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Acute Isolated Near Vision Difficulty in Patients With COVID-19 Infection

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We describe 3 COVID-19 patients with acute near vision difficulty.

Case 1, a 46-year-old man, presented with severe, generalized headache, fever, sore throat, anosmia, dysgeusia, and chest discomfort. The following day, nasopharyngeal swab for SARS-CoV-2 reverse transcriptase polymerase chain reaction was positive. He then noticed difficulty reading his quarantine documents. He had no other visual, neurological, or dysautonomic complaints. His pupil sizes were 3 mm bilaterally with no anisocoria in light and darkness. Pupillary reaction to light was normal but impaired to near stimulus, worse on the right eye. Near vision was N6 in the right eye and N5 in the left eye. Convergence was normal. Details are in Table 1.

Case 2, a 40-year-old man, developed cough and acute blurring of near vision; and was diagnosed with COVID-19 infection. He did not have dysgeusia, anosmia, neurological, or autonomic symptoms. Examination on day 6 of illness revealed borderline anisocoria (right pupil: 2.5 mm and left pupil: 2 mm). The left pupil became eccentric in shape a few days later. Pupillary reaction to light was sluggish compared with near stimulus. Near vision was N10 in the right eye and N6 in the left eye. Both were correctable to N5 with +1.00 glasses. Convergence and other eye movements were intact. There was no eye retraction on upgaze (Table 1). On day 18 of illness his ocular findings remained the same, but he was reading comfortably using +1.00 glasses. More formal evaluations, including cyclorefraction, were planned on deisolation. He has yet to return for review.

Case 3, a 28-year-old man, was diagnosed with COVID-19 when he presented with fever, sore throat, cough, anosmia, and dysgeusia. He developed near vision difficulty approximately 2 weeks later and was readmitted on day 33 for resultant headaches. He had no other neurologic, autonomic, or sudomotor symptoms. His pupils were symmetric, 5 mm, and reacted poorly to light but briskly to near stimulus. Near vision was N5 bilaterally but accommodation amplitude were reduced for age. Convergence was intact. Slit-lamp examination revealed subtle sectoral contraction of the left pupil, without iris atrophy. His ankle reflex was reduced, and tibial H-reflex was absent on nerve conduction studies. His autonomic function tests revealed postural tachycardia; the heart rate rose from 91 to 122 beats/min on standing and from 83 to 114/min during the tilt-table test without postural hypotension or other signs of dysautonomia (Table 1).

We describe 3 patients with COVID-19 infections who developed acute near vision difficulty with asymmetric accommodation defects. In Case 1, the pupils were of normal size and reacted better to light than near stimulus—the "inverse" Argyll Robertson pupil. Case 2 had the more typical Argyll Robertson pupils: small, slightly irregular pupils that reacted better to near stimulus than light. Case 3 had features of Adie's pupils and with reduced ankle reflex —the Adie syndrome. Convergence was intact; and accommodative convergence to accommodation ratio not significantly raised, suggesting that the near vision difficulty was independent of convergence. The patients had no signs of dorsal midbrain pathology, diffuse peripheral neuropathy, or generalized autonomic dysfunction.

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T. Umapathi, K. Z. Li: conceptualization, case evaluation and manuscript preparation. C. F. Chin, R. Agrawal, K. Vijakumar, G. S. E.Tan, P. H. Ung, T. K. Yeo: case evaluation and manuscript preparation.

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The 3 patients with localized ocular dysautonomia described in this paper and , 1 case of more diffuse autonomic dysfunction have been included in the comprehensive survey of COVID-19 neurological manifestations in Singapore: Neurology of COVID-19 in Singapore https://doi.org/10.1016/j.jns.2020.117118

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TABLE 1. Tabular representation of key ophthalmic findings and laboratory investigations in 3 patients with COVID-19 infection

A: Ophthalmic and Neurologic Examination	Case 1		Case 2		Case 3	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
Distance VA (unaided)	6/6	6/6	6/9	6/9 + 1	6/6	6/6
Near VA* (unaided)	N6	N5	N10 (with difficulty)	N6 (with difficulty)	N5	N5
Near VA* (+1.0D)	N5	—	N5	N5	—	—
Near point of convergence	32 cm		6 cm		To nose	To nose
Near point of accommodation	37 cm	31 cm	14–18 cm		22–25 cm	29–33 cm
Accommodative amplitude	2.7D	3.2D	5.5–7.1D		4–4.5D	2.9–3.5D
AC/A	Not performed		Not performed		5.4	
Accommodation facility	Not performed		Not performed		15–18 cycles per minute using ±0.5D; *Patient was tested with but unable to perform using ±1.00D, ±1.50D and ±2.00D*	
Autorefraction	−0.25/−0.25 × 154	0.00/−0.25 × 58	Not performed		Not performed	
Refraction	Not performed		Not performed		Plano	
Ocular examination	Both eyes: Clear cornea and lens; Optic disc 0.5; No retinopathy		Both eyes: Clear cornea and lens; Optic disc 0.4; No retinopathy		Both eyes: Clear cornea and lens; Optic disc 0.3; No retinopathy	
Eye movements (convergence, pursuit, and saccade)	Normal		Normal		Normal	
Deep tendon reflexes	Intact		Intact		Absent ankle	
Other neurological findings	Nil		Nil		Absent H reflex	
Signs/symptoms of dysautonomia	Nil		Nil		Postural tachycardia	
Pilocarpine 0.125% test	Not performed		Not performed		No reaction	No reaction

B: Pertinent clinical and laboratory features	Case 1		Case 2		Case 3	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
Medical history	Hypertension, hyperlipidemia, and migraine		Nil		Nil	
Medications, including eye drops	Lisinopril 20 mg/day		Nil		Nil	
White blood cell ($\times 10^9$/L)	3.5		3.9		8.8	
CRP (mg/L)	2.8		0.6		Not performed	
ESR (mm/hr)	10		Not performed		2	

(Continued)

B: Pertinent clinical and laboratory features	Case 1		Case 2		Case 3	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
LDH (U/L)	462		342		Not performed	
HIV Antibody screen	Non-reactive		Not performed		Non-reactive	
Chest radiograph	No consolidation or other infective changes		No consolidation or other infective changes		No consolidation or other infective changes	
Anticardiolipin IgM/IgG	Negative		Not performed		Negative	
Anti-Ro/Anti-La antibody	Negative		Not performed		Negative	
Antiganglioside antibodies	Negative		Not performed		Negative	
Syphilis IgG/RPR	Negative		Not performed		Negative	
Brain MRI	Not performed		Not performed		Normal	

*Moorfields bar reading book.

AC/A, accommodative convergence/accommodation ratio; CRP, C-reactive protein; D, diopter; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; RPR, rapid plasma regain; VA, visual acuity.

Isolated internal ophthalmoplegia, with combined pupillary and accommodation abnormalities, has been reported after chicken pox infection (1). Tetanus can cause accommodation paralysis, usually in cephalic tetanus. Deficiency of near-reflex, similar to Case 1, was described in a 13-year-old boy about 3 weeks after onset of tetanus (2). Near vision was N36 in both eyes, correctable with +2 diopter lens. Pupillary reaction was brisk to light but sluggish to near stimulus, with no other ocular or neurological deficits. The deficit did not recover after 5.5 years. Inverse Argyll Robertson pupils were reported in 1 patient recovering from botulism (3). Acute *Corynebacterium diphtheriae* infection and treatment with diphtheria antitoxin can cause accommodation paralysis and "inverse" Argyll Robertson pupil (4,5). Usually bilateral, it occurs up to 3 to 4 weeks post-infection. Recovery may be delayed by years. A seminal postmortem study demonstrated segmental demyelination of peripheral nerves (6).

The absence of dorsal midbrain signs, the nonuniform contraction of the iris in Case 3, and the development of an eccentric pupil in Case 2 support our localization to the ciliary nerves rather than dorsal midbrain. However, we do not think the pathology is neuronal degeneration at the ciliary ganglia, as is the case with idiopathic Adie's pupils. The 9:1 predominance of accommodation to light reflex neurons should cause more consistent affliction of the light reflex. Rather, we posit the patchy nature of segmental demyelination at the ciliary nerves, as in diphtheria (6), allows for more random involvement of the 2 functional sets of parasympathetic nerves. This would conceptually explain the isolated yet mixed deficits in our 3 patients. COVID-19 seems to have a predilection for dysimmune cranial mononeuropathies, Miller Fisher syndrome (MFS), and Guillain–Barre syndrome (GBS) (7). In our patients with mild COVID-19 infection, we believe the ciliary nerve pathology is likely from analogous dysimmune segmental demyelination; although the short latency from onset of COVID-19 symptoms in 2 out of the 3 patients suggests direct viral injury.

The classic localized autonomic disorders of the eye - Adie's syndrome, and its expansion, Ross syndrome- are also postulated to have postinfectious and dysimmune etiology. Unsurprisingly, Adie's pupil has been associated with GBS, MFS, and antiganglioside antibodies too (8,9). Besides Adie's pupils, loss of ankle and tibial H-reflexes, Case 3 had orthostatic tachycardia, all signs of patchy involvement of the autonomic and somatic peripheral nervous system. We also encountered another COVID-19 patient with restricted autonomic dysfunction; he developed sweating abnormalities and orthostatic tachycardia. He did not have any signs of ocular dysautonomia (10). Interestingly, diphtheria is also associated with delayed, mainly cardiovagal, dysautonomia and hyperhidrosis (5,11).

Near vision difficulty is a relatively innocuous symptom that may be under-reported. Whilst deployed to care for COVID-19 patients, we encountered approximately 8 young to middle-aged patients with similar complaints. From a combination of lack of suspicion and infection control restrictions, they were not evaluated carefully. We attributed one to hyperglycemia, another to early onset presbyopia, and 2 to anticholinergic effects of medications; and several cases were labeled as dry eyes.

In conclusion, we would like to highlight the occurrence of accommodation and pupillary abnormalities in COVID-19 patients, as a manifestation of dysimmune localized dysautonomia.

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