Ischemic stroke associated with Multisystemic Inflammatory Syndrome in children after SARS-CoV-2 infection: a case report

José Caballero-Alvarado[1]^, Karla Rodríguez Millones[2]^, Mylenia Ruiz Gonzales[2]^, Annel B. Rojas Alvarado[2,3]^, Carlos Zavaleta Corvera[1]^, Joshuan J. Barboza[4]^

[1]School of Medicine, Antenor Orrego Private University, Trujillo, Peru; [2]School of Medicine, Antenor Orrego Private University, Piura, Peru; [3]Scientific Society of Medical Students, Antenor Orrego Private University, Piura, Peru; [4]Research Vice-Rectorate, Norbert Wiener University, Lima, Peru

Contributions: (I) Conception and design: J Caballero-Alvarado, K Rodríguez Millones, M Ruiz Gonzales, AB Rojas Alvarado; (II) Administrative support: J Caballero-Alvarado, K Rodríguez Millones, M Ruiz Gonzales, AB Rojas Alvarado; (III) Provision of study materials or patients: J Caballero-Alvarado, K Rodríguez Millones, M Ruiz Gonzales, AB Rojas Alvarado; (IV) Collection and assembly of data: J Caballero-Alvarado, K Rodríguez Millones, M Ruiz Gonzales, AB Rojas Alvarado; (V) Data analysis and interpretation: J Caballero-Alvarado, C Zavaleta Corvera, JJ Barboza; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Carlos Zavaleta Corvera, MD, MHs. School of Medicine, Antenor Orrego Private University, Trujillo 13008, Peru.
Email: czavaletac3@upao.edu.pe.

Background: Multisystemic Inflammatory Syndrome in children (MIS-C) is a rare pediatric complication of coronavirus disease 2019 (COVID-19) which results in inflammation of various organ systems. Neurological involvement is a very rare compromised in children and only few cases of the ischemic cerebrovascular disease have been reported. Our objective is to analyze ischemic cerebrovascular disease in the context of multisystem inflammatory syndrome through a review of therapeutic approaches. Because acute ischemic stroke is uncommon in pediatric patients an opportune diagnose and treatment can reduce the morbidity and mortality. So, it is critical that clinicians are aware of the risk of stroke in the context of MIS-C.

Case Description: A 5-year-old boy was admitted to the pediatric emergency room with a history of cough and fever. A private physician requested a serologic test for COVID-19 reporting reactive immunoglobulin G (IgG). He presented to the emergency room (ER) with bilateral eyelid edema, diffuse erythematous spots, cracked lips, and joint pain. Physical examination showed dry oral mucosa, raspberry-like tongue, conjunctival injection, and generalized polymorphous exanthema. The diagnosis of MIS-C was made. On the third day of hospitalization appeared facial asymmetry, right hemiplegia, hypotonia, osteotendinous reflexes 2/4, right positive Babinski, decreased muscle strength ⅘, dysarthria and paresis of the VII. A brain computerized tomography (CT) scan shown diffuse hypodensity at the level of the caudate nucleus, predominantly in the left parietal region, lenticular ganglion, anterior and posterior arm of the internal capsule on the left side. Based on the diagnosis of acute ischemic stroke, treatment was started with acetylsalicylic acid, enoxaparin, captopril and physiotherapy and rehabilitation. In the following days, the evolution was favorable. He was discharged with remarkable clinical improvement; in his outpatient controls, only a slight decrease of strength in the right hand was evidenced. The child has shown clinical improvement and is at home attending to his controls.

Conclusions: It is important to keep in mind that children can develop a multisystem inflammatory syndrome and complications such as ischemic stroke, which requires early recognition and diagnosis to initiate timely treatment.

Keywords: Multisystemic inflammatory syndrome in children (MIS-C); stroke; severe acute respiratory syndrome

^ ORCID: José Caballero-Alvarado, 0000-0001-8297-6901; Karla Rodríguez Millones, 0000-0003-1238-5473; Mylenia Ruiz Gonzales, 0000-0002-7484-528X; Annel B. Rojas Alvarado, 0000-0001-7105-2180; Carlos Zavaleta Corvera, 0000-0001-5918-8261; Joshuan J. Barboza, 0000-0002-2896-1407.

coronavirus 2 (SARS-CoV-2); coronavirus disease 2019 (COVID-19); case report

Received: 06 September 2022; Accepted: 31 March 2023; Published online: 19 April 2023.
doi: 10.21037/pm-22-43
View this article at: https://dx.doi.org/10.21037/pm-22-43

Introduction

Coronavirus disease 2019 (COVID-19), declared a pandemic by the World Health Organization (WHO) in March 2020, is caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). As of June 26, 2022, more than 543.5 million cases and more than 6.3 million deaths have been reported worldwide (2). Currently, although different vaccines are already available and even fourth doses have been administered, SARS-CoV-2 mutations may increase infectivity and therefore spread, diminish the protective effect of antibodies present after infection, vaccination, or antibody treatment, and may also increase the risk of infection (3), situations that are associated with the presence of fourth or fifth waves of contagion.

Since the beginning of the pandemic, it became evident that children infected with SARS-CoV-2 remain mostly asymptomatic or mildly symptomatic. In general, children with COVID-19 have a lower risk of hospitalization and life-threatening complications (4). However, some cases of severe disease or a post-infectious Multisystemic Inflammatory Syndrome in children (MIS-C) have been described (5,6). On the other hand, children with this complication may present with respiratory, gastrointestinal, lymphatic, hepatic, cardiac, or neurological symptoms or signs, although the latter are infrequent in children and were related to headache, syncope, convulsions, and seizures (7).

We present the case of an otherwise healthy 5-year-old boy who developed a multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection that progressed to ischemic cerebrovascular disease (8-13). Because acute ischemic stroke is uncommon in pediatric patients, there can be a delay in diagnosis leading to high morbidity and mortality. So, it is critical that clinicians are aware of the risk of stroke in MIS-C. We present this case in accordance with the CARE reporting checklist (available at https://pm.amegroups.com/article/view/10.21037/pm-22-43/rc).

Highlight box

Key findings

- Analyze ischemic cerebrovascular disease in the context of multisystem inflammatory syndrome following severe acute respiratory syndrome coronavirus 2 infection.

What is known and what is new?

- The mechanism of Multisystemic Inflammatory Syndrome in children (MIS-C) is not well understood up to now and the most that is known is from cases in adults, which has allowed us to propose that there is an effect on the endothelium associated with infection by viruses such as SARS-CoV-2.
- Children can develop a multisystem inflammatory syndrome and complications which requires early recognition and diagnosis to initiate timely treatment. We exposed additional information concerning the diagnosis and treatment of this important event

What is the implication, and what should change now?

- Neurological involvement must be taken into account in the evaluation of a patient with probable Multisystemic Inflammatory Syndrome in children (MIS-C), which requires early recognition and diagnosis to initiate timely treatment and obtain better results in children.

Case presentation

A 5-year-old boy was admitted on January 21st, 2022 to the pediatric emergency department of a hospital in northern Peru with a productive cough and fever of 39 to 40 ℃ for the last 7 days. On the day of admission, bilateral eyelid edema, diffuse erythematous spots on different parts of the body, cracked lips, and joint pain was added, and he was taken to the hospital. The mother reported that a month ago she had mild respiratory symptoms (cough, rhinorrhea, febrile fever) that coincided with some cases of COVID-19 at school, and in those same days she had received the first dose of the Pfizer vaccine. The mother denies any history of head trauma in the child. On admission, tests were performed to rule out dengue (non-reactive) and a serological test for COVID-19, which was reactive for immunoglobulin G (IgG); other laboratory tests were performed: C-reactive protein (CRP) of

Table 1 Laboratory tests requested with abnormal results during the patient's evolution

Day/laboratory test	Admission	Day 3	Day 9	Reference values
Dengue rapid test	Non-reactive	–	–	–
COVID-19 antibodies	Reactive IgG; non-reactive IgM	–	–	–
PCR test for COVID-19	9.19 mg/dL	23.13 mg/dL	0.3 mg/dl	<2 mg/dL
Hemoglobin	10.3 gr/dL	9.3 gr/dL	11.4 gr/dL	>11.5 gr/dL
Hematocrit	30.8%	28.2%	34.3%	35–42%
VCM	76.7 fL	77.4 fL	79.4 fL	75–87 fL
MCH	25.7 pg	25.5 pg	26.5 pg	25–33 pg
Leukocytes	15,740/mm^3	25,000/mm^3	15,970/mm^3	5,500–15,500/mm^3
Neutrophils	29.59/mm^3	21.04/mm^3	9.74/mm^3	1.5–8.5/mm^3
Lymphocytes	0.66/mm^3	2.51/mm^3	5.43/mm^3	2–8/mm^3
Platelets	194,000/mm^3	278,000/mm^3	607,000/mm^3	150,000–400,000/mm^3
PDW	9.7 fL	8.3 fL	7.8 fL	17.6 fL
PCT	0.221%	0.224%	0.471%	<0.5%
AST	41.6 UI/L	–	–	10–50 UI/L
ALT	54.4 UI/L	–	–	5–45 UI/L
Dimero D	6.37 µg/mL	–	–	<0.5 µg/mL
Fibrinogen	–	507 mg/dL	–	1.62–4.01 mg/dL
Thromboplastin time	65 seconds	46.70 seconds	27 seconds	33.6–43.8 seconds
Prothrombin time	11.8 seconds	10.80 seconds	9.50 seconds	12.1–14.5 seconds
Glucose	82.4 mg/dL	113 mg/dL	–	60–100 mg/dL
Urea	–	14 mg/dL	–	6–20 mg/dL
Complete urine test	Scanty epithelial cells and mild proteinuria	Scarce epithelial cells and mucoid filament in regular quantity	–	–

COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; VCM, medium corpuscular volume; MCH, medium corpuscular hemoglobin; PDW, platelet distribution width; PCT, procalcitonin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; IgG, immunoglobulin G; IgM, immunogobulin M.

9.19 mg/dL, leukocyte count of 15,000/mm^3 with deviation to the left, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (41.6 and 54.4 U/L respectively), and D-dimer of 6.37 µg/mL (*Table 1*).

Physical examination revealed an irritable child with a heart rate of 162 beats per minute, respiratory rate of 50 breaths per minute, and oxygen saturation of 93% on room air. In addition, he had dry oral mucous membranes, raspberry tongue, conjunctival injection, generalized exanthema with a polymorphous pattern, cervical and axillary lymphadenopathy; and chest auscultation showed rhonchi in both lung fields. The rest of the examination was unaltered.

Other laboratory tests were performed and yielded hemoglobin 10.3 g/dL, glucose 150 mg/dL, leukocyte count 31,000/mm^3 with left shift, and CRP 10.65 mg/dL (*Table 1*). Cholesterol, triglycerides, total protein, albumin, bilirubin, and liver enzymes, creatinine, urea, glucose and electrolytes, urine examination, electrocardiogram, abdominal ultrasound, blood gas analysis and chest X-ray were reported within normal. No more respiratory tests were considered to perform. Echocardiography reported mild left atrial dilatation and laminar pericardial effusion without hemodynamic compromise. From the beginning, a diagnosis of MIS-C was proposed, and treatment with human

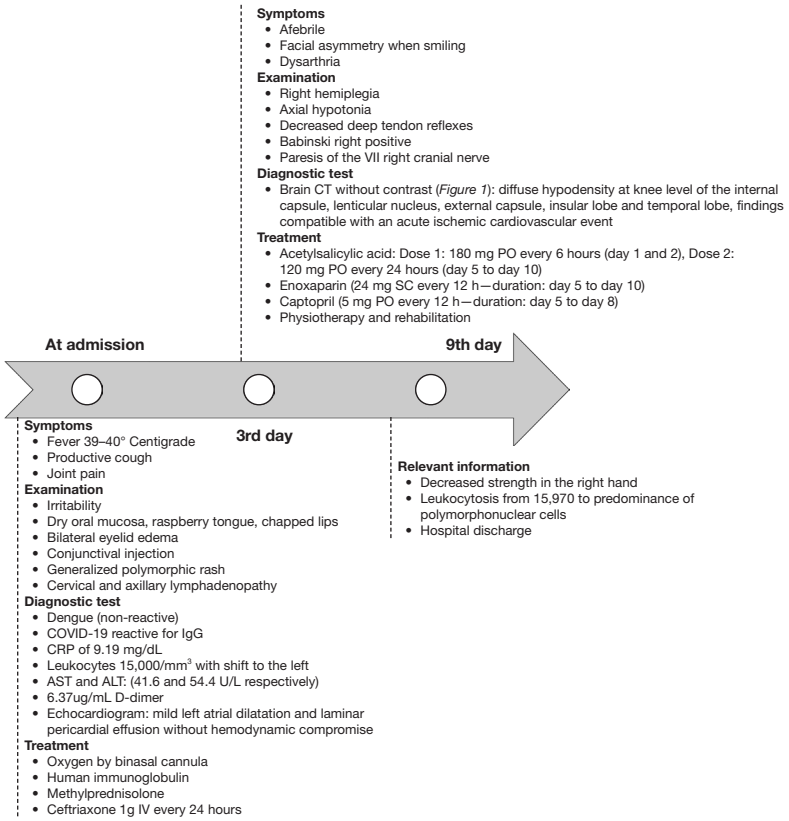

Figure 1 Timeline of the relevant events in the patient's history in chronological order. CT, computed tomography; PO, orally; SC, subcutaneous; COVID-19, coronavirus disease 2019; IgG, immunoglobulin G; CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; IV, intravenous.

immunoglobulin, methylprednisolone, ceftriaxone 1 g IV e//24 hours, and oxygen by binasal cannula was initiated (*Figure 1*).

On the third day of hospitalization, he no longer presented fever, however, the mother reported that the child presented facial asymmetry when smiling. On examination it was found: right hemiplegia, axial hypotonia, diminished osteotendinous reflexes, positive right Babinski, dysarthria, and paresis of the right VII cranial nerve. A brain CT scan without contrast was requested (*Figure 2*) and diffuse hypodensity was found at the level of the knee of the internal capsule, lenticular nucleus, external capsule, insula lobe, and temporal lobe, in addition, asymmetry of lateral ventricles, the smaller size of the left ventricle and effacement of the left Sylvian fissure, findings compatible with acute ischemic cardiovascular event. A control CT scan with contrast three days later showed the same alterations (*Figure 3*), the AngioTEM performed later did not provide further information.

Based on the diagnosis of acute ischemic stroke, treatment was started with acetylsalicylic acid: Dose 1: 180 mg PO every 6 hours (day 1 and 2), Dose 2: 120 mg PO every 24 hours (day 5 to day 10), enoxaparin [24 mg SC every 12 h—duration: day 5 to day 10], captopril (5 mg PO every 12 h—duration: day 5 to day 8), physiotherapy and rehabilitation. In the following days, the evolution is good. He was discharged with remarkable clinical improvement; in his outpatient controls, only a slight decrease of strength in the right hand was evidenced.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

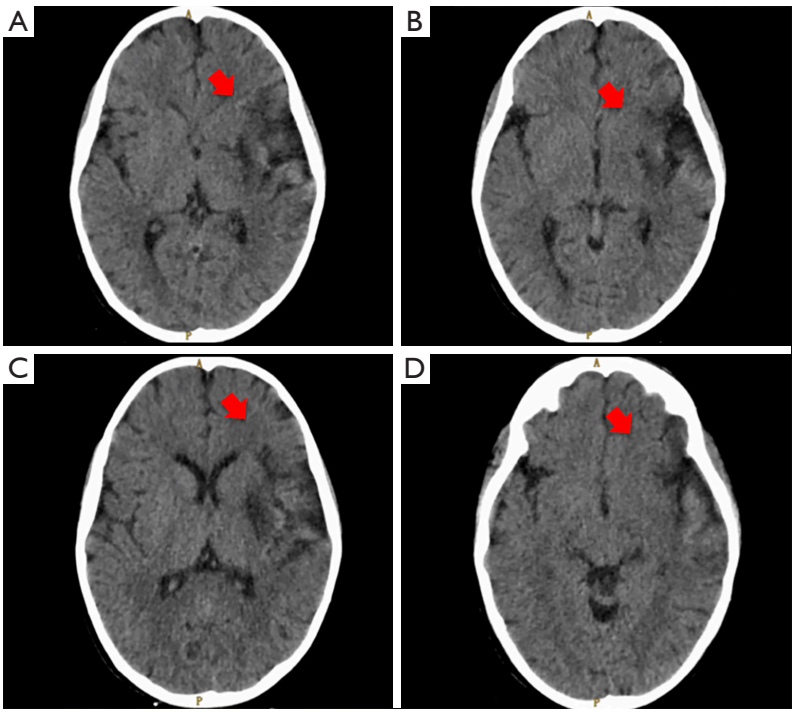

Figure 2 Contrast-enhanced brain computed tomography (transverse sections A, B, C, and D). Arrows show ischemic infarction affecting the internal capsule knee, lenticular nucleus, external capsule, insula lobe, and temporal lobe.

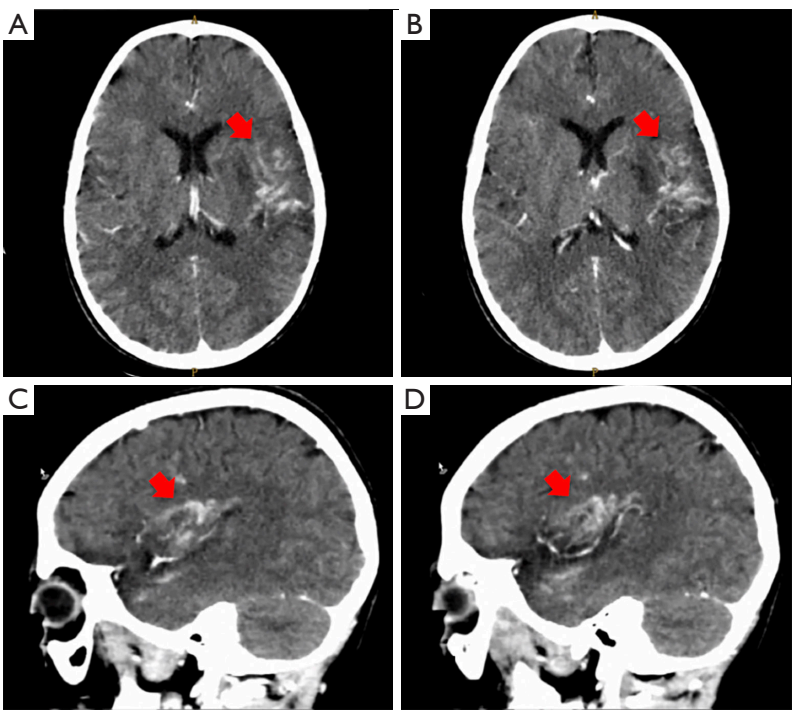

Figure 3 Computed Tomography of the brain with contrast (transverse section A and B, sagittal section C and D). Arrows show centripetal and centrifugal reinforcement at the knee of the internal capsule, lenticular nucleus, external capsule, insula lobe, and temporal lobe; the area of involvement is the left middle cerebral artery.

Discussion

The COVID-19 pandemic has affected millions of people worldwide. In most of the cases, children have milder clinical symptoms and better prognosis than the adult population (14). However, since April 2020, reports from the United Kingdom reported a clinical presentation in children similar to Kawasaki disease, but not necessarily meeting all established criteria for Kawasaki diagnosis, determining it as Kawasaki-Like or Kawasaki incomplete (15). Severe COVID-19 generally occurs in the initial and acute phase of infection with the SARS-CoV-2 virus. Severe COVID-19 is contagious. MIS-C commonly occurs three to six weeks after a mild or asymptomatic case of COVID-19 or an exposure to someone who has had COVID-19. MIS-C is not contagious. Kawasaki disease is an illness that has no known cause. It is suspected that exposure to a virus (not necessarily SARS-CoV-2) may trigger the condition, but this has not been confirmed. Kawasaki disease is not contagious (16,17). The relationship among Kawasaki and coronavirus is not yet specific, however, it has been associated with an altered immune response against the virus in a picture mediated by an excessive cytokine storm after acute infection; this condition has been called MIS-C, pediatric hyperinflammatory syndrome or pediatric multisystem inflammatory syndrome associated with SARS-CoV-2 (PIMS-CoV-2) (10). Most children with this condition have a positive serology for SARS-CoV-2 predominantly IgG, with a negative PCR test (as in the case of our patient), strengthening the theory of an irregular immune process triggered after an acute infection (18). However, there are reports of children with positive serology and PCR test, or with both tests negative (18-20). To date, the time to onset of MIS-C ranges from one to several weeks after acute infection (21).

The operational definition of this disease is characterized by presenting with fever >38 degrees for at least 3 days, with at least 2 of the following criteria: conjunctival rash, mucosal inflammation, myocardial dysfunction and/or hypotension, coagulopathies (prolonged prothrombin, thromboplastin activated and elevated D-dimer), gastrointestinal disturbances; in addition, there must be elevated inflammatory markers, predominantly C-reactive protein, evidence of SARS-CoV-2 infection (either with a rapid test, predominantly IgG, molecular test or epidemiological contact) and absence of another cause that justifies the inflammatory process (22). In this case report, the patient met all the criteria mentioned above (except hypotension and gastrointestinal problems), in addition, the association with coronavirus infection is reaffirmed by the history of epidemiological contact, respiratory symptoms described by the mother, and serology with a predominance of IgG, as well as the age of presentation in children older than 5 years compared to the classic that prevails in children under 5 years, in addition, there is greater cardiac involvement and especially high elevation of acute phase reactants (23).

Then, as mentioned above, during the pandemic period, MIS-C was reported, with characteristics similar to Kawasaki disease. However, the mechanism of MIS-C in the context of COVID-19 is not well understood. It has been suggested that is the result from an abnormal I macrophage activation syndrome and cytokine release syndrome. Among the clinical features of the case reports and reviews, there was fever, rash, dilation of conjunctival blood vessels, cervical lymphadenopathy, redness of the oropharynx, and neurological symptoms such as headache and altered mental status (24,25). It was reported that as much as there were similarities, differences could also be found, such as a higher incidence of gastrointestinal symptoms, myocarditis, shock, and coagulopathy (24).

The complications reported in MIS-C are classified according to the organ affected, being found at the cardiovascular level; myocarditis, pericarditis, shock, coronary artery anomalies, among others; at the respiratory level; pulmonary nodules, pleural effusion, empyema, etc.; and at the nervous system level, behavioral changes and irritability (13–35%), aseptic meningitis, peripheral facial nerve palsy and cerebrovascular accidents (3%) have been reported (25,26), the latter being the affectation presented by our patient.

The pathophysiology of acute ischemic stroke in MIS-C has not yet been fully elucidated, however, what is known in adults has allowed us to propose that there is an effect on the endothelium associated with SARS-CoV-2 infection in different organs, mainly in the lung, but also in the kidney, heart, intestine and also in the cerebral vessels (27). Possible mechanisms that can trigger ischemic cerebrovascular event (CVE) could be post-infectious immune processes, direct infection of the central nervous system (CNS) by the virus, and virus-induced hyperinflammatory and hypercoagulable states. Hemorrhagic and ischemic strokes, encephalitis, meningitis, acute disseminated encephalopathy, endothelitis, and venous sinus thrombosis are some cases of COVID-19 CNS disease (28). Although an immune-mediated inflammatory response stimulated by macrophages, neutrophils, and monocytes, followed by

Table 2 Cerebrovascular complications in patients with Kawasaki-like Multisystemic Inflammatory Syndrome

Author, year	Country	Type of study	Sample	Diagnostic method	Type of stroke	Type of treatment	Treatment results
Chang *et al.*, 2022 (8)	United States	Case series	2	Brain CT Agio CT of the head and neck	Ischemic stroke	IVIG 2 g/kg and IV methylprednisolone 2 mg/kg/day ×5 days, followed by a gradual reduction of oral prednisone for 3 days and therapeutic enoxaparin 1 mg/kg twice daily	Patient 1: subtle right hemiparesis that resolved on day 30. Patient 2: complication: DVT in the right lower extremity associated with a catheter. Mild expressive aphasia and mild right hemiparesis
Shala *et al.*, 2021 (9)	Kosovo	Case Report	1	MRI and MRA of the brain	Ischemic stroke (terminal branches of the left middle cerebral artery)	IVIG (2 g/kg) along with low dose aspirin therapy and methylprednisolone 40 mg twice daily	The complete resolution, except for discrete right-sided hemiparesis (4/5 muscle strength)
Coronado Munoz *et al.*, 2022 (10)	Peru	Cases and controls	47	Brain CT	5 hemorrhagic strokes and 1 ischemic stroke	Intravenous immunoglobulins. Low-dose methylprednisolone (does not refer to exact dose)	4 of 6 patients died. One patient with hemorrhagic stroke and one patient with ischemic stroke survived, but had significant sequelae
Salik *et al.*, 2021 (11)	United States	Case Report	1	Brain CT; magnetic resonance imaging	Right basal ganglia ischemic stroke with hemorrhagic transformation	IVIG 2 g/kg, methylprednisolone 2 mg/kg/day, and anakinra for suspected COVID-19 cytokine storm	Mental status gradually improved throughout the hospital stay, although the patient had residual left hemiparesis
Scala *et al.*, 2022 (12)	Italy	Case Report	1	CT and MRI of the skull	Ischemic stroke: ischemia of the right middle cerebral artery	Heparin and acetylsalicylic acid bridging systemic thrombolysis followed by endovascular thrombectomy. Emergency DHC	Neurological examination at discharge was Glasgow 14 with persistent severe left-sided hemiparesis
Tiwari *et al.*, 2021 (13)	India	Case Report	1	Non-contrast computed tomography and cerebral CT angiography	Ischemic stroke	IV immunoglobulin (2 g/kg for 2 days), methylprednisolone (30 mg/kg IV for 5 days), dexamethasone (0.15 mg/kg per day for 2 weeks), remdesivir (5.0 mg/kg by IV infusion over 1 hour, followed by 2.5 mg/kg per day by IV infusion for 5 days), and low molecular weight heparin (1 mg/kg SC twice daily for 2 weeks followed by once daily for 1 week)	His clinical status improved progressively, and mechanical ventilation was withdrawn on day 12. His serum CRP, ferritin, and lactate dehydrogenase values returned to normal

CT, computerized tomography; MRI, magnetic resonance imaging; MRA, magnetic resonance angiography; IVIG, intravenous immunoglobulin; IV, intravenous; COVID-19, coronavirus disease 2019; DHC, decompressive right hemicraniectomy; SC, subcutaneous; DVT, deep venous thrombosis; CRP, C-reactive protein.

antibody production by plasma and B cells, is generated in children, especially in those with MIS-C late after the initial infection, this appears to be more likely pathogenesis than the direct viral invasion of tissues (8). Patients benefit from intravenous immunoglobulin, methylprednisolone, and enoxaparin, although some patients require thrombolysis and even surgery. The literature reports a few cases of patients with MIS-C and debuting with acute ischemic CVE, some of them achieving full recovery, others with sequelae, and others who died (*Table 2*) (8-13).

In the present investigation, a rare and unusual presentation syndrome is reported. Therefore, through the present review, we exposed additional information concerning the diagnosis and treatment of this important event. However, its usefulness for medical decision-making is still limited, so we hope it will be a valuable resource of new information that can encourage and serve in the future to carry out research studies with a higher level of evidence.

Conclusions

The pandemic of COVID-19 continues in all countries,

with fourth, fifth, and sixth waves; and with the appearance of new variants. Infections in children are rare, however, they can occur and very few of them develop a complication called MIS-C. In this scenario, although very rare, few cases of ischemic CVE have been reported, such as the one we present. In this sense, this neurological involvement should be taken into consideration, which requires early recognition and diagnosis to initiate timely treatment and obtain better results in children.

Acknowledgments

We are grateful to all of those with whom we have had the pleasure to work during this and other related projects.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://pm.amegroups.com/article/view/10.21037/pm-22-43/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://pm.amegroups.com/article/view/10.21037/pm-22-43/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Forchette L, Sebastian W, Liu T. A Comprehensive Review of COVID-19 Virology, Vaccines, Variants, and Therapeutics. Curr Med Sci 2021;41:1037-51.
2. COVID-19 Map - Johns Hopkins Coronavirus Resource Center n.d. Available online: https://coronavirus.jhu.edu/map.html (accessed August 19, 2022).
3. Hemmer CJ, Löbermann M, Reisinger EC. COVID-19: epidemiology and mutations: An update. Radiologe 2021;61:880-7.
4. Nikolopoulou GB, Maltezou HC. COVID-19 in Children: Where do we Stand? Arch Med Res 2022;53:1-8.
5. Ashraf S, Abbasi FS, Atiq M. Kawasaki Shock Syndrome and Covid-19. J Coll Physicians Surg Pak 2021;31:135-7.
6. Giacalone M, Scheier E, Shavit I. Multisystem inflammatory syndrome in children (MIS-C): a mini-review. Int J Emerg Med 2021;14:50.
7. Kornitzer J, Johnson J, Yang M, et al. A Systematic Review of Characteristics Associated with COVID-19 in Children with Typical Presentation and with Multisystem Inflammatory Syndrome. Int J Environ Res Public Health 2021;18:8269.
8. Chang J, Bulwa Z, Breit H, et al. Acute Large Vessel Ischemic Stroke in Patients With COVID-19-Related Multisystem Inflammatory Syndrome. Pediatr Neurol 2022;126:104-7.
9. Shala N, Jashari F, Boshnjaku D, et al. A 14-Year-Old Male Patient with Kawasaki Disease Presented with Stroke after COVID-19. Case Rep Infect Dis 2021;2021:5576440.
10. Coronado Munoz A, Tasayco J, Morales W, et al. High incidence of stroke and mortality in pediatric critical care patients with COVID-19 in Peru. Pediatr Res 2022;91:1730-4.
11. Salik I, Jacoby M. Carotid Artery Dissection and Hemorrhagic Stroke in the Setting of Multisystem Inflammatory Syndrome in Children. Cureus 2021;13:e13640.
12. Scala MR, Spennato P, Cicala D, et al. Malignant cerebral infarction associated with COVID-19 in a child. Childs Nerv Syst 2022;38:441-5.
13. Tiwari L, Shekhar S, Bansal A, et al. COVID-19 associated arterial ischaemic stroke and multisystem inflammatory syndrome in children: a case report. Lancet Child Adolesc Health 2021;5:88-90.
14. Sood M, Sharma S, Sood I, et al. Emerging Evidence on Multisystem Inflammatory Syndrome in Children

Associated with SARS-CoV-2 Infection: a Systematic Review with Meta-analysis. SN Compr Clin Med 2021;3:38-47.
15. Riphagen S, Gomez X, Gonzalez-Martinez C, et al. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet 2020;395:1607-8.
16. Webinar May 19, 2020 - Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19) n.d. Available online: https://emergency.cdc.gov/coca/calls/2020/callinfo_051920.asp (accessed August 19, 2022).
17. Henderson LA, Canna SW, Friedman KG, et al. American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 3. Arthritis Rheumatol 2022;74:e1-e20.
18. Giraldo-Alzate C, Tamayo-Múnera C, López-Barón E, et al. Síndrome inflamatorio multisistémico en niños asociado a COVID-19. Revisión narrativa de la literatura a propósito de un caso. Acta Colombiana de Cuidado Intensivo 2022;22:137-48.
19. Coll-Vela LE, Zamudio-Aquise MK, Nuñez-Paucar H, et al. COVID-19-associated multisystem inflammatory syndrome in children: case series at a pediatric hospital in Peru. Rev Peru Med Exp Salud Publica 2020;37:559-65.
20. Belhadjer Z, Méot M, Bajolle F, et al. Acute Heart Failure in Multisystem Inflammatory Syndrome in Children in the Context of Global SARS-CoV-2 Pandemic. Circulation 2020;142:429-36.
21. Aldawas A, Ishfaq M. COVID-19: Multisystem Inflammatory Syndrome in Children (MIS-C). Cureus 2022;14:e21064.
22. Hennon TR, Yu KOA, Penque MD, et al. COVID-19 associated Multisystem Inflammatory Syndrome in Children (MIS-C) guidelines; revisiting the Western New York approach as the pandemic evolves. Prog Pediatr Cardiol 2021;62:101407.
23. Zhang QY, Xu BW, Du JB. Similarities and differences between multiple inflammatory syndrome in children associated with COVID-19 and Kawasaki disease: clinical presentations, diagnosis, and treatment. World J Pediatr 2021;17:335-40.
24. Sharma C, Ganigara M, Galeotti C, et al. Multisystem inflammatory syndrome in children and Kawasaki disease: a critical comparison. Nat Rev Rheumatol 2021;17:731-48.
25. Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nat Rev Immunol 2020;20:453-4.
26. Rife E, Gedalia A. Kawasaki Disease: an Update. Curr Rheumatol Rep 2020;22:75.
27. Uginet M, Breville G, Hofmeister J, et al. Cerebrovascular Complications and Vessel Wall Imaging in COVID-19 Encephalopathy-A Pilot Study. Clin Neuroradiol 2022;32:287-93.
28. Jha NK, Ojha S, Jha SK, et al. Evidence of Coronavirus (CoV) Pathogenesis and Emerging Pathogen SARS-CoV-2 in the Nervous System: A Review on Neurological Impairments and Manifestations. J Mol Neurosci 2021;71:2192-209.

doi: 10.21037/pm-22-43
Cite this article as: Caballero-Alvarado J, Rodríguez Millones K, Ruiz Gonzales M, Rojas Alvarado AB, Zavaleta Corvera C, Barboza JJ. Ischemic stroke associated with Multisystemic Inflammatory Syndrome in children after SARS-CoV-2 infection: a case report. Pediatr Med 2023;6:40.