Tonic Pupil Following COVID-19

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Abstract:
A 37-year-old female patient presented in the ophthalmic emergency department with sudden onset decreased vision with a history of being treated for COVID 19 3 weeks earlier. On examination, she was found to have a tonic right pupil, which was confirmed with a dilute pilocarpine test. As tonic pupils are known to be caused by neurotropic viruses and our current understanding of the SARS-CoV-2 is that it does affect the nervous system, we feel that the tonic pupil in our patient may be secondary to COVID 19.

Journal of Neuro-Ophthalmology 2021;41:e764–e766
doi: 10.1097/WNO.0000000000001221
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A 37-year-old female patient presented in the ophthalmic emergency department with sudden onset decrease in right eye vision of 5–6 days duration associated with pain over the right brow. The patient also complained of discomfort in bright light. She had no pain on ocular movement and no associated tinnitus, vomiting, diplopia, or transient visual obscurations. Magnetic resonance imaging (MRI) and magnetic resonance angiography of the brain and orbit done 2 days earlier showed no significant abnormality.

She gave a history of high fever, cough, and anosmia three weeks earlier, a nasal swab reverse transcription polymerase chain reaction (RT PCR) was positive for SARS-CoV-2 and a high-resolution computed tomography (HRCT) of the chest showed patchy infiltrates. Her D dimer level was 530 ng/mL, erythrocyte sedimentation rate was 63 mm in 1 hour, and C
reactive protein was 42.1 mg/L. She had been hospitalized and treated with remdesivir, intravenous antibiotics, dexamethasone, and deriphylline. A repeat nasal swab RT PCR 2 weeks after the onset of symptoms was negative. She had no other symptoms of cranial or autonomic nervous dysfunction.

On examination her best-corrected visual acuity was 6/6, N6 in both eyes with intact color vision and full and painless ocular movements. Pupillary evaluation revealed anisocoria with the right eye pupil being 5.5 mm in ambient light and the left 3.5 mm (Fig. 1A). Right eye pupil showed a sluggish reaction to direct light with vermiform movements and segmental constriction on slit-lamp evaluation (Fig. 2). There was a sluggish reaction to near response as well. The left eye reacted briskly to light and near reflex. There was no relative afferent pupillary defect. All other anterior and posterior segment findings and visual fields were within normal limits. Her deep tendon reflexes were brisk and bilaterally symmetrical.

Despite the poor near response, a provisional diagnosis of right eye tonic pupil was made and denervation supersensitivity tested and proved with dilute pilocarpine (0.1%) (Fig. 1C). When reviewed 3 weeks later, she complained of difficulty in focusing near objects with her right eye. Her anisocoria and light reaction were unchanged; however, the near response showed tonic contraction of the right pupil. The patient was advised to use glasses for near vision and review after 2 months.

Tonic pupil is a common cause for anisocoria and is characterized by poor or absent reaction of the pupil to light, a slow and tonic response to near and cholinergic supersensitivity. It occurs because of damage to the ciliary ganglion or short ciliary nerves in the retrobulbar space or intraocular, suprachoroidal space resulting in internal ophthalmoplegia and is followed by appropriate and inappropriate reinnervation (1). The characteristic light near dissociation is because of inappropriate reinnervation and seen after a few weeks to a few months of onset of the disease (2).

Reported etiology include infections, autoimmune process, choroidal and orbital tumors and trauma, including surgery, to the globe and orbit. Often it is idiopathic and known as Adie Syndrome. Occasionally, it may represent one manifestation of a widespread, peripheral, and autonomic neuropathy (1) and the involvement in such cases is often bilateral. Among infectious causes, viral etiology due to herpes zoster (3), chickenpox, and influenza have been reported. These viruses are known to invade the nervous system and it has been hypothesized in these cases that the virus infects the ciliary ganglion or the short ciliary nerves leading to their damage (4).

SARS-CoV-2 is a virus belonging to the Coronaviridae family and the causative agent of the current COVID 19 pandemic. It has shown neural invasion (5) and anosmia or hyposmia is a common symptom of COVID 19. This may be because of direct invasion of the olfactory nerve and olfactory bulb or because of indirect involvement by the activation of immune-mediated mechanisms (6). There are a number of reports of neuro ophthalmic association of COVID 19 in the form of external ophthalmoplegia (7), optic neuritis (8), and autonomic dysfunction in the form of Miller Fisher and polyneuritis cranialis (9). Dinkin et al (7) hypothesized that the manifestations were because of direct invasion by the virus; while in latter reports (8,9) it was presumed to be a postviral immune-mediated injury as cause for the denervation.

At the time of diagnosing our patient, there were no known reports of SARS-CoV-2 causing tonic pupil; however, subsequently Ordas et al reported a case of concurrent tonic pupil and trochlear nerve palsy in COVID-19 (10) and considered an immune-mediated mechanism as cause for the same. In our patient, MRI brain and orbit did not show any lesion along the ciliary ganglion or short ciliary nerves; furthermore, CSF was not tested for the presence of SARS-CoV-2 so the possibility of a direct invasion is unlikely, but cannot be ruled out. The occurrence of tonic pupil following COVID 19 may be coincidental; however, in view of the timeline of her symptoms, the known association of tonic pupil with viral infections and the reports of neurological associations of COVID 19 (6), we feel that there is a possibility that the tonic pupil in our patient was caused by SARS-CoV-2 secondary to a postinfectious immune response.

STATEMENT OF AUTHORSHIP
Category 1: a. Conception and design: M. Gopal, S. Ambika, and K. Padmalakshmi; b. Acquisition of data: M. Gopal, S. Ambika, and K. Padmalakshmi; c. Analysis and interpretation of data: M. Gopal, S. Ambika, and K. Padmalakshmi. Category 2: a. Drafting the manuscript: M. Gopal; b. Revising it for intellectual content: M. Gopal, and K. Padmalakshmi. Category 3: a. Final approval of the completed manuscript: S. Ambika.

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