• Letter to the Editor •

Acute bilateral anterior uveitis in paediatric inflammatory multisystem syndrome temporally associated with COVID-19

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Dear Editor,

We report the case of a young child who presented with bilateral acute anterior uveitis in the context of suspected paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS).

The study was conducted in accordance with the principles of the Declaration of Helsinki. Written consent obtained from father as the patient is a minor.

PIMS-TS is a novel condition that has emerged during COVID-19 pandemic, first reported in the United Kingdom in April 2020. Conjunctivitis is the most common ocular manifestation.

A 9-year-old girl presented to the local Accident and Emergency Department with a 5-day history of fever and cervical lymphadenopathy, accompanied by abdominal pain, diarrhoea and reduced oral intake. She required intubation and was transferred to our hospital. In Intensive Care Unit (ICU), she required triple inotropes (noradrenaline, adrenaline, and milrinone). Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) polymerase chain reaction (PCR) and immunoglobulin G (IgG) were negative on admission. Chest radiography (XR) showed moderate bilateral perihilar bronchial wall thickening, but no effusion and no lymph node enlargement seen. C-reactive protein (CRP) was elevated (307 mg/L). D dimer, fibrinogen, ferritin, troponin 1, triglyceride and pro-B- type natriuretic peptide were also elevated. Interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) were not evaluated. Echocardiogram showed moderate global systolic dysfunction and diastolic dysfunction with mild mitral regurgitation, small pericardial effusion, and normal coronaries. Inferior vena cava was distended. Other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes and infections associated with myocarditis such as enterovirus were excluded. As laboratory results supported PIMS-TS, protocol was activated and she was started on intravenous methylprednisolone, dalteparin, vitamin D, milrinone and adrenaline. Noradrenaline was weaned.

She was extubated 4d later and was stepped down from Paediatric Intensive Care Unit (PICU). At that moment, her eyes were noted to be red, and she complained of blurry vision and sore eyes, so she was referred to Ophthalmology. Best corrected visual acuity was 0.0 logMAR in both eyes. Examination revealed bilateral conjunctival hyperaemia, fine keratic precipitates (KPs) in both eyes and 1+ cells on the right eye with 0.5+ cells on the left eye based on Standardization of Uveitis Nomenclature (SUN) classification[1] (Figure 1). Crystalline lens and vitreous were clear in both eyes. No abnormalities were found in the retina and intraocular pressure was within normal limits in both eyes. She was started on topical steroids 4 times a day and reviewed one week later. The inflammation was successfully resolving with only a residual faint flare bilaterally. Her visual function was normal, therefore topical steroids were tapered. She was seen one month later when the ocular inflammation had completely resolved.

To our knowledge, this is the first reported case of bilateral anterior acute uveitis in a PIMS-TS child in the UK.

A cluster of children with hyperinflammatory shock and features similar to Kawasaki disease was first reported in the UK in April 2020[2]. Subsequently, many countries reported similar presentations.

Preliminary definitions of this syndrome were published by the UK Royal College of Paediatrics and Child Health (RCPCH) and included 3 main criteria[3]. First, a persistent fever with inflammation (neutrophilia, elevated CRP and lymphopenia) and evidence of single or multi-organ dysfunction (shock, cardiac,

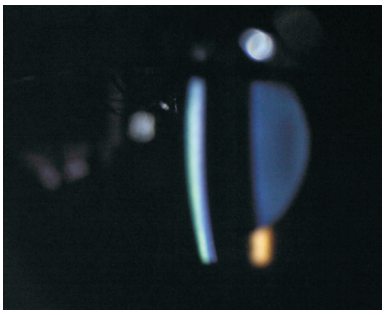

Figure 1 Anterior segment picture showing 1+ cells in the right eye.

respiratory, renal, gastrointestinal or neurological disorder) should be confirmed. Second, any other microbial cause should be excluded. And, last, SARS-CoV-2 PCR testing may be positive or negative.

In addition, an exaggerated cytokine storm may lead to increased vascular hypermeability, multiorgan failure and eventually death if the elevated cytokine concentrations remain over time[4].

Our patient met these 3 criteria, so diagnosis was made, and prompt management was started. Due to the severity of her symptoms, and although her eyes were noted to be red in PICU, ophthalmology referral was only placed once patient was extubated. She then complained of blurry vision and sore eyes.

Ocular findings on COVID-19 patients have been reported, suggesting the ocular surface could serve as an entry point and a reservoir for viral transmission[5]. Acute conjunctivitis is the most common ocular manifestation. Keratoconjunctivitis has also been described in a young female after travelling to a high-riskarea[6]. She presented with a 1-day history of unilateral conjunctivitis, photophobia, and watery discharge along with rhinorrhoea and nasal congestion. Eye and nasopharyngeal swab were positive for SARS-CoV-1 virus and negative for chlamydia, gonorrhoea with negative bacterial cultures. She had 20/20 vision both eyes (OU), conjunctival injection, follicles, 1 small pseudodendrite and subepithelial infiltrates with overlying epithelial defect, but no signs of intraocular inflammation.

Xia *et al*[7] reported a case where the patient was diagnosed with COVID-19 and conjunctivitis and had a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test from conjunctival swab. Our patient did not have follicular conjunctivitis, so we did not perform tear conjunctival swab.

A case of ophthalmia neonatorum as the presenting sign of COVID-19 has also been reported in the literature[8]. Mucopurulent discharge was noted on day 3 of life after an uncomplicated pregnancy and preventive erythromycin ointment applied at birth. Both parents had negative COVID-19 testing on admission, but mother did become positive after the event. Patient had positive nasopharyngeal and conjunctival SARS-CoV-2 PCR. Conjunctivitis resolved within 8d after a course of intravenous ceftriaxone, oral azithromycin, and topical erythromycin. Patient did not develop systemic disease.

In the Netherlands, a very similar case report has recently been published in the literature[9]. A 12-year-old boy with suspected PIMS-TS reported blurry vision with conjunctival hyperaemia. He was found to have mild anterior chamber reaction (1+ cells) and was successfully treated with topical steroids.

Furthermore, a case series of 5 children diagnosed with multisystem inflammatory syndrome secondary to COVID-19 and bilateral anterior acute uveitis has been reported in Turkey[10]. Three of these patients also had severe corneal punctate epitheliopathy. All of them were successfully treated with topical steroids.

List *et al*[11] examined the aqueous and vitreous samples of 16 patients who died from respiratory failure due to SARS-CoV-2 infection. All individuals included in this study were positive for the SARS-CoV-2 in nasopharyngeal swab test, but it was not found in the post-mortem aqueous and vitreous samples. Our patient's SARS-CoV-2 PCR and IgG were negative, so we did not perform aqueous or vitreous samples. Goel *et al*[12] reiterate in their study the rate of aqueous humour turnover is estimated to be 1.0% to 1.5% of the anterior chamber volume per minute, so all aqueous is re-secreted within a few hours.

This first reported case of bilateral anterior acute uveitis in association with PIMS-TS in the UK, along with the reported case from the Netherlands found in the literature, confirm uveitis is an ocular manifestation in children diagnosed with paediatric inflammatory multisystem syndrome temporally associated with COVID-19.

We encourage a multidisciplinary approach of these patients and a referral to ophthalmology for any child with conjunctival hyperaemia to rule out intraocular inflammation and to prevent possible ocular complications resulting from this.

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Conficts of Interest: Arruti N, None.

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