



# Acute panuveitis after COVID-19 mRNA booster vaccination following cataract surgery

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## ABSTRACT

**Purpose:** To report a case of presumed COVID-19 Pfizer third dose (booster) vaccination leading to severe panuveitis mimicking acute endophthalmitis in the early postoperative period following routine cataract extraction and intraocular lens implantation.

**Observations:** A 68-year-old female with mild refractive error who previously received 2 doses of the BNT162b2 vaccine underwent routine cataract extraction and intraocular lens implantation in the right eye. On postoperative day (POD) 2 the patient received her BNT162b2 booster vaccination. On POD 3 the patient's vision was hand motion at face with photophobia. Anterior segment examination was significant for 2+ conjunctival injection, mild stromal edema, 4+ cell and flare with trace hypopyon, and 4+ anterior vitreous cell without any wound leak. Subsequent Gram staining, culture for aerobic and anaerobic bacteria, KOH preparation, and PCR testing for infectious organisms were also obtained, all of which were found to be negative. ESR and CRP values were also negative. The patient was started on intravitreal injections of vancomycin and ceftazidime, as well as oral moxifloxacin, fortified vancomycin and tobramycin drops, prednisolone acetate 1%, and atropine 1%. On POD 5 the patient reported significant improvement of her vision and was found to have 20/80 vision. On POD 12 her vision improved to 20/25, and improved further on POD 19 to 20/20 vision with a completely normal examination. Cultures remained negative throughout the entire course.

**Conclusions and importance:** This is the first report to suggest a possible association between the BNT162b2 booster vaccination and development of acute panuveitis in the postoperative period after routine cataract extraction and intraocular lens implantation. This condition may mimic acute bacterial postoperative endophthalmitis and may portend a more favorable prognosis, but the authors believe such cases should nonetheless be treated aggressively as presumed infection.

## 1. Introduction

Since being identified in 2019, the SARS-CoV-2 virus has been responsible for an unprecedented global pandemic and public health emergency. In response to the initial spread of the virus, efforts to quickly develop a suitable vaccine began, and in December 2020 the Food and Drug Administration issued an Emergency Use Authorization for the Pfizer-BioNTech COVID-19 (BNT162b2) and Moderna COVID-19 vaccines.<sup>1</sup>

As vaccination rates increase, greater attention is now being paid to the adverse effects of these vaccines. These typically include systemic and inflammatory effects such as headache, fatigue, chills, diarrhea, fever, arthralgia, myalgia, and nausea.<sup>2–4</sup> Specific ocular adverse effects

have also been associated with the BNT162b2 vaccine<sup>5</sup> including corneal graft rejection,<sup>6–8</sup> anterior uveitis,<sup>9</sup> panuveitis,<sup>10,11</sup> posterior uveitis,<sup>12</sup> central serous chorioretinopathy,<sup>13</sup> and abducens nerve palsy.<sup>14</sup> Additionally, data suggest patients may experience increased systemic adverse effects<sup>15–17</sup> as well as increased organ-specific effects after additional doses of the vaccine as compared to after the first dose.<sup>18–20</sup>

We present a case of presumed COVID-19 Pfizer third dose (booster) vaccination leading to severe panuveitis mimicking acute endophthalmitis in the early postoperative period following routine cataract extraction and intraocular lens implantation (CEIOL).

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## 2. Case report

A 68-year-old Caucasian female patient was referred to the ophthalmology clinic for cataract evaluation. Past ocular history was negative except for mild myopic refractive error. Past medical history was significant for nephrectomy secondary to a perinephric abscess in her youth as well as blunt force trauma as a child to the right orbit. The patient was otherwise healthy with no history of systemic disease and not taking any medications. The patient denied any COVID-19 symptoms since the start of the pandemic and had received 2 doses of the BNT162b2 vaccine prior to the operation. She also reported a negative nucleic acid amplification test result (Hologic Aptima® SARS-CoV-2 assay) five days prior to her scheduled surgery.

Preoperatively, she had a best corrected visual acuity of 20/70 and 20/50 in her right and left eye, respectively. Pupils were equally round and reactive. Intraocular pressure (IOP) was 23 and 18 mm Hg in both eyes. Anterior segment examination with slit lamp was significant for 3+ cortical, 2+ nuclear sclerotic, and 1+ posterior subcapsular cataracts in both eyes. Fundus examination was significant for mild asymmetry of the cup to disc ratio at 0.4 and 0.6 for the right and left eyes, respectively. The risk and benefits of cataract surgery were explained to the patient and she elected to proceed with her right eye first.

Intraoperatively, it was noted that she had 1-2 clock hours of zonular dialysis presumably due to her prior right orbital trauma. Thus, after nuclear removal, a capsular tension ring was placed prior to insertion of an SN60WF monofocal lens in the lens bag. No signs of prolapsed vitreous were noted intraoperatively including by triamcinolone staining and miotic intracameral injection at the end of the case.

On postoperative day (POD) 1, the patient reported excellent vision and no pain. She was found to have 20/20 vision in the right eye with a normal IOP. The cornea was clear with only trace cell in the anterior chamber (AC) and the intraocular lens was well centered within the bag. There was no vitreous cell.

On the morning of POD 2 the patient elected to receive her BNT162b2 booster. By night, she reported that she had started to develop systemic symptoms including mild fever, joint pain and headache. She also noted that her vision in her operated eye was mildly blurred. The patient attributed this to being tired and went to bed after taking acetaminophen.

On the morning of POD 3 the patient awoke with fever, body aches, and poor vision, and was seen emergently in the clinic. She reported a significant decrease in vision with photophobia, but denied any pain. Her vision was found to be hand motion at face with normal IOP. Anterior segment examination was significant for 2+ conjunctival injection, mild stromal edema, 4+ cell and flare with trace hypopyon, and 4+ anterior vitreous cell without any wound leak. No view to the posterior pole could be obtained and a B-scan demonstrated an attached retina with dense vitreous cell (Fig. 1). Due to the high suspicion of acute postoperative endophthalmitis, an intravitreal tap was attempted using a 25-gauge needle on a 3-mL syringe but was unsuccessful. An anterior chamber paracentesis was performed using a 30-gauge needle and 150  $\mu$ L of fluid was obtained for culture. Subsequent Gram staining, culture for aerobic and anaerobic bacteria, KOH preparation, and PCR testing for infectious organisms were also obtained, all of which were found to be negative. ESR and CRP values were also negative. One mg of vancomycin and 2 mg of ceftazidime each in 100  $\mu$ L were injected intravitreally. She was also started on oral moxifloxacin 400 mg daily, fortified vancomycin and tobramycin drops four times a day, prednisolone acetate 1% four times a day, and atropine 1% twice a day.

On POD 5 the patient reported significant improvement of her vision, photophobia and systemic symptoms and was found to have 20/80 vision. Her anterior segment examination had improved to 1+ injection, 1+ punctate epithelial erosions, 1-2+ Descemet's folds, 2+ mixed cells in the AC without hypopyon or fibrin, and 2+ vitreous cell. On POD 12 the patient reported complete improvement of her vision with no symptoms. Her vision had improved to 20/25 with a normal IOP. Her

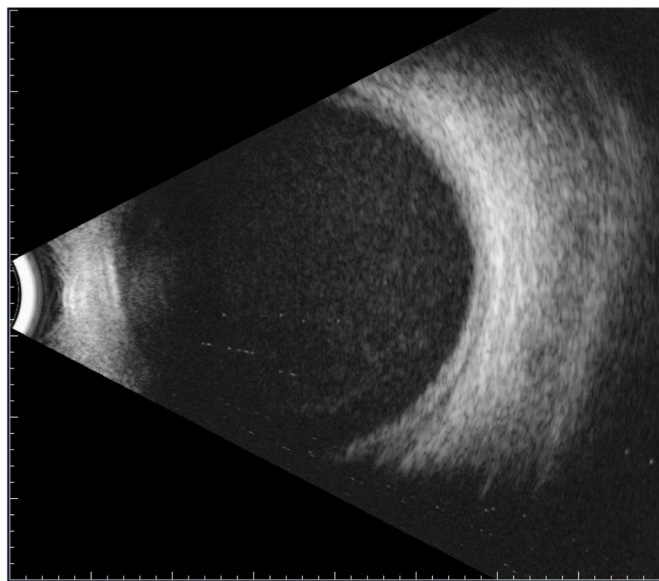


Fig. 1. B-Scan ultrasound of posterior segment of right eye. Right eye demonstrates an attached retina and the presence of dense vitreous cell.

examination was significant only for trace injection, few residual stellate keratic precipitates, and trace cell with a normal posterior pole. On POD 19, she achieved 20/20 vision with a completely normal examination. Dilated fundus examination was also normal. Cultures remained negative throughout the entire course.

## 3. Discussion

We present a case of acute panuveitis which developed shortly after receiving a booster immunization with the Pfizer-BioNTech mRNA COVID-19 vaccine during the postoperative period that was treated as acute postoperative endophthalmitis. To the best of our knowledge, this is the first report of panuveitis after a booster dose of mRNA COVID-19 vaccine postoperatively after cataract surgery.

Although the patient presented in the classic window for acute postoperative bacterial endophthalmitis, several characteristics in the clinical course make us consider immunization as the primary contributor to the patient's presentation: Firstly, the temporal association between the immunization, the patient's systemic symptoms, and subsequent intraocular inflammation; secondly, the rapid visual recovery from hand motion vision to 20/80 in less than 48 hours after the tap and injection; thirdly, the eventual recovery to better than 20/40 vision, which occurs in less than 13-33% of cases of bacterial endophthalmitis<sup>21-23</sup>; and finally, although a vitreous tap could not be successfully obtained, the absence of bacterial infection.

There has been increasing evidence that uveitis may be associated with vaccinations. A comprehensive systematic review compiling reports of vaccine-related uveitis identified 289 cases of uveitis from 1984 to 2015 after a variety of vaccinations.<sup>24,25</sup> These included the hepatitis B virus, human papillomavirus, influenza, Bacille Calmette-Guerin, measles-mumps-rubella, varicella virus, and hepatitis A vaccines. Additionally, of the patients whose gender was recorded, more than two-thirds were female.

Recently, an increasing number of uveitis cases have also been reported following vaccination with the BNT162b2 vaccine. One retrospective study found twenty-one cases of mild-to-moderate anterior uveitis within  $7.5 \pm 7.3$  days following either the first or second dose of the BNT162b2 vaccine.<sup>12</sup> A study also reported two cases of multiple evanescent white dot syndrome after the BNT162b2 vaccine.<sup>26</sup> Furthermore, a study of 686 patients with autoimmune inflammatory rheumatic diseases receiving two doses of the BNT162b2 vaccine

reported two cases of uveitis within 2–6 weeks of receiving the second dose.<sup>27</sup> Another report identified a patient who developed panuveitis 3 days after a second dose of the BNT162b2 vaccine.<sup>10</sup>

Determining serum or ocular markers associated with vaccine-related uveitis may help to determine the pathophysiology of uveitis after administration of the BNT162b2 vaccine. A recent study has identified a signature serum cytokine profile after administration of the BNT162b2 vaccine, and found increases in IL-15, IFN- $\gamma$ , and IP-10/CXCL10 after the first dose with a subsequent rise in TNF- $\alpha$  and IL-6 after the second dose.<sup>28</sup> The presence of IP-10/CXCL10, IL-6, and TNF- $\alpha$  have been associated with uveitis in both murine and human models. Increased IP-10/CXCL10 levels have been found in the aqueous humor,<sup>29,30</sup> and tears<sup>31</sup> of patients with active uveitis. Additionally, elevated levels of IL-6 in the vitreous fluid have been found in patients with uveitis,<sup>32,33</sup> with IL-6 inhibition demonstrating improvement in uveitis symptoms.<sup>33,34</sup> Elevated levels of TNF- $\alpha$  have also been found in the ocular fluid of patients with uveitis,<sup>35</sup> with anti-TNF- $\alpha$  treatment showing effectiveness in curbing inflammation in uveitis patients.<sup>36,37</sup>

IL-1 is known to cause many of the same systemic side effects seen after vaccination with BNT162b2, such as fever, chills, headache, nausea, vomiting, and myalgia.<sup>38–42</sup> The development of autoimmune uveitis has also been linked to IL-1 levels in patients. Increased secretion of IL-1 $\beta$  in the retina by neutrophils, macrophages, and dendritic cells is present in murine experimental autoimmune uveitis.<sup>43</sup> Anti-IL-1 antibody treatments such as anakinra and canakinumab have also been successful in treating uveitis in humans.<sup>44,45</sup>

Although previously reported cases of uveitis tended to occur 3 or more days after vaccination,<sup>9,10,46</sup> the shorter temporal relationship in our patient may be compounded by the post-inflammatory response after CEIOL. Cataract surgery represents a form of trauma to the eye, which has been demonstrated to cause postoperative inflammation.<sup>47–49</sup>

One of the proposed mechanisms is due to weakening of the blood aqueous barrier from increased postoperative levels of intraocular prostaglandin E and F $2\alpha$ .<sup>50,51</sup> Such factors may have led to expedition of the systemic cytokine to penetrate the intraocular milieu, resulting in the earlier onset of symptoms relative to other reports.

The major limitation in our report was the unsuccessful vitreous tap. Vitreous taps tend to have positive culture rates of 64% for bacterial endophthalmitis while aqueous taps are lower at 32%.<sup>52</sup> Obtaining a vitreous tap would have allowed us greater confidence in ruling out an infectious etiology. Additionally, the patient had a history of zonular dehiscence, which is a risk factor for infectious endophthalmitis and might increase the possibility that this patient may have had endophthalmitis over panuveitis.<sup>53</sup>

#### 4. Conclusions

This report suggests a possible association between the BNT162b2 booster vaccination and the development of acute panuveitis in the postoperative period after cataract surgery. This condition may mimic acute bacterial postoperative endophthalmitis and may portend a more favorable prognosis, but the authors believe such cases should nonetheless be treated aggressively as presumed infection.

#### Patient consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying image.

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#### Authorship

All authors attest that they meet the current ICMJE criteria for

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#### Declaration of competing interest

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