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ORIGINAL ARTICLE

Bilateral multifocal central serous retinopathy following mRNA COVID-19 vaccine

Choriorétinopathie séreuse centrale bilatérale suivant le vaccin à ARN-m anti-COVID 19

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Summary We present a case of acute bilateral multifocal CSCR in a young healthy Caucasian female occurring 3 days after receiving the first dose of the Pfizer-BioNTech BNT162b2 COVID-19 mRNA vaccine. The true incidence of this adverse reaction might be underreported in asymptomatic unilateral or paracentral cases. We believe that the post-COVID-19 vaccination occurrence of CSCR is not a sufficient reason to withhold the second dose of the vaccine. Further studies are required to ascertain the best way to prevent and manage this complication.

MOTS CLÉS
Choriorétinopathie séreuse centrale ;
Rétine ;

Résumé Nous présentons un cas de choriorétinopathie séreuse centrale (CRSC) bilatérale aiguë chez une jeune patiente caucasienne trois jours après avoir reçue la première dose du vaccin à ARN-m anti-COVID-19 Pfizer-BioNTech BNT162b2. L'incidence réelle de cet effet indésirable semble être sous-estimée dans les cas paracentraux ou unilatéraux

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Pfizer-BioNTech

asymptomatiques. L'apparition de CSRC post-vaccination anti-COVID-19 ne contre-indique pas l'administration de la deuxième dose vaccinale. Des études supplémentaires sont nécessaires afin de standardiser les moyens de prévention et de prise en charge de cette complication.

Introduction

The introduction of different vaccine technologies has helped in stemming the worldwide coronavirus SARS-CoV-2 epidemic. Various systemic side effects related to the vaccine such as fatigue, fever, headache, myalgias and arthralgias have been described, and exceptional adverse events such as lymphadenopathy, ventricular arrhythmia and paresthesia were reported [1]. Two cases of unilateral acute central serous retinopathy (CSR) occurring in a previously healthy young males 3 to 7 days after the first dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine were reported [2,3]. We present herein a case of acute bilateral multifocal CSR in a young healthy Caucasian female occurring 3 days after receiving the first dose of mRNA COVID-19 vaccine.

Case report

A 32-year-old healthy Caucasian female presented to our department with a 2-day history of bilateral progressive painless loss of vision. She reported having received the first dose of the Pfizer-BioNTech mRNA COVID-19 vaccine 3 days prior to the onset of her symptoms. She had no past medical or ocular history and she denied taking any medication including corticosteroids or hormone therapy. She also reported pain at the vaccine injection site on her arm and a general fatigue that lasted for 24 hours after the injection.

At presentation, her best-corrected visual acuities were 20/60 in both eyes. Her pupils were equally round and reactive to light and accommodation. Slit lamp examination revealed normal anterior segments and her intraocular pressure was 12 mmHg in both eyes. Fundoscopy showed evidence of bilateral multifocal serous retinal elevations. No hemorrhages or vascular abnormalities were noted (Fig. 1).

A fluorescein angiogram (FA) demonstrated multifocal single point leakage bilaterally (Fig. 2) and macular OCT confirmed the bilateral neurosensory retinal serous detachment in the posterior pole (Fig. 3a and Fig. 4a) and temporal pigment epithelial detachment with subretinal fluid in the left eye (Fig. 4b).

In order to rule out active COVID-19 infection, a nasopharyngeal swab and blood sample were obtained at presentation and the patient tested negative for SARS-CoV-2 through polymerase chain reaction and immunoglobulin M and G testing for which seroconversion usually occurs 5—7 days after active infection. The patient was discharged without treatment and followed up closely.

After one month, her BCVA had improved to 20/30 on the right and 20/20 on the left with a reduction in the thickness of the serous detachment on OCT. At the 6 weeks visit, her BCVA was 20/25 and 20/20 in the right and left eye respectively with a further reduction in the subretinal fluid on OCT (Fig. 3b and Fig. 4c). At about the same time, a blood test revealed that her antispike IgG antibodies level was 27 UI/mL (> 1 UI/mL threshold for anti-COVID-19 immunity). After discussing pros and cons, the patient decided to have her second dose of COVID-19 vaccine, as planned, 7 weeks after her initial presentation and was followed-up closely. She didn't develop any ocular nor systemic side effects subsequently and her CSR continued to improve clinically and on OCT. Three weeks following the second vaccine dose, her BCVA was 20/20 in both eyes and her OCT was dry centrally with a small persistent PED temporally but no subretinal fluid in the left eye (Fig. 3c and Fig. 4d).

Discussion

To the best of our knowledge, this is the first reported case of bilateral multifocal CSR occurring a few days after the Pfizer-BioNTech mRNA COVID-19 vaccine. Various ocular and orbital manifestations of COVID-19 infection have been described including dacryoadenitis, conjunctivitis, blepharitis, episcleritis, anterior, intermediate or posterior uveitis, retinitis, optic neuritis, retinal vascular arterial or venous occlusion, and even neuro-ophthalmological events such as cranial nerve palsies [4].

On the other hand, only few cases of intraocular complications related to the vaccine have been reported in the literature. The first case is an acute endothelial graft rejection after Descemet membrane endothelial keratoplasty (DMEK) occurring 7 days after the first dose of the BNT162b2 mRNA SARS-CoV-2 (BioNTech/Pfizer) vaccination [5]. Two cases of acute unilateral acute CSR few days after receiving first dose of Pfizer mRNA COVID-19 vaccine [2,3].

A direct relationship between vaccination and development of bilateral CSR should be considered in our patient. Firstly, her simultaneous bilateral symptoms started 3 days after receiving mRNA COVID-19 vaccine without any prior known risk factors for developing this condition. Moreover, CSR is much less common in females than males [6] and bilateral acute CSR is an extremely rare condition [7,8]. In addition, one case of unilateral CSR associated with mRNA COVID-19 vaccine has already been reported in a young Hispanic male patient three days after receiving the first dose of the same vaccine [3].

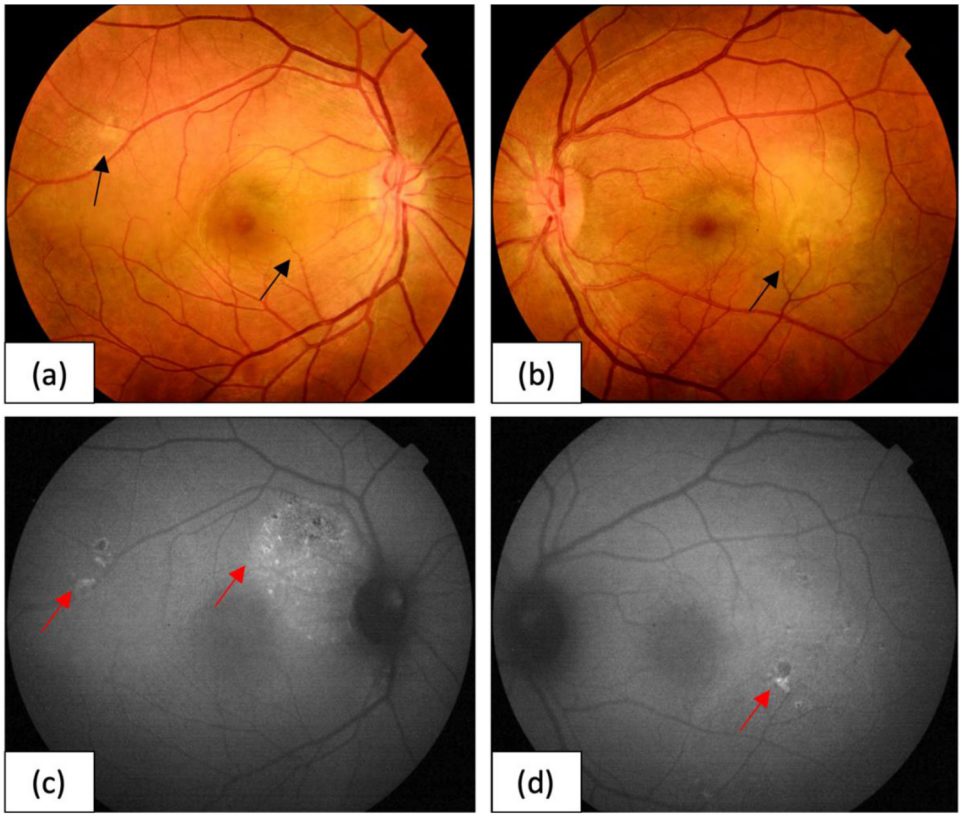

Figure 1. (a) and (b): fundus color photo of both eyes at the time of presentation showing multifocal serous retinal detachment with pigmentary changes (black arrows); (c) and (d): autofluorescence imaging of the posterior pole at the time of presentation showing multiple areas or hyper and hypo-autofluorescence.

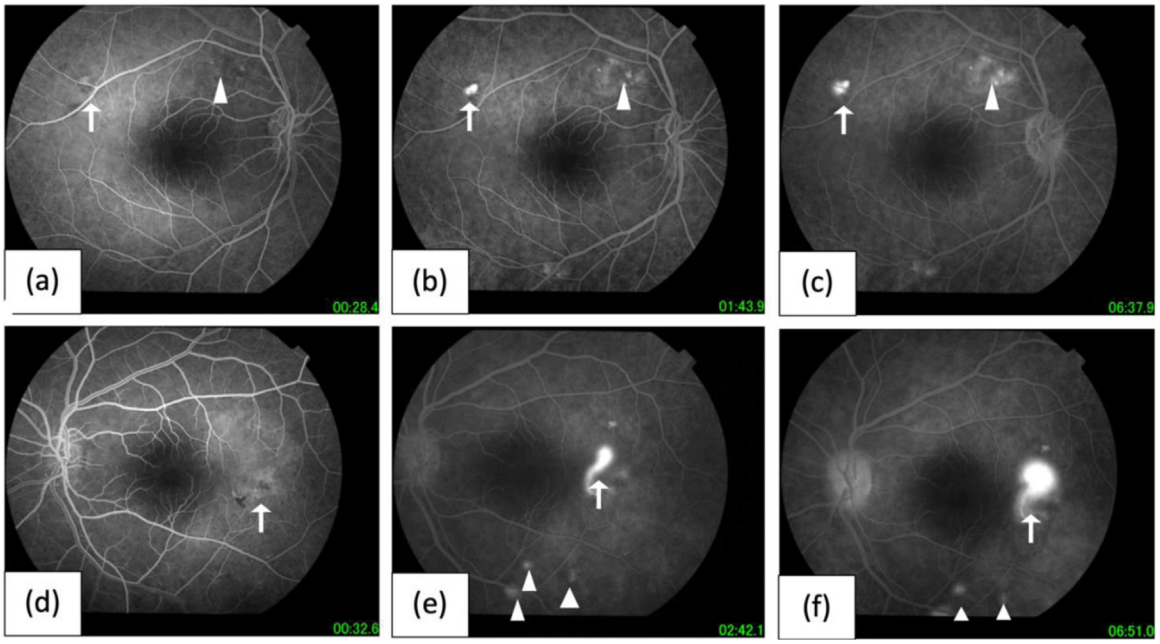

Figure 2. Fundus fluorescein angiography at the time of presentation showing bilateral multifocal leakage: in the right eye (a)—(c) and left (d) and (e) eyes.

The systemic side effects of mRNA COVID-19 vaccines are rare and appear to be associated to an increased systemic immune response especially in young patients. They seem to occur within one week of receiving the second dose usually and they include pericarditis, myocarditis and multisystem inflammatory syndrome in children (MIS-C) [9—11]. Patients previously infected with COVID-19 seem to develop stronger adverse effects after the first dose of the vaccine,

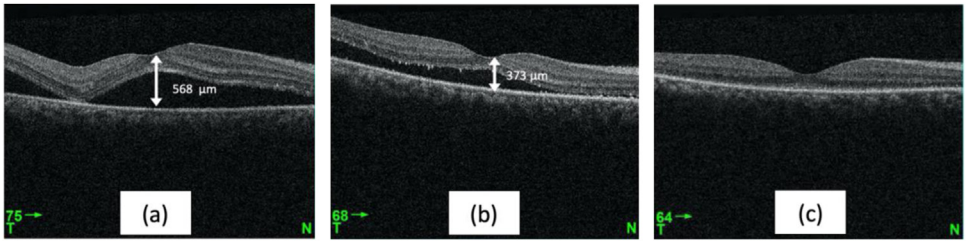

Figure 3. Macular OCT of the right eye: (a) at presentation with serous macular detachment; (b) at 6 weeks with a decrease in subretinal fluid and CRT (up-down arrows); and (c) at 10 weeks (3 weeks after receiving the second dose) with dry macula.

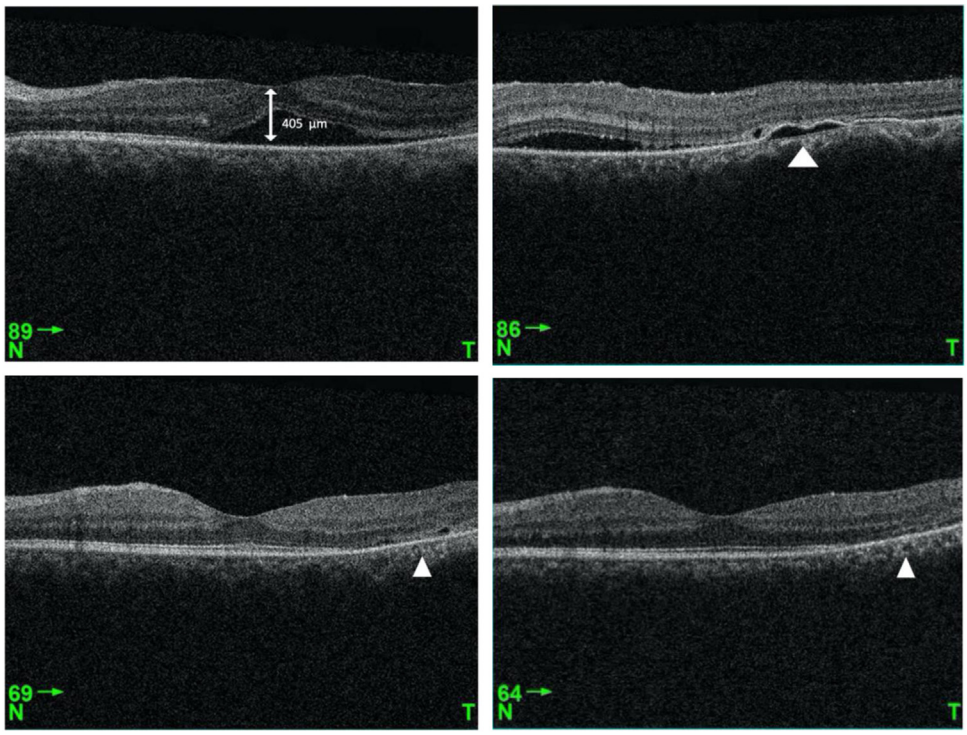

Figure 4. Macular OCT of the left eye: at presentation (a) and (b) serous macular detachment and PED; at 6 weeks (c) spontaneous resolution of CSR and alteration of outer retinal layers (head of arrows); at 10 weeks (d) flat macula and no recurrence of CSR. Note that temporal PED (b) persisted throughout follow-up but SRF disappeared.

presumably due to a previous sensitization of the immune system that triggers an extensive and misadapted cytokine storm, leading to inflammatory damages within the host organs. Our patient may have had an asymptomatic infection previously that may have triggered the reaction after the first dose. Polymerase chain reaction ruled out active infection with SARS-CoV-2 virus at the time of presentation and her bilateral CSR was proven to be related to the vaccine rather than an active COVID-19 infection.

The development of CSR post-vaccination may have a similar underlying immunopathophysiological mechanisms as other various systemic adverse effects. A sudden increase in the systemic immune response may lead to a sharp rise in circulating inflammatory cytokines which may in turn target the choroidal circulation and increase its permeability [12]. Other agents associated to the vaccine such as free extracellular mRNA, polyethylene glycol, and elevated serum cortisol may also increase choroidal permeability [3]. Free extracellular mRNA is known to increase mediated endothelial cell permeability and may lead to diffuse vascular endothelial leak [13]. Polyethylene glycol (PEG) is the biocompatible polymer used as a drug carrier in Pfizer-BioNTech mRNA COVID-19 vaccine and the glycation of the PEG nanoparticles in the body also increases vascular permeability [14]. Moreover, the systemic response to vaccination is often accompanied by a rise in serum cortisol level which may predispose to an increase in choroidal hyperpermeability and development of CSR with particular bilateral predilection [8,15,16].

Conclusion

In conclusion, this is the first report of an acute bilateral multifocal CSR following mRNA COVID vaccination. It is possible that the true incidence of this adverse reaction might be underreported in asymptomatic cases if the disease occurs outside the macular area or unilaterally in the non-dominant eye. Occurrence of post-COVID 19 vaccination CSR doesn't justify withholding second dose administration.

Further studies are required to ascertain the true incidence of this complication in addition to the best way to prevent and manage it.

Disclosure of interest

The authors declare that they have no competing interest.

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