CASE REPORT

UNILATERAL ADIE'S TONIC PUPIL AFTER CORONAVIRUS DISEASE-19 (COVID-19): A CASE REPORT

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ABSTRACT

Introduction: *Adie's tonic pupil is a neuro ophthalmological disorder characterized by dilated pupil, which is unresponsive to light. It is caused by damage to postganglionic fibers of the parasympathetic innervation of the eye. Recent events of the coronavirus disease 2019 (COVID-19) pandemic had suggested that severe acute respiratory syndrome coronavirus-2 infection (SARS-CoV-2) had neurotropic and neuroinvasive capabilities.*

Purpose: *To report a rare case of unilateral Adie's tonic pupil after COVID-19.*

Methods: *A single case report study.*

Case Report: *A 31-year-old woman presented with a glare on the right eye 3 months ago. No other symptom was reported. No prior history of using any eye drops and trauma. Further investigation revealed a history of asymptomatic SARS CoV-2 infection. Her best-corrected visual acuity of both eyes was 1.0, but we observed an impairment of accommodation on the right eye. A fixed dilated right pupil, 8 mm in diameter, was observed without any constriction on near reflex. Slit lamp and funduscopy examination were within normal limits on both eyes. Pilocarpine 0.1% test was positive on the right eye. Neurological examinations and brain imaging was within normal limits. The patient was diagnosed with Adie's tonic pupil. She was treated with pilocarpine 0.1% once daily. After 2 months of follow up, her complaint of glare was diminished but no improvement of near acuity was seen on the right eye.*

Conclusions: *This case report was one of the first few cases of Adie's tonic pupil possibly associated with COVID-19.*

Keywords: *Adie's tonic pupil, COVID-19, anisocoria, pilocarpine.*

INTRODUCTION

Since coronavirus disease 2019 (COVID-19) was recognized as a pandemic in December 2019, different neurological symptoms have been reported in a few cases after COVID-19 infection.[1] The prevalence of neurological manifestation after COVID-19 infection was various. Emerging clinical evidence suggests neurological involvement is an important aspect of the disease.[2] The underlying mechanisms can include both direct invasion and inflammatory responses. Coronavirus infections have been associated with neurological manifestation. Neurotropic and neuroinvasive capabilities of coronaviruses have been described in humans. Several routes of CNS invasion can be used by viral pathogens, among the hematogenous route, peripheral nerves, or olfactory sensory neurons. Neurotrophic characteristics of coronavirus

have been described, but the mechanism of damage is yet to be elucidated. Most recently, pupillary involvement associated with the virus has been reported.[3-5]

Adie's tonic pupil is neuro ophthalmological disorder characterized by a large, regular pupil with decreased reaction to light but a strong and tonic pupillary response to near vision (light-near dissociation).[6] The pupil experiences a slow tonic redilation on looking from near to far distance. Other characteristics include sectoral palsy of the iris sphincter, accommodative paresis, and denervation cholinergic supersensitivity. It is caused by damage to the ciliary ganglion or short ciliary nerves (postganglionic parasympathetic nerve injury produces an Adie tonic pupil.[7]

Approximately 70% of patients are women 20-40 years of age and tonic pupils are unilateral in 80% of cases.[8] Pharmacological testing can be used to confirm the diagnosis of Adie's tonic pupil. The diagnosis was confirmed with the rapid miotic response of the affected pupil to pilocarpine 0.1% drop.[9] 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,[10] that the tonic pupil in our patient may be secondary to COVID-19. Here we present a curious case of unilateral Adie's tonic pupil after SARS-CoV-2 infection.

CASE REPORT

A 31-year-old woman presented with a glare on the right eye 3 months ago. She denied having any symptoms of blurry vision, ptosis, diplopia, and headache. No prior history of using any eye drops and trauma. Further investigation revealed a history of asymptomatic SARS CoV-2 infection based on a positive rapid antibody test and close contact with a confirmed COVID-19 patient 2 months prior she first noticed her ocular symptom. No prior history of autoimmune disease such as rheumatoid arthritis, systemic lupus eritematous (SLE), Multiple sclerosis (MS), or Guillain Barre Syndrome. Ophthalmology examination revealed best-corrected visual acuity of both eyes was 1.0 using S-1.75 OU, but an impairment of accommodation was observed on the right eye by using rule. A dilated pupil, 8 mm in diameter, was observed on the right eye without any constriction under direct and indirect illumination, furthermore, this anisocoria was greater in bright light. Near reflex did not produce any constriction on the right eye. No signs of ocular injury were observed. The ocular movement did not show any limitation as seen in figure 3. Slit lamp and funduscopy examination was within normal limits on both eyes.

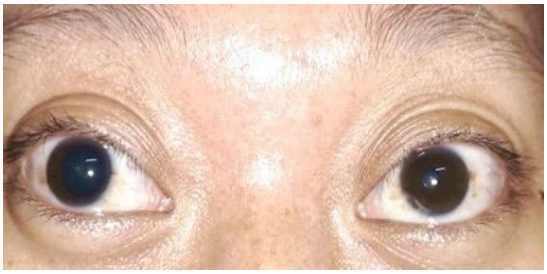

Figure 1. Right pupil was dilated and not reactive to light. In bright light, anisocoria was greater.

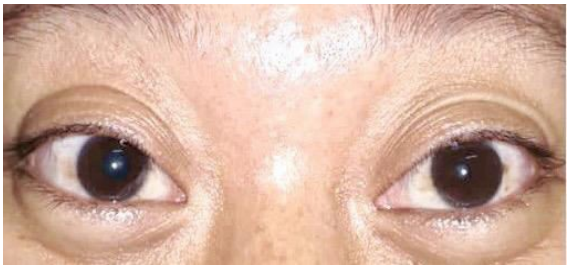

Figure 2. A miotic right pupil after instillation of diluted pilocarpine 0.1%.

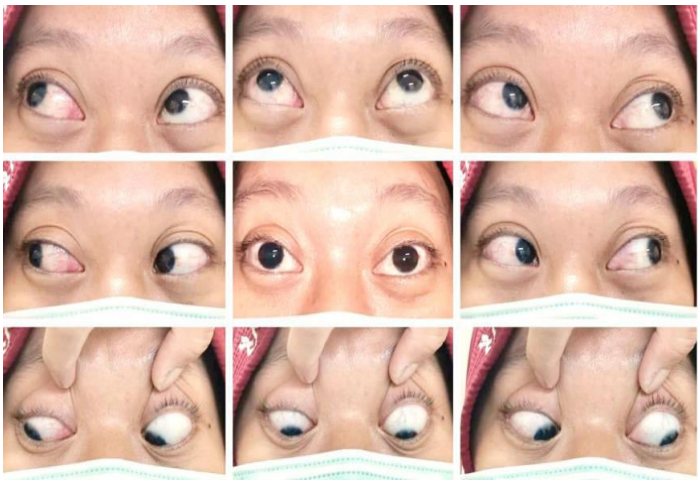

Figure 3. The ocular alignment and movement were within normal limits**.**

She was given one drop of pilocarpine 0.1% and after 30 minutes, the pupil diameter of the right eye became 4 mm in bright light, whereas the left eye showed no reaction. She was referred to a neurologist to evaluate any neurological deficit. Detailed neurological examinations, including cranial nerve functions and deep tendon reflexes, were normal. Blood tests were normal, including hematological routine, urea, creatinine, blood glucose, and lipid profile. She underwent brain imaging, such as MRI, MRA, MRV, and the result was within the normal limits as shown in figure 4.

The patient was diagnosed with Adie's tonic pupil on the right eye. She was treated with diluted pilocarpine 0.1% once a day. After the follow-up period for 2 months, the right pupil

size was 4 mm but still did not show any contraction on accommodation. Near vision was also not improved on the right eye. The near addition of S+1.50 on the right eye improved her near acuity to N8 on 33 cm.

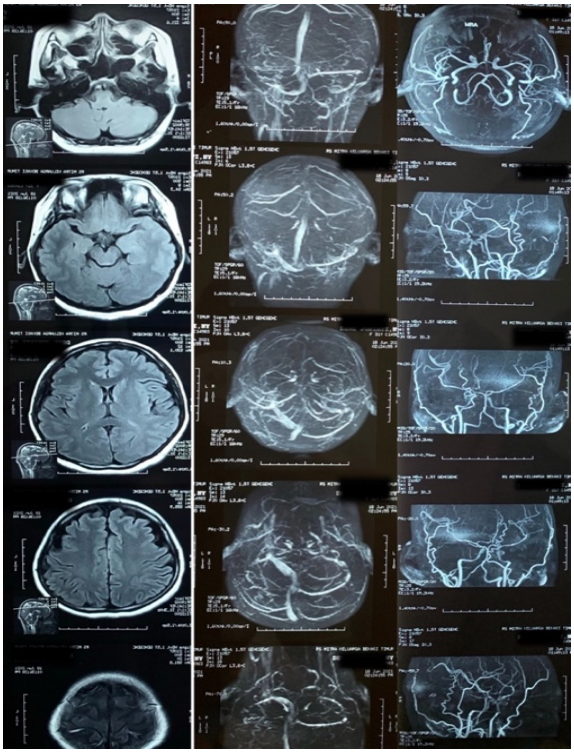

Figure 3. Compression and ischemic lesions were absent on MRA, MRI, and MRV**.**

DISCUSSION

Coronavirus disease 2019 (COVID-19) has become a global pandemic, affecting millions of people. Coronavirus is one of the major viruses that primarily targets the human respiratory system, but also has neuroinvasive capabilities and spread from the respiratory tract to the central nervous system (CNS). [1] Neuroophthalmology manifestations associated with SARS-CoV-2 have also been identified.[2] Wang et al. described dysautonomic syndrome as a new finding due to COVID-19, including Adie's tonic pupil, in their study.[3] Recently, 2 cases of Adie's tonic pupil associated with (SARS-CoV-2) have been reported his is thought to occur due to a direct invasion of the ciliary nerves or ganglion by the virus due to its neurotropism, or due to a delayed immune-mediated mechanism.[11]

Adie's tonic pupil has a prevalence of 2 per 1000 population and occurs in a 6:1 female to male ratio with an average age of onset of 32 years.[12] This disease is mostly idiopathic with no identifiable cause but may rarely be caused by local disorders involving the orbit that affect the ciliary ganglion including infections, ischemia, migraine, autoimmune disorders such as Guillain- Barre syndrome, and orbital tumor. The main differential diagnosis to consider for a large pupil is a third nerve palsy, pharmacological mydriasis, Adie's tonic pupil and iris

trauma.[13,14] It is thought to be a result of damaged postganglionic parasympathetic nerve fibers of the ciliary ganglion most commonly by an inflammatory process or idiopathic. Pupillary symptoms result from damage to the postganglionic parasympathetic supply innervating the ciliary body and iris which first travel as preganglionic fibers along with the oculomotor nerve to synapse at the ciliary ganglion within the orbit.[15]

Neuroopthalmologic manifestations associated with SARS-CoV-2 have been identified. Seller et al. reported a case of inflammatory chorioretinopathy and bilateral tonic pupil two days after COVID-19 infection.[2] Ordas *et* al. reported a case of fourth cranial nerve palsy with tonic pupil developing 2 weeks after a SARS-CoV-2 infection.[11] Tutar *et* al. in their case report described Neuroophthalmology manifestation associated with SARS-CoV-2 have been identified.[16] Nieto *et* al. reported SARS-CoV-2 infection related to bilateral tonic pupil with a presumed immune- mediated mechanism.[17] Gopal *et* al. reported SARS-2-CoV infection following by tonic pupil after 3 weeks infection, which was confirmed with dilute pilocarpine test.[18] In our patient, the onset of Adie's tonic pupil was 2 months after SARS-CoV-2 infection. This case was regarded as a possible COVID-19-related tonic pupil based on probable SARS-CoV-2 infection just prior to ophthalmologic complaints, after excluding all possible causes.

Lee et al. reported that light-near dissociation was seen in 88.2% of Adie's tonic pupil cases.[19] The disease also shows hypersensitivity to muscarinic receptor agonists (e.g., pilocarpine 0.1%) due to supersensitivity of the damaged postganglionic ciliary nerve fibers. The diameter of pupil with this disease will reduce after being given a small concentration of parasympathomimetic.[20] However, some pupils in third nerve palsy also respond to 0.1% pilocarpine, and therefore, the diagnosis of a tonic pupil should not be based on pharmacologic testing of pupils alone. Specific workup for each patient will depend on the associated manifestations. Magnetic resonance imaging scans may be useful to exclude other conditions that can mimic or cause Adie's tonic pupil.[7] After thorough ophthalmological and neurological examinations, we found no abnormalities suggesting an oculomotor nerve palsy in this patient.

Most patients with Adie's tonic pupil do not require any treatment.[7] Patients with an underlying systemic cause should have treatment directed at their other autonomic neuropathies. The treatment for impairment of the eyes (due to accommodative paresis) is to prescribe reading glasses. Almost all patients with Adie's tonic pupil had an accommodative paresis at the time of onset, and accommodative symptoms are difficult to treat and usually resolve during several months of onset. The reason for light-near dissociation is the ciliary body has much denser neuronal innervation than iris sphincter. In this case, after follow-up for 2 months, accommodative symptoms are not yet improved. Topical low-dose pilocarpine drops

may be administered as a treatment as well as a diagnostic measure.[20] Before initiating therapy, a consideration of risk-benefit ratio is mandatory. Patients should be informed about potential side effects such as chronic conjunctival irritation, cataract, and even systemic toxicity. Batawi and Micieli prescribed pilocarpine 0,1% three times a day to be used for the patient with Adie's tonic pupil for symptomatic relief.[21] Due to the long-term nature of this disease, the patient was given a diluted pilocarpine eye drop 0.1% once daily to minimize unwanted side effect of the drug. Although Adie's tonic pupil usually does not require treatment, dilute pilocarpine can be considered as a therapy in patient with glare or blurred vision. After follow-up for 2 months, no side effect was noted and the patient felt significant improvement in her symptoms, but unfortunately her accommodation was not yet improved. Although we initiated therapy in our patient using pilocarpine 0.1%, we do not suggest this is ideal initial therapy for all patients with Adie's tonic pupil.

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CONCLUSION

The diagnosis of Adie's tonic pupil was made through careful history taking and neuro ophthalmological examinations. Pilocarpine 0.1% once a day was sufficient to reduce glare without compromising long-term safety. To our knowledge, this was one of the first few cases of Adie's tonic pupil possibly associated with SARS-CoV-2 infection, therefore the disease could be added to the already long list of COVID-19 manifestations. Further investigations should be done to find the causal relationship between Adie's tonic pupil with this devastating novel virus.

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