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Acquired Brown syndrome following COVID-19 infection in a child

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Coronavirus disease 2019 (COVID-19) is a highly virulent multi-system disease caused by the SARS-CoV-2 virus. Symptoms of COVID-19 infection commonly include fever, malaise, cough, and shortness of breath. Numerous manifestations affecting nearly every organ system have been described. Ophthalmic manifestations, though rare, have been reported, including, most commonly, conjunctivitis in both adults and children, which often occurs as part of a multisystem inflammatory syndrome in children. However, pediatric ocular findings of COVID-19 are poorly understood. We present a case of acquired Brown syndrome in a child following COVID-19 infection.

Case Report

A 12-year-old girl with no significant past medical or ocular history presented at a local urgent care facility for fever (100.4F), headache, chills, and myalgias. Ocular examination at that time was described as “normal,” without mention of conjunctival injection. The patient tested positive for COVID-19 on real-time polymerase chain reaction testing and was discharged in stable condition without treatment. At that time, she began to experience intermittent vertical diplopia, blurry vision, and dull right-sided peribulbar pain.

Two weeks after her COVID-19 diagnosis, she was evaluated emergently for 2 days of constant vertical diplopia, worsening right peribulbar pain, and an inability to “move the right eye upward.” At that time, review of systems was negative for recent fevers, chills, numbness, tingling, weakness, abdominal pain, diarrhea, joint pains, dermatologic rashes, oral or genital ulcers, or other symptoms. Family history was notable for congenital nystagmus and esotropia requiring surgical intervention in her mother and rheumatoid arthritis in her maternal grandmother.

On examination, visual acuity was 20/20 in both eyes, pupillary examination was normal, and intraocular

pressure was 10 mm Hg in the right eye and 11 mm Hg in the left eye. External examination revealed mild tenderness to palpation of the superomedial corner of the right orbit overlying the trochlea. She was orthotropic in primary position and downgaze; however, on attempted upgaze, there was limited elevation of the right eye, worse in adduction than abduction (Figure 1A).

Magnetic resonance imaging (MRI) of the brain and orbits revealed focal enhancement of the right trochlea, without inflammation of the muscle belly or surrounding tissue, consistent with trochleitis (Figure 1B-C). No sinus disease was present, and no other intracranial or vascular abnormalities were identified. Laboratory work-up was notable for white blood cell count of 8.7 K/ μ l with leukopenia (30.7% neutrophils) and lymphocytosis (60.8% lymphocytes). Extensive infectious and autoimmune testing was negative, including a comprehensive metabolic panel, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies, rheumatoid factor, antineutrophil cytoplasmic antibody, rapid plasma reagin, and tuberculosis interferon gamma release assay.

She was diagnosed with acquired Brown syndrome of the right eye secondary to trochleitis in the setting of recent COVID-19 infection and discharged. Follow-up in the pediatric ophthalmology clinic 1 week later revealed persistent Brown syndrome, with a 10^A right hypotropia on elevation in abduction increasing to 25^A on elevation in adduction, and significant tenderness with palpation of the trochlea. She was otherwise orthotropic in all other gazes with preserved stereopsis and no abnormal head position. She was prescribed a methylprednisolone taper (Medrol Dosepak, Pfizer, New York, NY) because of symptomatic diplopia in upgaze. After 1 month, minimal improvement in alignment was noted, with complete resolution of periorbital pain. Four months later, the patient reported improving diplopia in upgaze, without pain. Given the manageable symptoms and family hesitation to try further pharmacological intervention, the patient and her mother opted for continued observation.

Discussion

COVID-19, initially thought to be a respiratory illness, is now known to affect nearly every organ system. Ocular manifestations of COVID-19 primarily consist of conjunctivitis, although cases of extraocular muscle dysfunction and/or orbital inflammation primarily in adults have been reported.^{1,2} We report a case of Brown syndrome secondary to trochleitis following recent COVID-19 infection in a child.

Brown syndrome, a restriction of oculomotor elevation in adduction, results from dysfunction of the superior oblique tendon and trochlea complex. Symptoms include diplopia, reduced stereopsis, and sometimes periorbital pain, which is often worse with extraocular movements. An abnormal head position may be seen to maintain fusion in both congenital and acquired cases. It is caused either by

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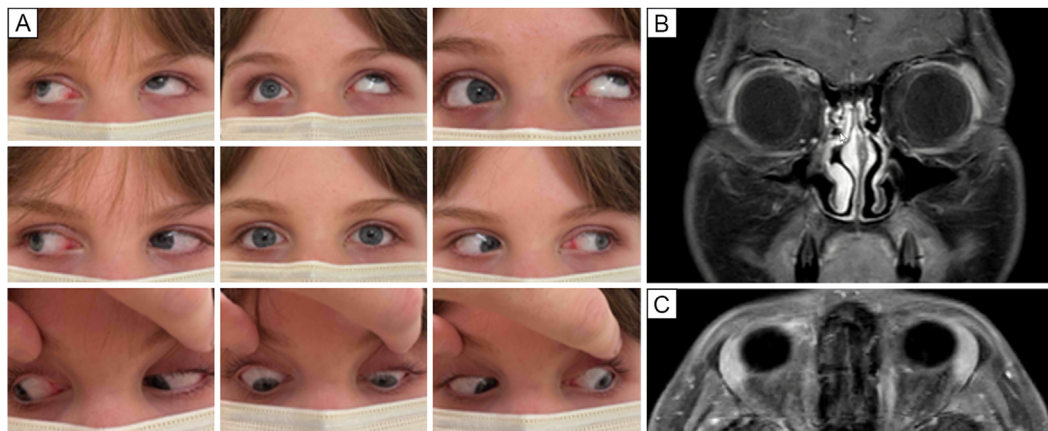


FIG 1. A, Sensorimotor examination showing limitation of adduction in elevation of the right eye, 3 weeks after COVID-19 diagnosis. B-C, Magnetic resonance imaging of the intracranial space and orbit on the day of presentation. Focal enhancement of the right trochlea is noted on post-contrast T1-weighted coronal (B) and axial (C) images (arrows) without involvement of the right superior oblique muscle or right orbit.

congenital abnormalities of the superior oblique muscle, tendon, trochlea and/or surrounding extraocular muscle pulleys or acquired secondary to trauma, infection including sinusitis, or inflammatory diseases affecting the orbit.³⁻⁵

When an inflammatory etiology is suspected, a systemic workup should be performed. Rheumatologic workup can include complete blood count, comprehensive metabolic panel, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies, rheumatoid factor, thyroid panel, antimicrobial antibodies, and angiotensin converting enzyme to investigate associated systemic disorders, such as rheumatoid arthritis, juvenile idiopathic arthritis, and systemic lupus erythematosus, as well as mimics, such as thyroid disease and sarcoidosis. Less commonly associated pathologies include psoriasis and enteropathic arthropathy. Most cases of trochleitis are idiopathic and a negative workup is not uncommon.^{6,7} Furthermore, most inflammatory cases resolve spontaneously; thus, treatment is largely conservative. Indications for surgery include persistent diplopia in primary position and abnormal head position.⁸

We present a case of acquired Brown syndrome in a child that was associated with a diagnosis of COVID-19. Only one previous case report by Kızıltunç and colleagues⁹ describes similar findings in an adult with notable differences. First, this 12-year-old patient presented with mild COVID-19 symptoms without a systemic inflammatory response, in contrast to the published adult case who developed trochleitis in the setting of a multisystem inflammatory syndrome treated with intravenous steroids. Second, neuroimaging of the adult described by Kızıltunç and colleagues⁹ showed diffuse orbital inflammation, which likely influenced the development of trochleitis. Our case, by comparison, showed inflammation strictly limited to the trochlea without myositis or inflammation

of the surrounding orbit. Self-limited ophthalmic manifestations of COVID-19 in the absence of multisystem inflammatory syndrome have been documented, including a report of acquired abducens palsy following COVID-19 infection.¹⁰ This report additionally notes focal tenderness overlying the trochlea and relevant negative testing results.

Short- and long-term effects of SARS-CoV-2 are still being discovered 2 years after the initial outbreak and discovery of the virus. Given the high phenotypic variability and often unpredictable nature of COVID-19, it is important to continue reporting on the various infectious and autoimmune manifestations seen in the population.

References

1. Sen M, Honavar SG, Sharma N, Sachdev MS. COVID-19 and eye: a review of ophthalmic manifestations of COVID-19. *Indian J Ophthalmol* 2021;69:488-509.
2. Case SM, Son MB. COVID-19 in pediatrics. *Rheum Dis Clin North Am* 2021;47:797-811.
3. Hong H, Lyu IJ. Pediatric trochleitis associated with paranasal sinusitis: a case report. *BMC Ophthalmol* 2019;19:16.
4. Elhusseiny AM, Gise R, Mantagos IS. Trochleitis presenting with double vision in a patient with juvenile idiopathic arthritis. *Orbit* 2021;40:342-3.
5. Chanlalit W, Teeyapant C, Soodchuen S. Trochlear pain: clinical characteristics and treatment outcomes. *J Neurol* 2018;265:376-80.
6. Jarrín E, García-García Á, Hurtado-Ceña FJ, Rodríguez-Sánchez JM. Clinical characteristics, treatment, and outcome of trochleitis. *Strabismus* 2017;25:1-4.
7. Pareja JA, Sánchez del Río M. Primary trochlear headache and other trochlear painful disorders. *Curr Pain Headache Rep* 2006;10:316-20.
8. Lambert L. Taylor and Hoyt's Pediatric Ophthalmology and Strabismus. 5th ed. Edinburgh: Elsevier; 2016.
9. Kızıltunç PB, Seven MY, Atilla H. Diplopia due to acquired Brown syndrome after COVID-19 infection. *J AAPOS* 2021;25:366-8.
10. Knoflach K, Holzapfel E, Roser T, et al. Case report: unilateral sixth cranial nerve palsy associated with COVID-19 in a 2-year-old child. *Front Pediatr* 2021;9:756014.