

“Vitreous Hemorrhage and Long-Lasting Priapism After COVID-19 m-RNA Based Vaccine: A Case Report”

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Abstract

Purpose: To report a case of possible multi-district thromboembolic event involving the eye of a patient with several cardiovascular risk factors, following a second inoculation of SARS-CoV-2 m-RNA based vaccine.

Case-report: A 60-year-old man presented with blurred vision in the left eye lasting 1 month but started within 24 hours from the 2nd dose of BNT162b2 vaccine inoculation. He also reported a long-lasting but self-limiting priapism which started about 4 h after the vaccination. Patient's medical history included: acute lymphoblastic leukemia, treated with chemotherapy and HLA-identical sibling donor transplant 18 months earlier; subsequent cytomegalovirus posterior outer retinal necrosis (PORN) resolved with antiviral treatment; type II diabetes and erectile dysfunction. Ocular examination of the affected eye revealed vitreous hemorrhage which limited the observation of details of the fundus. After a 2-week follow-up without any clinical improvement, parsplana vitrectomy (PPV) with cataract extraction was performed. Surgical aspiration of a large preretinal hemorrhage revealed intraretinal flame-shaped hemorrhages and some cotton wool spots. Further intraoperative examination and post-operative fluorescein angiography excluded the rhegmatogenous and the neovascular origin of the intraocular bleeding.

Conclusions: Due to the several predisposing factors such as diabetes, aspirin assumption, history of blood dyscrasia and infectious retinitis, the relationship between the acute intraocular bleeding and the BNT162b2 inoculation remains difficult to ascertain in this patient. However, the occurrence of lasting priapism and vitreous hemorrhage within 24 h from the vaccination is a critical event which deserves to be mentioned.

Keywords

Vascular anomaly, Sars-CoV-2 vaccine, priapism, BNT162b2 vaccine, COVID-19 thrombosis

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Introduction

Sars-CoV-2 (COVID 19) infection is frequently associated with a broad spectrum of thromboembolic complications, ranging from microinfarcts to deep vein thrombosis, ischemic stroke and acute coronary syndrome.^{1,2}

Ischemic priapism, caused by focal thrombosis due to hypercoagulability and hyperviscosity in patients with COVID-19 has also been reported.^{3,4}

Ocular manifestations have been reported in several case reports and a single case series, suggesting a possible connection between COVID-19 disease and ocular complications related to retinal vein occlusion (CRVO), such as

cotton wool spots and multiple flame-shaped peripheral retinal hemorrhages, but evidence is still controversial.⁵

Within 1 year from the World Health Organisation's declaration that the outbreak of COVID-19 was a global pandemic, multiple vaccines (BNT162b2, mRNA-1273, Ad26.COV2.S, and ChAdOx1 nCoV-19) were developed

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and distributed (beginning in December 2020) using several, different technologies to prevent COVID-19 disease.

According to the most recent data, the large majority of the Italian population has received at least two vaccine inoculations. Mild or severe adverse effects reported mainly include neurological, muscular and vascular complications.⁶

We report a case of a 60-year-old patient who suffered a vitreous hemorrhage associated with priapism within 24 h of receiving the second dose of the BNT162b2 vaccine.

Case report

In July 2021, a 60-year-old man was referred to our Eye Clinic after following extended blurred vision in his left eye (lasting 1 month). The patient had received a second dose of the BNT162b2 (COMIRNATY; lot number EX3599) vaccine inoculation 24 hours prior to ocular symptoms onset. Further, the patient reported having also suffered self-limiting priapism, which began 4 hours after the same vaccination lasting around 7 h. During this time interval, he closely monitored his blood pressure which remained within normal range (< 135/ 75 mmHg). As visual loss did not resolved, the patient's hematologist, responsible for his clinical follow-up of previous acute lymphoblastic leukemia ph+, referred the patient to our Eye Clinic for consultation. The patient was previously treated with chemotherapy and HLA-identical sibling donor transplant in December 2019. Four months after transplantation, the patient suffered cytomegalovirus-related posterior outer retinal necrosis (PORN) but limited to an inferior retinal quadrant of the left eye. Antiviral systemic treatment combined with 4 intravitreal Ganciclovir injections (0.02 mg/0.08 mL) allowed the

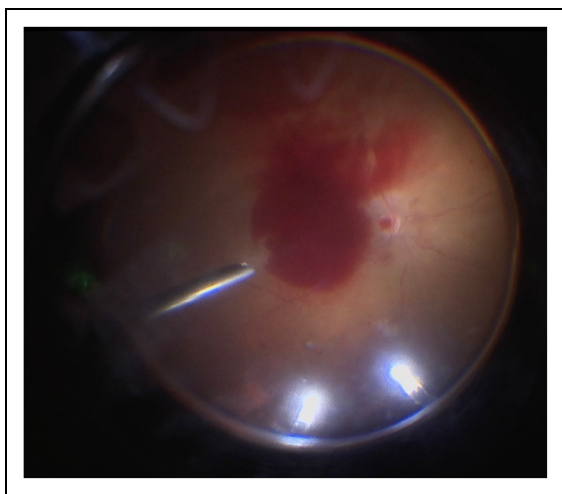


Figure 1. Intraoperative colour photograph of the affected eye showing pre-retinal hemorrhage involving the posterior pole with flame-shaped hemorrhages and cotton wool spots.

complete resolution of the PORN within 8 weeks with restoration of the pre-PORN visual acuity (0.4 LogMAR). The patient is diabetic (type II insulin-dependent diabetes) without evidence of diabetic retinopathy. The referring hematologist excluded any hematological disease recurrence. We were also informed that the patient has suffered medically untreated erectile dysfunction. The patient's medical treatment included: ramipril 5 mg daily, ursodeoxycholic acid 450 mg daily, lansoprazole 30 mg daily, aspirin 100 mg daily, aciclovir 800 mg daily, trimethoprim-sulfamethoxazole (160 mg + 800 mg) 2 compresses on alternate days. No adverse event or remarkable disturbances were reported after the first vaccine injection.

On our initial examination, best corrected visual acuity (BCVA) was hand motion in his left eye (0.2 LogMAR in his right eye). Pupils were equal, round and reactive to light with a mild afferent defect in the left eye. On slit-lamp examination, nuclear cataract was documented in both eyes, whereas the rest of the anterior segment was within normal limits, including intraocular pressure.

Dilated fundus examination showed no sign of diabetic retinopathy in the right eye and vitreous hemorrhage in the left eye. Ocular B-scan ruled out retinal detachment and tractional tears.

Laboratory evaluation for hypercoagulability markers such as activated partial thromboplastin time, prothrombin time, International, normalized ratio, Protein C activity, Protein-S antigen, factor V Leiden and hyperhomocysteinemia were within normal ranges. Fibrinogen and D-dimer were 552 mg/dL and 578 ng/mL respectively (Fibrinogen reference interval 150–400 mg/dL; D-dimer cut-off point: 500 ng/mL). The patient was PCR negative for Sars-CoV-2.

As the vitreous hemorrhage in the left eye did not improve 6 weeks from symptoms onset (that is 2 weeks from our first examination), a parsplana vitrectomy (PPV) with silicone oil tamponade combined with cataract extraction was prescribed. Silicone oil was applied as a preventative measure for post-operative bleeding, which also acts as a stabilizer for vascular anomalies and as a transparent medium if further intensification laser treatment is required. Intraoperatively, a preretinal hemorrhage, numerous intraretinal flame-shaped hemorrhages and some cotton wool spots were documented (Figure 1), while the retina was confirmed attached without tears.

Post-operative fluorescein angiography examination was performed 10 weeks from the acute bleeding episode (when the media transparency and post-operative course allowed the examination). The patient's left eye revealed delayed arteriovenous transit and persisting, widespread capillary nonperfusion at the posterior pole and in the mid and peripheral 360° retina (Figure 2). There was no detection of neovascular hyperfluorescence, or remarkable cystoid macular edema. This ischemic pattern was very

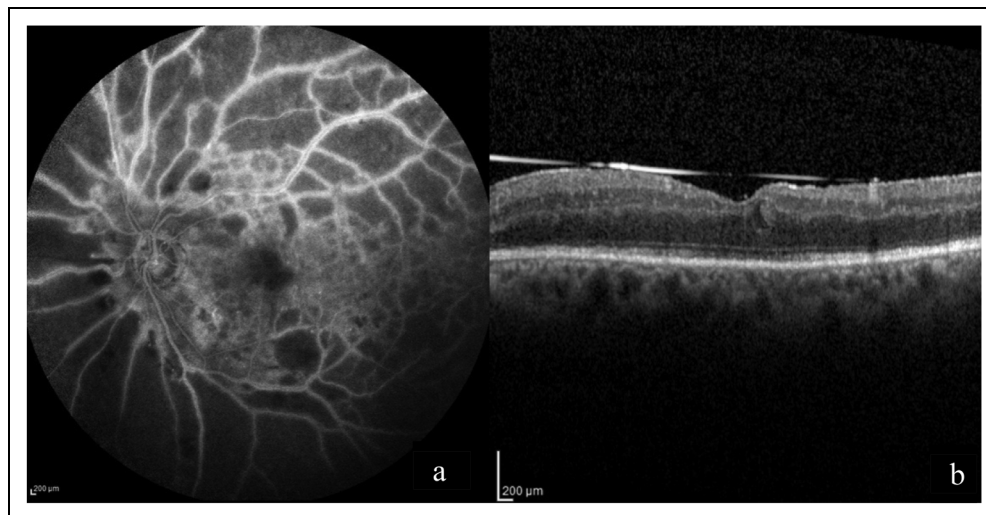


Figure 2. Post-operative (a) fluorangiography and (b) optical coherence tomography images of the left eye taken 10 weeks from vaccination. They show silicon oil filling the vitreous chamber and extensive nonperfusion of the macula and peripheral retina in the late phase of the examination. There is no evidence of retinal neovascularization or significant macular edema.

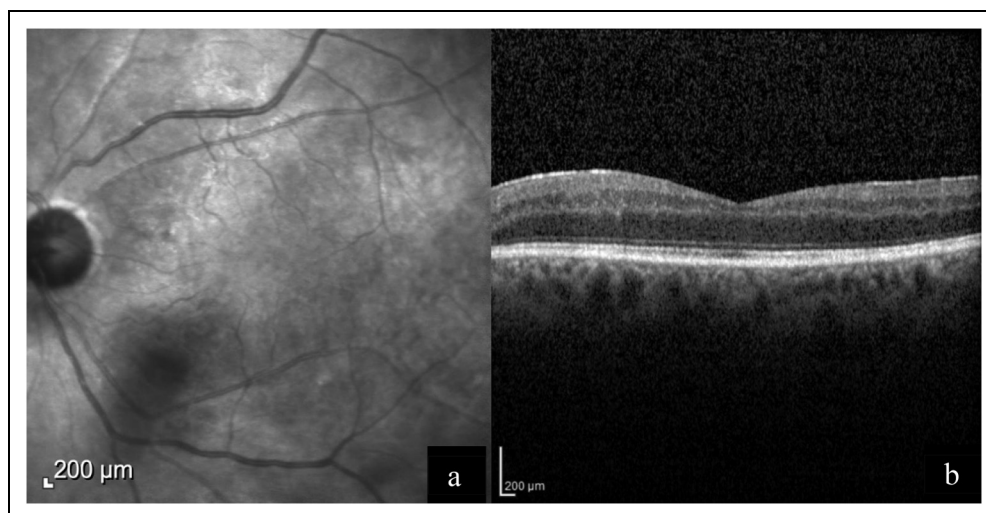


Figure 3. Pre-operative (a) infrared fundus photograph and (b) optical coherence tomography macular scan of the left eye as it appeared 2 months before vitreous hemorrhage onset.

likely absent, or at least much less severe, in a pre-operative fundus imaging performed during the last follow up visit for the prior PORN (Figure 3). Unfortunately, pre- and post-operative imaging techniques do not correspond, which limits our conclusions. Hence, adjunctive laser treatment was required before tamponade removal. Eight weeks after PPV the silicon oil was uneventfully removed and BCVA restored to 0.6 logMAR.

Discussion

A wide range of vaccine-related thromboembolic events associated with thrombocytopenia have been described

following Sars-CoV-2 adenovirus-vector based vaccinations, especially in the intracranial district.^{7,8} One possible case of central retinal vein occlusion in a healthy subject has been reported, immediately following the inoculation of an m-RNA-based vaccine.⁹

To our knowledge, other cases of vitreous hemorrhage after the second dose of BNT162b2 vaccine have not previously been published. The patient in our case report had multiple risk factors for vascular occlusive events, given his history of leukemia, diabetes, retinal vasculitis related to PORN and erectile dysfunction. Although the origin of the acute bleeding is difficult to establish, especially in a patient with pre-existing retinal vascular complications,

and the observation of the fundus in detail possible only after 6 weeks from the onset of the hemorrhage, we think that a retinal vascular obstruction, particularly affecting the venous district, could be the causative event. The timing of sudden priapism and intraocular bleeding within 24 h from the second dose of BNT162b2 vaccine may indicate a relationship.

The authors hypothesize that a transient blood hypercoagulability or hyperviscosity phase may follow COVID-19 m-RNA-based vaccination. This phase, which for most healthy subjects resolves uneventfully, in a patient at high risk of occlusive events may decompensate an unstable vascular equilibrium, thus leading to potential thrombotic accidents.

Conclusions

We advocate strict follow-up of blood coagulation for patients at high cardiovascular risk (including oncohaematologic patients) receiving BNT162b2 vaccine. This evaluation is especially important whilst a third dose of vaccine is now recommended worldwide.

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Consent for publication

The Local Ethical Committee “Area Vasta Emilia Nord (AVEN)” does not require official approval for the publication of single case reports. Written informed consent to publish information and images included in this report was obtained from the patient.

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