

## Initial anterior uveitis event associated with recent novel SARS-CoV-2 (COVID-19) infection in the setting of HLA-B27

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### ABSTRACT

**Purpose:** To describe an atypical ocular manifestation following SARS-CoV-2 infection.

**Observations:** A 27-year old previously healthy male with no past ocular history presented with pain, photophobia and red eye in his left eye (OS). His only notable mention on review of systems was a positive SARS-CoV-2 infection three weeks prior. Slit lamp examination demonstrated fine inferior keratic precipitates (KPs) in the inferior cornea and 3+ anterior chamber cells OS. There was no vitritis or chorioretinal lesions. The patient was diagnosed with his first event of acute anterior uveitis. Standard ocular inflammatory panel returned positive for HLA-B27. The postulated mechanism of initial anterior uveitis attack in the setting of COVID-19 infection was dysregulation of inflammatory cells and mediators in a patient with baseline elevated risk for ocular inflammation.

**Conclusions and Importance:** It is crucial to investigate patients for HLA-B27 following initial anterior uveitis event if infected by SARS-CoV-2, as patients with HLA-B27 are at baseline higher risk of ocular inflammatory dysregulation.

### 1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected 140 million individuals worldwide as of April 25, 2021.<sup>1</sup> Medical specialities are attempting to understand the possible sequelae of this disease while daily case rates, and death, continue to rise.<sup>1</sup> During the viral cycle, SARS-CoV-2 particles bind to angiotensin-converting-enzyme-2 (ACE-2) receptors to enter host cells.<sup>2</sup> These receptors can be found in ocular structures such as the conjunctiva, choroid and optic nerve.<sup>3</sup> Conjunctivitis, full-thickness retinitis, optic neuritis, and anterior uveitis have all been identified as ocular manifestations of coronavirus infection in feline hosts.<sup>3</sup> Of these ocular diseases, follicular conjunctivitis has been well documented in the setting of adult SARS-CoV-2 infections, even demonstrating positive conjunctival swab specimen results.<sup>4,5</sup> Despite the alarming number of COVID-19 positive tests, anterior uveitis has been sparsely reported in literature following recent SARS-CoV-2 infection.<sup>6–8</sup> We describe a case of an adult patient presenting with anterior uveitis temporally associated with SARS-CoV-2 infection.

### 2. Findings

A 27-year-old previously healthy male was referred urgently to a tertiary ophthalmology clinic for assessment of ocular pain, photophobia and redness in his left eye (OS). The patient noted OS redness with no irritation or discharge two-days prior to presentation, followed by ocular pain, and extreme photophobia OS one day later. He denied any past ocular history or trauma and confirmed no previous history of ocular inflammatory conditions. However, he recently tested positive for SARS-CoV-2 on nasopharyngeal swab three weeks prior. His only symptom at the time was fever, which resolved over four days. No residual SARS-CoV-2 symptoms, including cough, dyspnea, loss of smell or gastrointestinal manifestations were appreciated. The patient completed a two-week quarantine with no subsequent sick contacts. The patient denied SARS-CoV-2 vaccination prior to or during the clinical course. No relevant family history was noted.

On examination, his best-corrected distance visual acuity (BCVA) was 20/20 in the right eye (OD) and 20/20 OS with intraocular pressure of 18 mmHg OD and 15 mmHg OS. Pupil and extraocular motility examination was unremarkable. Slit lamp examination of the anterior

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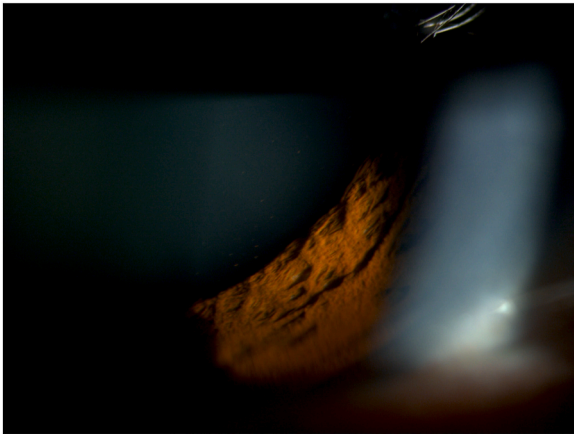
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**Fig. 1.** Slit lamp photo of the left eye demonstrating ciliary injection, fine inferior keratic precipitates and 3+ cells.

segment was within normal limits OD, but OS demonstrated ciliary conjunctival injection, fine inferior keratic precipitates (KPs) in the inferior cornea and 3+ anterior chamber cells; no posterior synechiae were present (Fig. 1). Fundus examination was unremarkable in both eyes (OU), notably with no signs of vitritis or optic disc. Fundus autofluorescence OS was unremarkable. Spectral-domain optical coherence tomography of the macula OU was unremarkable.

Based on the negative review of systems and first anterior uveitis event, the presumptive diagnosis was isolated unilateral SARS-CoV-2 induced anterior uveitis. The patient was started on Prednisolone 1% gtts 6 times daily OS and Atropine sulfate 1% gtts bid OS.

Despite the patient denying sacroiliac pain or previous uveitic events, a comprehensive uveitis panel was conducted and found the patient to be HLA-B27 positive. The remaining panel, including rheumatoid factor, angiotensin converting enzyme, anti-nuclear antibody, anti-neutrophil cytoplasmic autoantibody, complete blood count, creatinine, and chest X-ray.

One week following initial presentation, the patient demonstrated resolution of ocular pain, red eye and photophobia. His vision was 20/20 OU with pressures within normal limits. Slit lamp examination showed interval improvement in fine inferior KPs OS with trace cells in the anterior chamber. One-month follow-up demonstrated resolution a deep and quiet anterior chamber with interval improvement of KPs and conjunctival injection. The patient continued to deny joint pain or systemic symptoms consistent with HLA-B27 throughout the follow-up period.

### 3. Discussion

This case demonstrates an interesting presentation of an adult patient with his first episode of anterior uveitis temporally associated with a recent SARS-CoV-2 infection. We hypothesize that this patient had an increased baseline risk of anterior uveitis due to HLA-B27,<sup>9</sup> and when infected by SARS-CoV-2, a viral-induced inflammatory cascade was initiated that superseded the homeostatic threshold for anterior uveitis. Leukocyte and inflammatory mediator migration through the blood-ocular barrier, in conjunction with possible direct infection via ocular ACE2 receptors,<sup>2</sup> ultimately led to the initial anterior uveitis event in this patient. COVID-19 infections have been demonstrated in case reports to also trigger inflammatory conditions such as giant cell arteritis<sup>10</sup> and graft rejection following penetrating keratoplasty.<sup>11</sup> A recent prospective cross-sectional study 19.4% of patients undergoing anterior segment surgery over an 102-day period having SARS-CoV-2 viral ribonucleic acid in the aqueous humour, demonstrating the propensity of this virus to reach the site of our patient's inflammatory activity.<sup>12</sup> However, it should be noted that there is no definitive way to

conclude a causal relationship between infection and this anterior uveitis event, as it may be possible that the HLA-B27 status alone led to ocular inflammation. Alternative infectious etiologies for this iritis event, such as herpetic uveitis, is also on the differential as it has been known to occur following SARS-CoV-2 infection; however, the patient denied prior herpetic signs and symptoms, and there was no hypertensive nature to the inflammatory event.

The case published by Bettach et al., in 2021 was the first to describe anterior uveitis in an adult patient temporally associated with COVID-19 infection.<sup>6</sup> This patient was a 54-year-old female admitted to the intensive care unit for septic shock, heart failure, fever and gastrointestinal symptoms secondary to SARS-CoV-2 infection.<sup>6</sup> Two weeks following initial presentation, this patient developed blurred vision due to anterior uveitis OU.<sup>6</sup> The Bettach et al. patient contrasts our patient as he only promoted four days of fever following COVID-19 infection and denied any history of shock or cardiovascular compromise.<sup>6</sup> One key similarity was that both patients developed anterior uveitis within 2–3 weeks of a positive SARS-CoV-2 test and began improving after a 1-week steroid and cycloplegic treatment regimen.<sup>6</sup> A more recent publication by Sanjay et al., in 2021 reported a 35-year-old male with a known history of HLA-B27 associated anterior uveitis, who presented with an iritis flare following SARS-CoV-2 infection after stopping his immunosuppressive therapy.<sup>7</sup> This case contrasts our case as their patient was already known to have HLA-B27, though the timeline of infection and onset of symptoms mirrors our patient.<sup>7</sup>

Another interesting case of anterior uveitis temporally associated with SARS-CoV-2 was in a pediatric patient with Kawasaki-like multi-system inflammation.<sup>8</sup> This case by Wong Chung et al., in 2021 described a 12-year old boy with a 6-day fever of unknown origin, strawberry tongue, macular exanthem on the skin, conjunctival hyperemia and abdominal pain.<sup>8</sup> Multiple inflammatory markers were elevated, including C-reactive protein, liver function tests, and ferritin.<sup>8</sup> The patient progressed to shock and decreased level of consciousness with a diagnosis of multisystem inflammatory disease or Kawasaki disease temporally associated with SARS-CoV-2.<sup>8</sup> One week following initial presentation, the boy demonstrated blurred vision secondary to bilateral anterior uveitis.<sup>8</sup> He was treated successfully with prednisolone acetate for 10 days.<sup>8</sup> Anterior uveitis has been well defined in patients with Kawasaki disease. Shiari et al. found that approximately 36.1% of children with Kawasaki disease present with anterior uveitis.<sup>13</sup> A study by Esteve-Sole et al., in 2021 implicated IFN- $\gamma$  in the pathogenesis of multi-system inflammatory syndrome in the setting of COVID-19.<sup>14</sup> Although no multi-system inflammatory syndrome was present in our patient's clinical course, our team hypothesizes that the inflammatory cascade initiated by SARS-CoV-2 infection likely triggered a first event anterior uveitis associated with HLA-B27.

Benito-Pascual in 2020 described a patient with SARS-CoV-2 infection implicated as the etiology of panuveitis and optic neuritis.<sup>15</sup> This 60-year-old female presented with anterior chamber cells, vitritis, optic disc edema and peripapillary subretinal fluid. These symptoms were followed 10 days later by cough and dyspnea with an accompanying positive SARS-CoV-2 nasopharyngeal swab.<sup>16</sup> This case contrasts ours as our patient had resolved COVID-19 symptoms three weeks prior to uveitic presentation and demonstrated clear vitreous. Further research should be conducted to investigate the pathophysiology and risk factors for patients developing uveitis, either prior to demonstrating alternative symptoms, or following resolved SARS-CoV-2 features.

In summary, this case represents an interesting presentation of acute anterior uveitis associated with recent SARS-CoV-2 infection in the setting of positive HLA-B27 serology and without multi-system inflammatory disorder. With literature demonstrating a well-known association between SARS-CoV-2 infections and follicular conjunctivitis, eye care professionals worldwide should be made aware of the possibility of this pathogen causing anterior uveitis, even in the absence of dermatological or cardiovascular compromise. Patients should be counselled on interval improvement of ocular pain, red eye and photophobia over a

week with topical steroid and cycloplegic medications.

#### Patient consent

The patient consented to publication of the case orally.

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#### Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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