

## Nodular scleritis-a rare presentation of COVID-19& variation with testing

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### ABSTRACT

**Purpose:** – To report a rare case of patient presenting with nodular scleritis and SARS-CoV2.

**Observations:** This case highlights a unique presentation of SARS-CoV2 positive patient with nodular scleritis as a presenting feature. Patient initially had ocular symptoms and developed only mild systemic features subsequently which did not require hospitalization. COVID testing done at different time points showed variable results which correlated with the ocular features. This patient was followed up during quarantine using tele-ophthalmology.

**Conclusion and importance:** This case highlights a possible rare presentation of a SARS-CoV2 patient with nodular scleritis and also importance of tele medicine during these unprecedented times.

### 1. Introduction

An important aspect of the current efforts to control and reduce the impact of the COVID-19 pandemic has been to reduce the transmission of virus between individuals. In this respect, it is vital to understand the routes and modes of transmission, including the possibility of spread via the ocular surface. Several clinical studies have reported the presence of SARS-CoV-2 in tear specimens from individuals with COVID-19.<sup>1</sup> There has been discordance in reports regarding the proportion of COVID-19 patients with presence of virus in ocular specimens, possibly relating to factors including sensitivity of tests, type of ocular specimen and timing of specimen procurement in patients. In a large study including 1099 hospitalised patients with laboratory-confirmed COVID-19 from 30 hospitals in China, conjunctival congestion was documented in 9 patients (0.8%).<sup>2</sup> In another study of patients diagnosed clinically as COVID-19, one third had ocular symptoms and signs, including conjunctival hyperaemia, chemosis and epiphora. Early recognition and detection of these cases can help in adequate protection and reduced transmission of the disease.<sup>3,4</sup> Although viral infection of ocular cells has not yet been reported in patients, a recent report found that SARS-CoV-2 can infect conjunctival epithelium in an ex-vivo culture system.<sup>5</sup> This case report highlights an unusual presentation of a patient positive for COVID-19 and the need for treating every patient with red eye in this pandemic with adequate precautions to prevent inadvertent cross infection.

### 2. Case report

A 39 year old male patient presented with redness and pain in the right eye since 2 days. On examination, the patient had minimal chemosis with congestion in the right eye. He was diagnosed as conjunctivitis (Fig. 1) and prescribed topical 0.5% moxifloxacin eye drops 4 times a day in the right eye. Since conjunctivitis has been described as a possible clinical feature in patients of COVID-19, the patient was tested for SARS-CoV2 with Real time-polymerase chain reaction (RT-PCR) on nasopharyngeal swab sample and was found to be negative.

2 days later, the patient developed fever and cough along with worsening of ocular involvement and was reviewed through video consultation. He was found to have localised congestion and swelling in the superomedial quadrant of the right eye and diagnosed to have possible nodular scleritis clinically. A repeat nasopharyngeal swab sample was taken to test for SARS-Cov2 RT-PCR and patient was started on tablet azithromycin with antipyretics-acetaminophen for symptomatic relief while awaiting test results. Repeat swab tested positive for COVID-19 but since patient had only mild symptoms and signs of systemic illness, and he did not require hospitalization and was advised home quarantine. Patient was started on topical betadine 0.25% drops and nepafenac eye drops twice a day. Systemic blood investigations to look for underlying autoimmune disorders which could cause a nodular scleritis (Complete blood count, Random blood sugars, RA factor, ANA, c-ANCA, p-ANCA, ESR, CRP, urine microscopy) were advised and found to be within normal limits. Patient was also advised Chest X-Ray which was

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normal and TPHA, HIV 1 and HIV 2 to rule out associated infections which also was negative. Patient was followed up via telemedicine during the quarantine period. Subsequently there was an exacerbation of redness and pain in the right eye but no worsening of systemic condition 5 days after onset of fever. Examination of the right eye via teleophthalmology showed increased conjunctival congestion with worsening of the nodular inflammation. Fever and cough had reduced significantly by this consultation. Owing to non-resolving inflamed conjunctival/episcleral nodule an MRI orbit was advised to look for other possible causes of such a nodule like neoplasms and to rule out orbital extension. The MRI, T1W image (Fig. 2) was reported as a nodular lesion with scleral thickening and a possible inflammatory etiology suggesting a diagnosis of nodular scleritis. Patient was started on topical 1% prednisolone eye drops 4 times a day along with 0.25% betadine drops along with oral NSAID (non-steroidal anti-inflammatory drug) – etoricoxib 60mg once daily and reported significant improvement in ocular symptoms and signs which was continued for a week followed by tapering of steroid eye drops and continuing oral NSAID. A repeat MRI (Fig. 2) orbit was done after 4 days showed resolution of inflammation and scleral thickening. The patient's systemic condition remained stable and resolved without worsening or requiring hospitalization. 12 days after onset of fever and COVID positive test, a repeat nasopharyngeal swab for SARS-CoV-2 was found to be negative.

### 3. Discussion

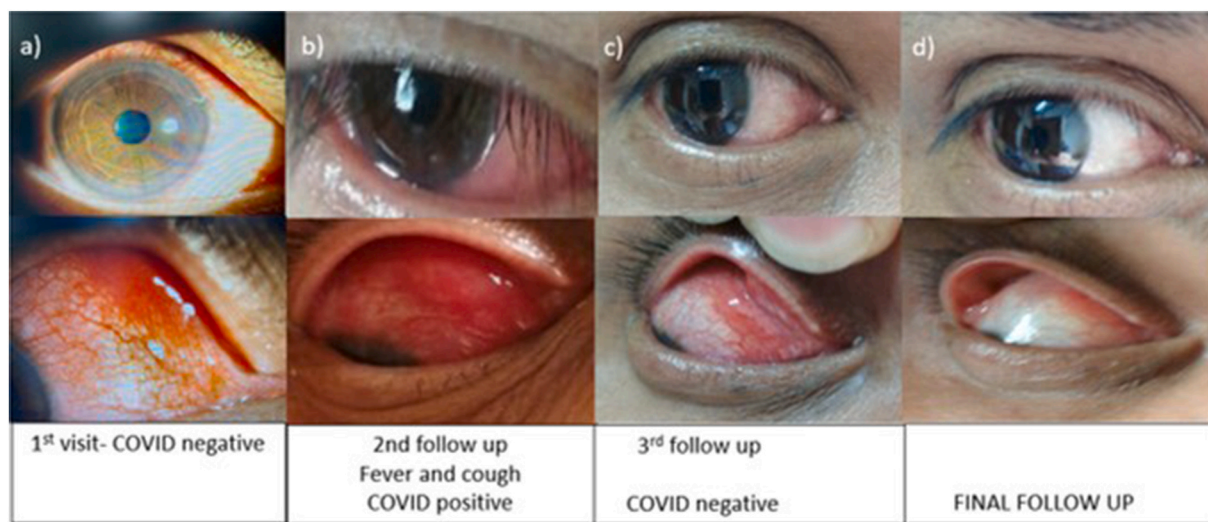
This is the first reported case of nodular scleritis being the presenting feature in a patient with COVID-19 infection. Another unusual feature of the case is that the patient had very mild systemic features with only ocular features which resolved with supportive treatment and did not require hospitalization.

There has been a report of 2 cases with confirmed COVID-19 developing anterior scleritis after their systemic symptoms improved and in these cases a thorough systemic workup did not identify any underlying autoimmune diseases.<sup>6</sup> One patient presented with necrotizing anterior scleritis and required intravenous cyclophosphamide, subcutaneous adalimumab in addition to oral prednisolone and the other patient had only sectoral anterior scleritis and responded to topical betamethasone and oral prednisolone.<sup>6</sup> There have also been reports of patients with COVID-19 developing acute follicular conjunctivitis, conjunctival hyperaemia, chemosis, epiphora, and increased ocular

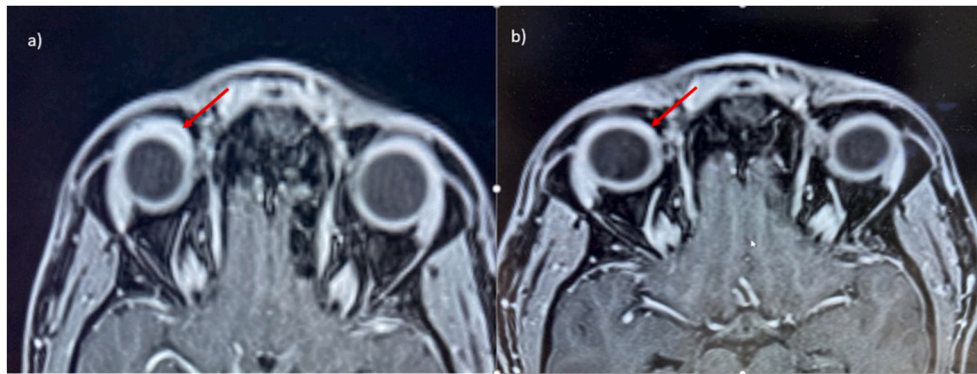
secretions.<sup>7,8</sup> These manifestations however have been observed more frequently in patients with severe pneumonia and during the middle phase of illness.<sup>4</sup> Only 1 patient in a series of 38 cases was reported to have conjunctivitis as the initial manifestation of the disease.<sup>4</sup> There has also been a case report of a patient presenting with conjunctival congestion and then rapidly worsening to develop severe acute respiratory illness within few hours.<sup>9</sup> This is a possible first report of an associated scleritis with an active SARS-CoV-2 infection. Though the patient did develop fever and cough, the patient was only mildly symptomatic requiring home quarantine and not hospitalization in contrast to earlier reports of ocular manifestations presenting in patients with severe respiratory distress often requiring admission to the intensive care unit.<sup>7</sup>

Scleritis is an inflammatory process involving the outer coating of the globe which is characterized by focal or diffuse hyperaemia, moderate to severe pain, and possible impairment of vision. The autoimmune scleritis constitutes the majority of cases of scleritis. Topical and/or systemic corticosteroids are the management of choice in these cases. Seldom, scleritis may be caused by an infectious etiology, seen in 5%–10% of cases. There has been an association of scleritis with herpes group of viruses, however there has been no evidence of association with SARS-CoV-2 yet.<sup>10</sup>

This case also highlights an unusual trajectory of the disease wherein the patient had a fluctuating COVID test positivity correlated with the fluctuating levels of ocular manifestations as well. It is important to try and decipher the possible reasons for the varying COVID test results. Negative test result immediately followed by a positive test result within a short period of time, could be due to a false-negative test result. RT-PCR is commonly used to detect SARS-CoV2 in samples. There are a number of reasons for false negative results. It is well known that results from real-time RT-PCR can be affected by the variation of viral RNA sequences.<sup>10,11</sup> In addition according to the natural history of the COVID-19 and viral load kinetics in different anatomic sites of the patients, sampling procedures can contribute to the false-negative results. A study has reported sputum as the most accurate sample for laboratory diagnosis of COVID-19, followed by nasal swabs, while throat swabs were not recommended for the diagnosis. The role viral load kinetics of SARS-CoV-2 has been documented in two patients in Korea where they have shown a variation, suggesting a different viral load kinetics from that of previously reported other coronavirus infections.<sup>12,13</sup> The virus was detected from upper respiratory tract (URT) and lower respiratory



**Fig. 1.** a) Diffuse anterior segment photographs reveal localised conjunctival congestion with dilated tortuous telangiectatic vessels in superior and superonasal conjunctiva. b) Shows additional violaceous hue appearance of the sclera in addition to conjunctival congestion and chemosis with dilated tortuous telangiectatic vessels with nodular swelling in the superonasal quadrant with dilated tortuous conjunctival vessels. c) and d) gradual resolution of conjunctival congestion and chemosis with resolving nodular swelling.



**Fig. 2.** MRI,axial T1W image of the patient shows. a) localised thickening of medial aspect of the right eyeball with localised area of hyporeflexivity suggestive of fluid accumulation within the sclera confirming the diagnosis of anterior nodular scleritis. b) resolution of scleral thickening post treatment.

tract (LRT) specimens 2 days after onset of symptoms, however an altered viral load led it to be negative after 5 days but on the 7th day due to a spike in the viral load the patient again turned out to be positive. These findings indicate the different viral load kinetics of SARS-CoV-2, suggesting that sampling timing and period of the disease development play an important role in real-time RT-PCR results.

Conjunctival swabs from patients with ocular manifestations have proven positive for SARS-CoV-2 5% in only 5% patients.<sup>14</sup> This low detection rate could indicate a low prevalence of the virus in conjunctival secretions and tears or viral loads below the detection thresholds of existing PCR diagnosis techniques.<sup>15</sup> This could explain the initial negative result on RT-PCR. One limitation of this case report was that we did not demonstrate the virus from conjunctiva to conclusively link the nodular inflammation to SARS-CoV2. Even though the virus was not detected, and low detection rates of SARS-CoV-2 from the conjunctiva is known,<sup>14</sup> it still can be a co-incidental finding of a nodular scleritis with a coexisting SARS-CoV2 infection even after ruling out other possible causes. Hence a larger cohort of patients presenting with scleritis and COVID-19 need to be evaluated to conclusively prove the association, however this case does represent an interesting association of the scleritis with a SARS-CoV2 infection.

This case also illustrates the usefulness and relevance of tele-ophthalmology procedures during the COVID-19 epidemics, which, in addition to preventing the transmission of SARS-CoV-2, could help detect potentially COVID-19 patients. Ophthalmologists should be aware of these unusual ocular presentations of COVID-19 since they could precede the development of systemic manifestations and help early identification and treatment of these cases.

#### Patient consent

Consent to publish this case report has been obtained from the patient in writing. This report does not contain any personal identifying information.

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#### Author contribution

All authors attest that they meet the current ICMJE criteria for Authorship. Dr. Arif Adenwala – Case imaging and data. Dr. Rohit Shetty

– Case imaging and concept. Dr. Sharon D'souza – Manuscript writing and data processing., Dr. Padmamalini Mahendradas – imaging interpretation, Dr. Gairik Kundu-manuscript writing and corresponding author.

#### Declaration of competing interest

The following authors have no financial disclosures: AA, RS, SD, PM, GK.

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