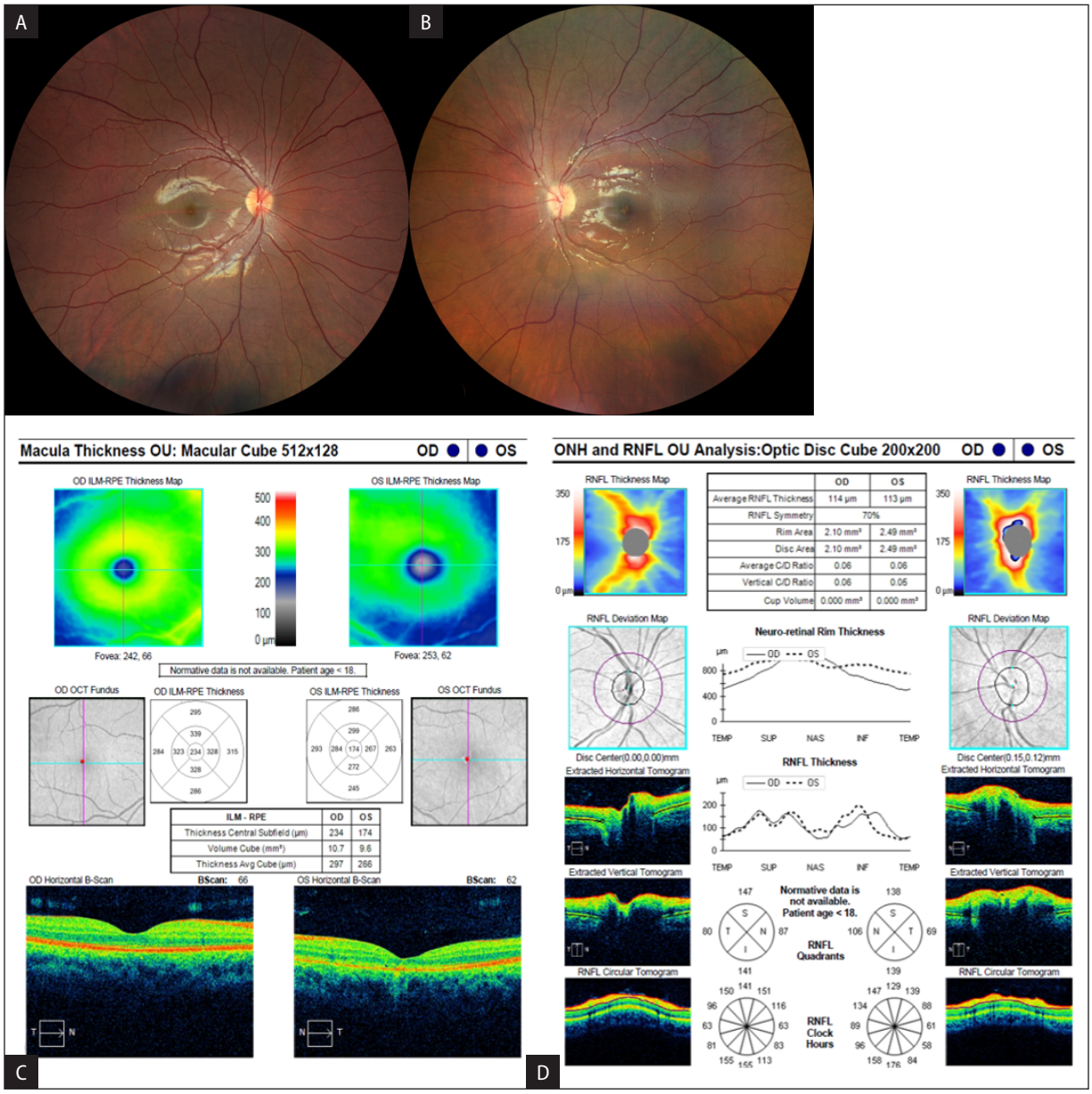

FIGURE 4. Clinical status 4-months following treatment. **A.** Right eye fundus photo; **B.** Left eye fundus photo; **C.** Optical coherence tomography (OCT) of macular cube; **D.** Optical coherence of the retinal nerve fibre layer (OCT RNFL) analysis demonstrating improvement of optic nerve head swelling, peripapillary, and subfoveal subretinal fluid

a relationship between vaccination and uveitis would be expected [3]. Pavesio et al. identified 70 patients presenting with ocular inflammatory events within 14 days following COVID-19 vaccination with a mean age of 51 [4]. Elhusseiny et al. reviewed fourteen reports involving 34 patients reporting uveitis after COVID-19 vaccination. The average age at the presentation time was 47.6 ± 16.3 years, with the average time from vaccination to development of ophthalmic symptoms 8.0 ± 8.6 days [3].

In a review of adverse ocular events from 2010 to 2020, optic neuritis was found to be the most common event associated with nine different vaccines, with a mean onset of 10.8 days post-injection. Five patients receiving COVID-19 vaccination were diagnosed with post-vaccination central nervous system inflammatory syndrome leading to neuroretinitis and papillitis. The mean age at the presentation time was 48.0 ± 21.5 years, and the average time from vaccination to development of ophthalmic symptoms was 8.6 ± 8.3 days. Three of them

presented with bilateral involvement. Significant improvement in symptoms and examination was achieved with the use of intravenous methylprednisolone.

Neuroretinitis is a focal inflammatory optic neuropathy characterised by unilateral optic disc oedema and macular exudates [5]. Both infectious and non-infectious aetiologies are recognised, with cat-scratch disease (*Bartonella henselae*) being the most common identifiable cause [6]. The patient presented had serial tests for *Bartonella henselae* with IgG titres being consistently < 64 with negative IgM results. Approximately 25% of neuroretinits cases are considered idiopathic, where no definitive cause is determined after thorough investigation [7]. The close proximity of the second Pfizer vaccine dose poses a temporal association with plausible causation. The patient was neither symptomatic nor tested positive for SARS-CoV-2 preceding the onset of his ocular symptoms. Lee et al. described a similar case report of unilateral neuroretinitis of an 83-year-old Korean woman following her second dose of the Pfizer vaccine [8]. Visual loss, to the point of hand-movement perception, occurred two days after receiving the second Pfizer vaccine with no background primary ocular history. She was commenced on three days of 1 g intravenous methylprednisolone, followed by oral prednisone taper [8]. Although initial visual improvement was witnessed during the first month of treatment, her vision remained finger-counting perception after six months. Lee et al. postulated that the low vision was at least partly due to photoreceptor disruption due to persistent subretinal fluid [8]. Likewise, while there was a considerable improvement in our patient's vision and status of the disc and macula over a four-month period, his visual acuity remained at 6/24-2, secondary to continued subfoveal photoreceptor disruption. Of note, in contrast to the case presented by Lee et al. our patient had the typical clinical features of neuroretinitis with the presence of a macular star. Although the demographics and visual outcomes of the two cases may differ, they share an interesting temporal similarity of ocular disease following the second Pfizer vaccine dose. Cheng and Margo et al., suggested that vaccine-related side effects, particularly within close proximity of initial administration, may be attributable to an immediate hypersensitivity-type reaction [9]. As the Pfizer vaccine is still relatively novel with respect to its known ocular side-effect profile, this case report poses a temporal relationship with high plausibility. Case reports such as these provide essential insight into potential rare side effects of a widely disseminated global vaccine.

Conflict of interests

The authors have no conflicts of interest to declare.

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