Ocular manifestations of COVID-19 in the pediatric age group

Muhannad A Alnahdi1,2,3 and Maan Alkharashi4,5,6

Abstract
The coronavirus disease 2019 (COVID-19) is now known to be associated with several ocular manifestations. The literature thoroughly discussed those that affect adults, with a lesser focus in the pediatric age group. We aim to outline the various pediatric ocular manifestations described in the literature. The manifestations may be divided into isolated events attributed to COVID-19 or occurring in the new multisystem inflammatory syndrome in children (MIS-C), a novel entity associated by COVID-19 infection. Ocular manifestations have virtually affected all ages. They manifested in neonates, infants, children, and adolescents. Episcleritis, conjunctivitis, optic neuritis, cranial nerve palsies, retinal vein occlusion, retinal vasculitis, retinal changes, orbital myositis, orbital cellulitis were reported in the literature with this emerging viral illness. Conjunctivitis was the most common ocular manifestation in MIS-C in nearly half of the patients. Other ocular manifestations in MIS-C were anterior uveitis, corneal epitheliopathy, optic neuritis, idiopathic intracranial hypertension, and retinitis. The clinical outcome was favorable, and children regain their visual ability with minimal or no deficits in most of the cases. Further follow-up may be warranted to better understand the long-term effects and visual prognosis.

Keywords
Pediatric ophthalmology, Neuro-ophthalmology, Orbital disease, Ocular surface, Anterior uveitis

Date received: 15 December 2021; accepted: 2 July 2022

Introduction
The World Health Organization declared coronavirus disease 2019 (COVID-19) as a pandemic in March 2020. The rapid spread of this illness across countries laid an unprecedented and excessive burden upon hospitals worldwide. The first COVID-19 associated conjunctivitis was reported in a healthcare provider who developed conjunctivitis after examining a patient who later tested positive.1 This shed light on the potential risk of transmitting the virus through the ocular surface, necessitating practicing full precautions including eye protection. Respiratory, systemic, and unusual presentations were described in both adult and pediatric age groups. The American College of Pediatrics reported more than four million children were infected as of July 2021.2 Children are less infected and tend to present with milder symptoms3–5. Nearly a quarter of infected children initially had no symptoms, while severe to critical cases represented around ten percent, and mortality is less than one percent in children.2,6

Coronaviruses are known to cause ocular alterations in murine and feline models. The known clinical features were conjunctivitis, anterior uveitis, retinitis, and optic neuritis.7 Prior epidemiological studies in humans did not show any ocular manifestations in Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome.7 So, most clinical implications were derived from animal models to better understand the possible

1Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada
2College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
3Department of Ophthalmology, King Abdulaziz Medical City, Ministry of National Guard-Health Affairs, Riyadh, Saudi Arabia
4Department of Ophthalmology, College of Medicine, King Saud University, Riyadh, Saudi Arabia
5Department of Ophthalmology, Boston Children’s Hospital, Boston, Massachusetts
6Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts

Corresponding author:
Muhannad A. Alnahdi, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada. Email: m1alnahdi@gmail.com
manifestations of COVID-19. COVID-19 was found to have a similar receptor-binding motif as SARS-COV, which allows the virus to infect the host cells via angiotensin-converting enzyme 2 (ACE2). This receptor is part of the renin-angiotensin system expressed in endothelial cells, and preliminary reports suggest the evidence of ACE2 expression in corneal and conjunctival cells, and maybe more in the inner epithelial layers of the eye, particularly within fibroblasts and dendritic cells.

We are still uncertain about the exact prevalence of ocular manifestations in COVID-19 patients. The existing reports suggest that the rate of conjunctivitis in COVID-19 patients may reach 31% in severe cases. A systematic review reports that dry eye, foreign body sensation, redness, tearing, itchiness, eye pain were the most common ocular symptoms of patients with COVID-19. The literature shows that adult patients can have various ocular manifestations associated with COVID-19, some of the reported ones are conjunctivitis, episcleritis, corneal graft rejection, orbital cellulitis, orbital inflammatory disease, dacyroadenitis, retinal vessels occlusions, retinopathy, maculopathy, endophthalmitis, cranial nerve palsies, optic neuritis, and uveitis with variable prognostic outcomes.

The thought of children having more benign outcomes than adults is not completely accurate as health authorities alerted pediatricians about an outbreak of Kawasaki-like disease associated with clinical evidence of COVID-19. Children presented with a severe constellation of fever and multi-organ symptoms. Lo et al. reviewed more than 1400 patients diagnosed with MIS-C, the most common systemic manifestations were fever, gastrointestinal symptoms, shock, rash, and neurological symptoms. Patients were showing higher positivity to serology compared to nasopharyngeal swaps (80% vs 37%, respectively). Also, patients tended to present one month after their viral illness, implying a potential post-infectious inflammatory storm as the underlying mechanism.

Attention to ocular features may increase the sensitivity of case detection as one in ten cases may show at least one ocular manifestation. Generally, ocular manifestations may be underreported because studies focus on the consequences of the respiratory tract as COVID-19 may lead to fatal respiratory failure. Nonetheless, the literature still contains numerous reports that aid in outlining the ocular implications of this emerging entity in the pediatric population. This article aims to cover the various ocular manifestations in the literature of pediatric COVID-19 patients.

Conjunctivitis
Conjunctivitis is an inflammation and swelling of conjunctival tissue with engorgement of blood vessels, epiphora, chemoisis, ocular pain, follicular reaction of the tarsal conjunctiva, and occasional regional lymphadenopathy. Conjunctivitis is one of the potential initial symptoms of COVID-19 not only in adults but also in pediatric patients. The presence of conjunctivitis was linked in adult patients with severe disease compared to non-severe disease, while children did not manifest such an association with adverse disease course.

Conjunctival manifestations can be found in newborns. A four-day-old baby presented with an acute onset of mucopurulent discharge with subconjunctival hemorrhage that was diagnosed as ophthalmia neonatorum. There were no other systemic manifestations. Although her parents tested negative before the mother’s admission for delivery, nasopharyngeal and conjunctival swabs were positive. Other investigations were noncontributory leading to attributing her ocular disease to COVID-19. Perez et al. in his cohort described 15 neonates who had COVID-19, eleven of them developed chemosis and hemorrhagic conjunctivitis. The author reasoned that such presentation may be due to an overlap between COVID-19 and co-morbidities of prematurity.

Wu et al. described a two-year-old boy who was diagnosed after a community screening test. He was initially asymptomatic but later developed conjunctivitis and eyelid dermatitis that subsided five days later. They attributed this manifestation as either a direct infection of the virus or as a coinciding bacterial infection. Also, Dashi et al. reported conjunctivitis seven days after diagnosing a three-year-old child based on respiratory, systemic, and laboratory evidence of the infection. His ocular symptoms were alleviated after five days. Valente et al. reported four children with mild conjunctival inflammation, and clinical resolution was achieved after three to five days from onset. These cases demonstrate the possible acute occurrence of conjunctivitis in pediatric patients. Conjunctivitis was evident as a part of MIS-C in nearly half of the patients as described by Lo et al. and other reviews echoed similar findings. Conjunctivitis in children is more likely induced by a systemic inflammatory reaction, specifically in the convalescent phase of the infection rather than a direct viral infection compared to adult patients.

Episcleritis
Episcleritis, inflammation of episcleral tissue and vessels, was described within the spectrum of manifestations in the literature in very few cases. It was evident in a 17-year-old boy who had an active illness with accompanying conjunctivitis, and another 13-year-old boy presented in the convalescent stage where he had positive IgG immunoglobulins upon testing and developed optic neuritis a few days after recovery. Episcleritis was earlier described in two adult patients who developed this manifestation as an initial presentation and amid the viral illness. Similarly to these cases, episcleritis was
previously linked to respiratory viral illnesses, thus, caution is needed in such times given the temporal association of such presentation with COVID-19.\textsuperscript{28}

\section*{Keratitis}

Corneal findings were found in few patients, although not as a sole finding but these cases add on the manifestations associated with COVID-19. Three patients suffered from severe corneal epitheliopathy that resolved after one week of treatment.\textsuperscript{30}

\section*{Orbital inflammatory disease}

Orbital inflammatory disease (OID) accounts for up to 6\% of orbital disease in general.\textsuperscript{31} OID’s exact cause remains unknown and has a highly varying clinical features that may target any orbital tissue as lacrimal glands, muscles, or fat. Amid the pandemic, authors described the emergence of peculiar orbital manifestations in children. Eleiwa et al. described a case of orbital myositis in a child who was found to be positive COVID-19. The child presented with unilateral progressive periorbital swelling, eyelid drooping, left gaze horizontal diplopia, and painful ocular movements. Imaging supported the diagnosis, and steroids led to complete recovery. Orbital inflammation was also reported by Christopher and colleagues in a six-month-old infant who presented with periorbital edema that recurred.\textsuperscript{32} She had an active COVID-19 infection. Orbital biopsy showed comparable findings to lung specimens seen in patients with COVID-19, thus, diagnosing bilateral orbital inflammation presumably caused by COVID-19. Also, Remppis et al. reported in his case series an infant who presented with orbital swelling, fever, and other gastrointestinal features.\textsuperscript{33} Perez et al. described 15 neonates diagnosed with COVID-19.\textsuperscript{18} All cases exhibited periorbital edema, which may be attributed to either COVID-19 or prematurity as per the authors.

\section*{Orbital cellulitis}

Orbital cellulitis occurred in two patients who had sinusitis and intracranial abnormalities and co-infection with COVID-19. Turbin et al. described two adolescent patients who presented similarly in 24 h in two different emergency departments.\textsuperscript{34} They presented with unilateral progressive orbital swelling, restricted extraocular movement, proptosis. Extensive investigations were unremarkable. Despite the eventful hospital course, the outcome for the aforementioned cases was favorable.

\section*{Retinal changes}

Few patients have been reported to manifest retinal pathology attributed to COVID-19. Quintana–Castanedo et al. described unilateral pathological retinal findings in an 11-year-old child presenting with cutaneous features.\textsuperscript{35} Fundus examination showed retinal vascular changes, exudate, and perivascular infiltrate. Abbinante et al. also reported retinal changes that persisted during follow-up without any visual complaints.\textsuperscript{36} These changes were vascular tortuosity, especially arterial vasculature, and cotton wool spots along the vessels visible on examination and ancillary tests such as OCT and angio-OCT. Retinal vasculitis was discovered because of vigilance to the potential thromboembolic risk of COVID-19.

Posterior segment manifestations were associated with MIS-C in two children.\textsuperscript{37} An eight-year-old child presented complaining of floaters, with an otherwise unremarkable history. His examination showed splinter-retinal hemorrhages around the left optic nerve, and several vitritis-like hyperreflective dots in the right posterior vitreous on Optical Coherence Topography (OCT). Another child presented with conjunctival hyperemia and periorbital rash. Her examination revealed nonpurulent conjunctivitis, dilation and minimal tortuosity of retinal vessels, and vitritis-like hyperreflective dots in both eyes. Both patients had positive serology, and their ocular manifestations regressed during follow-up.

\section*{Retinal vein occlusion}

Walinjkar et al. described unilateral retinal vein thrombosis in a 17-year-old girl.\textsuperscript{38} She presented with diminishing vision. Her examination and ancillary tests supported the diagnosis of central retinal vein occlusion. She improved after receiving multiple intravitreal anti-Vascular Endothelial Growth Factor injections. This clinical presentation may be attributed to COVID-19, as retinal vessels occlusions are repetitively found in the literature in adults and seems to be one of the most common retinal presentations of COVID-19 in adults. Despite this, thromboembolic risk in pediatric patients may be lower. A recent multicenter cohort found that the incidence of thromboembolic events in COVID-19 infected hospitalized pediatric patients was 2\%, in MIS-C was 6.5\% and 0.7\% in asymptomatic patients.\textsuperscript{39} Factors associated with thrombosis were age more than 12, presence of a central venous catheter, cancer, and MIS-C. The former three factors were already established in hospitalized pediatric patients.

\section*{Uveitis}

Uveitic manifestations were associated with MIS-C, and not as an isolated COVID-19 associated finding in pediatric patients. Anterior uveitis was reported in several cases as either an initial manifestation of the syndrome or days after diagnosis.\textsuperscript{30,40,41} Five patients with MIS-C were diagnosed with bilateral non-granulomatous anterior uveitis.\textsuperscript{30} Chung et al. reported a 12-year-old child who developed blurred vision while hospitalized as a case of multisystem inflammatory syndrome.\textsuperscript{40} Bilateral anterior uveitis was
diagnosed based on mild anterior chamber reaction and conjunctival hyperemia that was successfully treated by topical steroid. Another child presented with redness and tearing of eyes among other constellations of symptoms. Ophthalmological examination revealed bilateral non-granulomatous anterior uveitis with few keratitic precipitates, anterior chamber cells, and bilateral disc edema. Therapeutic intravenous immunoglobulins was started, however, the patient developed a new-onset retro-orbital pain. She persisted to have ophthalmic complaints, raising inflammatory markers, and high IgG titer for COVID-19, thus, they commenced oral prednisone. She fully recovered three months later. Anterior uveitis was reported in an adult patient who succumbed from the multi-system inflammatory syndrome, supporting uveitis as a potential manifestation of this syndrome not only in children but also in adults.

**Optic nerve abnormalities**

Pediatric optic neuritis is rare. Annual incidence reached 0.57 per one hundred thousand and increases with adolescents. Clinical variability is evident between pediatric and adult optic neuritis. Optic disc edema and bilateral involvement are observed more in children. Orbital pain is less frequent, but vision loss during an attack is more pronounced in children, however, recovery as regaining normal visual acuity is noticeably better. The exact pathophysiology behind the neurological manifestation in COVID-19 is uncertain. Discussed theories are: (1) direct invasion through hematogenous spread infecting endothelial cells of the blood-brain barrier through binding of spike protein and ACE2 receptor or direct access through the olfactory neurons and disseminates using retrograde axonal transport. (2) Post-infectious immune-mediated molecular mimicry inducing an autoimmune reaction in the body. (3) Indirect mechanism by the cytokine storm and overt inflammation leading to indirect viral disruption of the blood-brain barrier and pro-coagulable status.

Optic neuritis was described as an initial presentation of COVID-19. A previously healthy ten-year-old girl was diagnosed with unilateral optic neuritis and found to have a positive COVID-19 swab despite being asymptomatic. Another case presented with subacute visual loss that progressed with near blindness over seven days. The patient was diagnosed with anti-Myelin Oligodendrocyte Glycoprotein positive bilateral optic neuritis attributed to presumed infection with COVID-19. He was exposed to COVID-19 and suffered a febrile illness. Also, a 13-year-old boy presented to the hospital with a new-onset blurry vision in his right eye. Imaging studies supported optic neuritis. Extensive investigations were unremarkable except for positive serology for COVID-19; thus, the patient was labeled with post-infectious optic neuritis. Appropriate treatment with steroids led to the disappearance of symptoms within three weeks. Additionally, two teenagers suffered from optic neuritis (bilateral and unilateral cases), which was temporally associated with COVID-19 clinically and serologically. Overall, the patients did not have any demyelinating findings on imaging or previous history of neurological disease. They had favorable visual outcomes concuring the known prognosis of pediatric optic neuritis, without any reportable relapse indicating ongoing inflammatory processes.

**Figure 1.** Reported ophthalmic manifestations in published case-reports and case-series of COVID-19 & MIS-C.

*Conjunctivitis reported in review articles of MIS-C were not included.
Multisystem inflammatory syndrome in children was associated with Idiopathic intracranial hypertension. It was shown to have manifested with ophthalmic features as reported by Verkuil et al.50 A 14-year-old nonfebrile girl presented with a headache and right abducent nerve palsy. Her examination revealed bilateral papilledema. Brain imaging was consistent with elevated intracranial pressure, and serology proved evidence of COVID-19 confirming the diagnosis. She recovered after receiving acetazolamide and oral steroids. Baccarella et al. reported two cases,51 the first case presented with diplopia and a worsening headache following few days of a febrile illness, clinical examination revealed unilateral abducent nerve palsy without papilledema. A lumbar puncture (LP) showed high opening pressure. He was treated with acetazolamide and discharged with improving clinical status. The other patient presented with diplopia and persistent headache after being discharged after hospitalization due to MIS-C. He had unilateral abducent nerve palsy with bilateral papilledema due to elevated intracranial pressure. Brain and orbits imaging supported the diagnosis, however, lumbar puncture showed normal opening pressure. Diplopia resolved the day after the LP, but papilledema persisted. He was discharged with steroids and showed resolution of his illness during follow-up.51

Abnormal ocular motility
Other cranial nerves involvement has been rarely described in pediatric patients with confirmed COVID-19. A 15-year-old girl with serology confirmed COVID-19 was diagnosed with bilateral optic neuritis and unilateral abducent nerve palsy presenting as diplopia.59 A two-year-old girl presented with acute onset oculomotor nerve palsy.52 She tested positive for COVID-19 by a nasopharyngeal

Table 1. Summary of pediatric ocular manifestations attributed to COVID-19.

| MIS-C related manifestations |  |
|-------------------------------|---|
| Conjunctivitis                |  |
| Anterior uveitis              |  |
| Corneal epitheliopathy        |  |
| Optic neuritis                |  |
| Idiopathic intracranial hypertension |  |
| Retinitis                     |  |

| COVID-19 related manifestations |  |
|----------------------------------|---|
| Conjunctivitis                   |  |
| Ophthalma neonatorum             |  |
| Optic neuritis                   |  |
| Abducent nerve palsy             |  |
| Oculomotor nerve palsy           |  |
| Opsoclonus                       |  |
| Neuromyelitis Optica             |  |
| Orbital Inflammation Disease     |  |
| Orbital cellulitis               |  |
| Orbital myositis                 |  |
| Retinal vasculitis               |  |
| Retinal vein occlusion           |  |
| Asymptomatic retinal changes     |  |
swap, although no systemic symptoms were apparent. Both cases recovered completely and partially, respectively. Another unique clinical case, albeit not a true cranial nerve involvement, was described in a four-month-old infant who developed chaotic ocular movements associated with tongue thrusting after one month from her COVID-19 illness. She did not exhibit developmental regression and completely recovered after corticosteroids. Several reports have described cranial nerves involvement in adults. Several reports have described cranial nerves involvement in adults.54–58 Most cases had spontaneous regain of normal neurological function without deficits.

Conclusion

This review outlines the vast spectrum of ocular manifestations of COVID-19 in the pediatric age groups (Figures 1–2). Ocular manifestations maybe divided into two categories (Table 1): multisystem inflammatory syndrome related manifestations and COVID-19 related manifestations. The literature suggests that each has distinct pathophysiology. MIS-C may initially present with ocular manifestations; thus, ophthalmologists should be aware and have a high index of suspicion, specially when it presents with other systemic symptoms in order to promptly manage these cases interdisciplinary and limit potential deterioration in vision and health in general. The management is generally supportive and specific to each clinical manifestation. Ocular manifestations of MIS-C have a benign clinical course, and cases reported in the literature had uneventful visual recovery after receiving the treatment for each disease. The other isolated manifestations carried a similar benign outcome as patients regained any visual deficit and recovered to their normal status; however, the long-term prognosis is unknown just like MIS-C.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Muhammad A Alnahdi https://orcid.org/0000-0003-0839-4131

References

1. Lu Cw, Liu Xf and Jia Zf. 2019-nCoV Transmission through the ocular surface must not be ignored. Lancet (London, England) 2020; 395: e39.
2. Children and COVID-19: State-Level Data Report. https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/ (accessed August 14, 2021).
3. Ludvigsson JF. Systematic review of COVID–19 in children shows milder cases and a better prognosis than adults. Acta Paediatrica (Oslo, Norway : 1992) 2020; 109: 1088–1095.
4. Zimmermann P and Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. Pediatr Infect Dis J 2020; 39: 355.
5. Lee P-I, Hu Y-L, Chen P-Y, et al. Are children less susceptible to COVID-19? J Microbiol Immunol Infect 2020; 53: 371.
6. Li B, Zhang S, Zhang R, et al. Epidemiological and clinical characteristics of COVID-19 in children: a systematic review and meta-analysis. Front Pediatr 2020; 0: 709.
7. Seh A and Agrawal R. Can the coronavirus disease 2019 (COVID-19) affect the eyes? A review of coronaviruses and ocular implications in humans and animals. Ocul Immunol Inflamm 2020; 28: 1.
8. Wan Y, Shang J, Graham R, et al. Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus. J Virol Epub ahead of print March 17, 2020; 94. DOI: 10.1128/JVI.00127-20.
9. Willcox MD, Walsh K, Nichols JJ, et al. The ocular surface, coronaviruses and COVID-19. Clinical and Experimental Optometry 2020; 103: 418–424.
10. Wu P, Duan F, Luo C, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei province, China. JAMA Ophthalmol 2020; 138: 575–578.
11. Nasiri N, Sharifi H, Bazrafshan A, et al. Ocular manifestations of COVID-19: a systematic review and meta-analysis. J Ophthalmic Vis Res 2021; 16: 103–112.
12. Sen M, Honavark G, Sharma N, et al. COVID-19 and eye: a review of ophthalmic manifestations of COVID-19. Indian J Ophthalmol 2021; 69: 488.
13. Shah KK, Venkatramani D and Majumder PD. A case series of presumed fungal endogenous endophthalmitis in post COVID-19 patients. Indian J Ophthalmol 2021; 69: 1322–1325.
14. PICS Statement regarding novel presentation of multi-system inflammatory disease - Paediatric Critical Care Society. https://pccsociety.uk/news/pics-statement-regarding-novel-presentation-of-multi-system-inflammatory-disease/ (accessed August 14, 2021).
15. Lo T-C and Chen Y-Y. Ocular and systemic manifestations in paediatric multisystem inflammatory syndrome associated with COVID-19. J Clin Med 2021; 10: 2953.
16. Loffredo L, Pacella F, Pacella E, et al. Conjunctivitis and COVID–19: a meta-analysis. J Med Virol 2020; 92: 1413–1414.
17. Mechel E, Trinh M, Kodsi S, et al. Ophthalmia neonatorum as the presenting sign of SARS-CoV-2. Journal of Aapos. Epub ahead of print 2021. DOI: 10.1016/J.JAAPOS.2021.03.001
18. Pérez-Chimal LG, Cuevas GG, Di-Luciano A, et al. Ophthalmic manifestations associated with SARS-CoV-2 in newborn infants: a preliminary report. Journal of Aapos: the Official Publication of the American Association for Pediatric Ophthalmology and Strabismus 2021; 25: 102–104.
19. Wu P, Liang L, Chen C, et al. A child confirmed COVID-19 with only symptoms of conjunctivitis and eyelid dermatitis.
28. de la Maza MS, Jabbur NS and Foster CS. Severity of scleritis in children related to COVID-19: a systematic review. Eur J Pediatr 2020; 180: 1.

29. Otaif W, al Somali AI and al Habash A. Episcleritis as a possible presenting sign of the novel coronavirus disease: a case report. J APOS: the Official Publication of the American Society for Pediatric Ophthalmology and Strabismus 2020; 24: 212–215.

30. Öztürk C, Yüce Sezen A, Savas E, et al. COVID-19 associated multisystem inflammatory syndrome in children: a systematic review and meta-analysis. Iran J Allergy Asthma Immunol 2020; 19: 570–588.

31. Yuen SJA and Rubin PAD. Idiopathic orbital inflammation in children diagnosed with multisystem inflammatory syndrome secondary to COVID-19. Ocul Immunol Inflamm 2021; 29: 700–704.

32. Fernández Alcalde C, Granados Fernández M, Nieves Moreno M, et al. Ocular manifestations of multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection: a systematic review with meta-analysis. SN comprehensive Clinical Medicine 2021; 3: 38–47.

33. Remppis J, Ganzenmueller T, Kohns Vasconcelos M, et al. A case series of children and young people admitted to a tertiary care hospital in Germany with COVID-19. BMC Infect Dis 2021; 21: 1–6.

34. Turbin RE, Wawrzesin PJ, Sakla NM, et al. Orbital cellulitis, sinusitis and intracranial abnormalities in two adolescents with COVID-19. Orbit (Amsterdam, Netherlands) 2020; 39: 305–310.

35. Quintana-Castanedo L, Feito-Rodríguez M, Fernández-Alcalde C, et al. Concurrent chilblains and retinal vasculitis in a child with COVID-19. J Eur Acad Dermatol Venereol 2020; 34: e764–e766.

36. Abbinante G, Plaitano C, Gallo FG, et al. A case of retinal vascular involvement in a 6-year-old patient with COVID-19. Eur J Ophthalmol 2021; 112067212110270: NP1–NP5.

37. Arkan İ, Demir ST, Livan EH, et al. Ocular manifestations of multisystem inflammatory syndrome in children with COVID-19. Pediatr Infect Dis J 2021; 40(9): E356–E358.

38. Wafijnak JA, Mahjija SC, Sharma HR, et al. Central retinal vein occlusion with COVID-19 infection as the presumptive etiology. Indian J Ophthalmol 2020; 68: 2572–2574.

39. Whitworth H, Sartain SE, Kumar R, et al. Rate of thrombosis in children and adolescents hospitalized with COVID-19 or MIS-C. Blood 2021; 138: 190.

40. Chung JEREW, Engin Ö, Wolfs TFW, et al. Anterior uveitis in paediatric multisystem syndrome temporally associated with SARS-CoV-2. The Lancet 2021; 397: e10.

41. Karthika IK, Gulla KM, John J, et al. COVID-19 related multi-inflammatory syndrome presenting with uveitis - A case report. Indian J Ophthalmol 2021; 69: 1319–1321.

42. Bettach E, Zadok D, Weill Y, et al. Bilateral anterior uveitis as a part of a multisystem inflammatory syndrome secondary to COVID-19 infection. J Med Virol 2021; 93: 139–140.

43. Lock JH, Newman NJ, Bioussie V, et al. Update on pediatric optic neuritis. Curr Opin Ophthalmol 2019; 30: 418–425.

44. Pezzini A and Padovani A. Lifting the mask on neurological manifestations of COVID-19. Nature Reviews Neurology 2020; 16: 636–644.

45. Aghagoli G, Marin BG, Katchur NJ, et al. Neurological involvement in COVID-19 and potential mechanisms: a review. Neurocrit Care 2021; 34: 1062–1071.

46. Lin JE, Asfour A, Sewell TB, et al. Neurological issues in children with COVID-19. Neurosci Lett 2019; 699: 94–100.

47. Parvez Y, Alzarooni F and Khan F. Optic neuritis in a child with COVID-19: a rare association. Cureus Epub ahead of print January 19, 2021; 743. DOI: 10.1016/J.NEULET.2020.135567.

48. Parvez Y, Alzarooni F and Khan F. Optic neuritis in a child with COVID-19: a rare association. Cureus Epub ahead of print March 25, 2021; 13. DOI: 10.7759/CUREUS.14094.

49. Yuen SJA and Rubin PAD. Idiopathic orbital inflammation: distribution, clinical features, and treatment outcome. Arch Ophthalmol 2003; 121: 491–499.

50. Sánchez-Morales AE, Urrutia-Osorio M, Camacho-Mendoza E, et al. Neurological manifestations temporally associated with SARS-CoV-2 infection in pediatric patients in Mexico. Child’s Nervous System : ChNS : Official Journal of the International Society for Pediatric Neurosurgery 2021; 37: 2305–2312.
51. Baccarella A, Linder A, Spencer R, et al. Increased intracranial pressure in the setting of multisystem inflammatory syndrome in children, associated with COVID-19. *Pediatr Neurol* 2021; 115: 48–49.

52. Oliveira Md, Lucena ARVP, Higino TMM, et al. Oculomotor nerve palsy in an asymptomatic child with COVID-19. *J AAPOS* 2021; 25: 169.

53. Heald DL, Devine IM, Smith RL, et al. Opsoclonus after COVID-19 in an infant. *Pediatr Neurol* 2021; 117: 34.

54. Sawalha K, Adeodokun S and Kamoga GR. COVID-19-Induced acute bilateral optic neuritis. *J Investig Med High Impact Case Rep* Epub ahead of print 2020; 8. DOI: 10.1177/2324709620976018

55. Dinkin M, Gao V, Kahan J, et al. COVID-19 presenting with ophthalmoparesis from cranial nerve palsy. *Neurology* 2020; 95: 221–223.

56. Rodríguez-Rodríguez MS, Romero-Castro RM, Alvarado-de la Barrera C, et al. Optic neuritis following SARS-CoV-2 infection. *J Neurovirol* 2021; 27: 359.

57. Greer CE, Bhatt JM, Oliveira CA, et al. Isolated cranial nerve 6 palsy in 6 patients with COVID-19 infection. *Journal of Neuro-Ophthalmology: the Official Journal of the North American Neuro-Ophthalmology Society* 2020; 40: 520–522.

58. Woodhall M, Mitchell JW, Gibbons E, et al. Case report: myelin oligodendrocyte glycoprotein antibody-associated relapse with COVID-19. *Front Neurol* 2020; 11: 1479.