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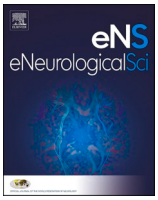

Case report

Stroke in a child with SARS-CoV-2 infection: A case report

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Some patients with COVID-19 show widely neurological manifestations including stroke. We report a child who was hospitalized due to seizures and was later diagnosed with COVID-19. Acute infarction was seen in the right putamen, globus pallidus, and the posterior part of the insula. A small focal dilatation within M1 segment of the left middle cerebral artery (MCA) was also observed. According to the present case report, COVID-19 infection may contribute to the occurrence and development of ischemic stroke.

1. Introduction

The novel coronavirus was first reported in Wuhan, China [1]. This virus is called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been called by the WHO as the coronavirus disease 2019 (COVID-19) [2,3].

The severity of COVID-19 in children is classified as mild, normal, severe, and critical [4,5]. Although there are reports that children are less likely to develop COVID-19 infection, it is important to monitor the symptoms and the course of the disease carefully [6]. In addition to the usual symptoms including fever and cough, coronavirus also has neurological symptoms such as hyposmia, hypogeusia, and headache [7]. After a nasal infection, coronavirus enters the CNS through the nasal route, causing neurological manifestations ranging from ischemic stroke to acute demyelination and encephalitis [8,9].

Stroke can be ischemic or hemorrhagic. Ischemic stroke is more frequently caused by arterial occlusion, however, it may also be caused by venous occlusion of cerebral veins or sinuses [10]. In children, multiple risk factors are involved in stroke including cardiac disease, sickle cell disease, prothrombotic disorders, arteriovenous malformations, syndromic and metabolic disorders, cerebral vasculitis, cancers, and trauma [10–12]. Besides such risk factors which can all contribute to stroke, viral infections can also lead to stroke [12]. The most common microorganisms which contribute to stroke include mycoplasma, chlamydia, enterovirus, influenza A, parvovirus 19, and coxsackie [13]. Virus infection triggers a cytokine cascade that aggravates ischemic brain damage [14–16]. There are reports that COVID-19 infection may contribute to the occurrence of ischemic stroke in adults [17]. In this article a pediatric case with the ischemic stroke subtypes related to the SARS-CoV-2 was reported.

2. Case presentation

A 10-year-old girl was referred to Besat Hospital of Kurdistan University of Medical Sciences, Sanandaj, Iran. She suddenly had a severe headache in the right temporal area followed by facial distortion, tonic movements of the shoulders and the right leg, and loss of consciousness for 5 min.

Body temperature at admission was 37.0 °C and blood pressure was 110/70 mmHg. The heart rate was 90 beats per minute and the number of breaths per minute was 20. The patient was fully conscious and when she came to the hospital she only had dysarthria and left-sided hemiparesis. One week before, she had had a low grade fever and gastrointestinal manifestations such as vomiting and abdominal pain for two days. She had no previous history of cough, shortness of breath, skin rash, or recent trauma. No one in her family had a known history of COVID-19 infection. In the context of COVID-19 pandemic, SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) was performed on a nasopharyngeal swab and the result was positive.

In the neurological examinations, ipsilateral cranial nerve VII (facial nerve) dysfunction was observed, however, the other nerves were normal. The muscle stretch was 3.5 for the left limb and 4.5 for the right limb. In this case, facial paralysis on the left side, and left lip curvature were observed.

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Table 1
Clinical findings in patient with ischemic stroke in the setting of COVID-19.

	In patient	Normal range
white blood cell	6.8 × 10^9/L	5 to 11 × 10^9/L
white blood cell differential	60% neutrophils	20.0%–50.0%
	40% lymphocytes	40.0%–75.0%
hemoglobin	13 g/dL	in children: 11–13 g/dL
prothrombin time (PT)	12 s	10–12 s
partial thromboplastin time (PTT)	was 26 s	25–35 s
factor XIII	more than 30%	50% to 150%
erythrocyte sedimentation rate (ESR)	12 mm/h	0 to 10 mm/h
lactate dehydrogenase (LDH)	318 units/L	60 to 170 units/L
D-dimer	was less than 200	for 2–12 year-old children: 4–227 ng/L)
triglyceride	119 mg/dL	150 to 199 mg/dL
cholesterol	149 mg/dL	below 200 mg/dL
LDL	125 U/L	140 to 280 units per liter U/L
HDL	43 mg/dl	less than 45 mg/dl
ammonia (plasma)	58 µmol/L	50 to 100 µmol/L
lactate (plasma)	1.4 mmol/L	for 2–18 year-old individuals: 1.0–2.4 mmol/L
pyruvate	0.95 mmol/L	0.08–0.16 mmol/L
anti-cardiolipin antibodies (ACA)	2.5	(reference range previously listed as IgG: 0–14 (negative) for IgG (immunoglobulin G
	3.1	(reference range previously listed as IgM: 0–12 (negative) for IgM (immunoglobulin M)
beta-2 glycoprotein 1 antibodies	1.4 for IgG	positive results: >40 U/mL for IgG
	0.4 for IgM	positive results: >40 U/mL for IgM
lupus anticoagulant	34.7	up to 46.1 s
aPTT-LA (lupus sensitive reagent)	31.6	31 to 47 GPL
protein C	0.73 U/ml	0.72–1.23 U/ml
Protein S	0.79 U/ml	0.60–1.60 U/ml
antithrombin III (ATIII)	133%	80% to 120%
Varicella-zoster virus (VZV)	686.90 for IgG	Less than 135 mlU/ml
	0.25 for IgM	Less than 0.4
fluorescent antinuclear antibodies (FANA)	negative	No reaction at 1/100
Anti-double-stranded (ds)DNA antibodies IgG	9.7	Less than 100 IU/ml

It should be noted that there was no sign of a recent history of chickenpox. Furthermore, cerebrospinal fluid analysis was normal in terms of cell count, biochemical studies, and bacterial culture. Cardiovascular examinations including echocardiography were normal. The thrombotic panel and the laboratory findings showed in Table 1.

The magnetic resonance imaging (MRI) also showed an acute infarction in the right putamen, globus pallidus, and the posterior part of the insula (Fig. 1). Cerebral venous thrombosis was not observed in the magnetic resonance venography (MRV) with contrast. Brain magnetic resonance angiography (MRA) showed small focal narrowing within the right middle cerebral artery (MCA).

Enoxaparin was prescribed until lack of thrombosis was confirmed (5 days) and then aspirin treatment was started. After a second echocardiogram and normal MRV results, treatment with anticoagulants was stopped and aspirin treatment with a dose of 3 mg/kg was started. The patient's clinical symptoms were relatively improved by the time of discharge. The patient is currently under our care and has been receiving aspirin for up to two years.

3. Discussion

Neurological signs have been observed in about 84% of the patients with COVID-19 [18]. Some COVID-19 patients develop stroke [19–21]. There are multiple, not mutually exclusive, possible mechanisms associating COVID-19 with ischemic stroke. Pulmonary angiopathy and thrombosis reported in severe COVID-19 pneumonia which can be related to stroke [22].

In the current case, acute infarction was seen in the right putamen, globus pallidus, and the posterior part of the insula. A small single focal dilatation within M1 segment of the MCA were also observed. In a related study, Mohammadifard et al. Reported a COVID-19 infection case with right hemiparesis and dysarthria. No history of shortness of breath, cough, fever, skin rash, hemoglobinopathy or recent trauma. Also in this case the serum ferritin, the C-reactive protein, the platelet count, the prothrombin time and the partial thromboplastin time were normal. The erythrocyte sedimentation rate contrary to our study has elevated. The major imaging finding in this patient is the presence of unilateral focal vasculopathy, characterized by focal irregular narrowing and banding of the proximal M1 segment of the left MCA associated with left basal ganglia and insula acute infarction [23]. In another study, a 41-year-old female with COVID-19 infection with occlusion of the M1 segment of left MCA with poor distal reconstitution has been reported. In another case, a 78-year-old man with positive diagnosis of COVID-19 was presented with a strong clinical concern for stroke and venous thromboembolic event [24]. Yaghi et al. observed a low rate of imaging-confirmed ischemic stroke in hospitalized patients with COVID-19 infection. Most strokes were cryptogenic, possibly related to an acquired hypercoagulability [25]. In the present case report, D-dimer level was normal. In the case report of Mohammadifard et al. about a pediatric patient with ischemic stroke due to SARS-CoV2, the D-dimer level has not been reported [23]. Some studies have reported that lactate dehydrogenase is elevated in ischemic stroke [26]. In the current case,

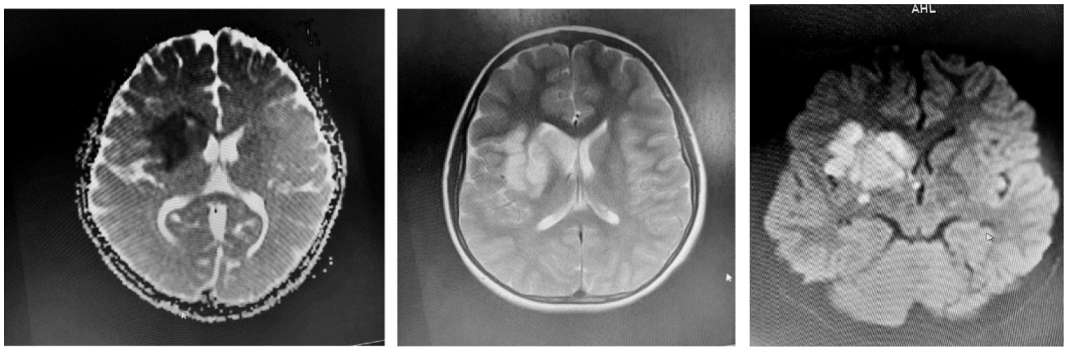

Fig. 1. Infarct areas in the brain.
These images are from patient with ischemic stroke in the setting of COVID-19. The MRI showed an acute infarction in the right putamen, globus pallidus, and the posterior part of the insula.

lactate dehydrogenase was elevated.

Stroke rates have increased during the COVID-19 pandemic [27]. Evidence suggests that COVID-19 can also affect the cerebrovascular systems [28]. It has been stated that 5% of COVID-19 adult patients have had a concomitant stroke [27]. In strokes following COVID-19, inflammatory and hypercoagulable mechanisms may play a role through thrombotic events [27,29]. The data of the current study can propose a causal relationship between SARS-CoV-2 and ischemic stroke since other risk factors were not present in this patient. Due to the absence of thrombotic events in this case, angiopathy caused by COVID-19 seems to have led to a stroke.

4. Conclusion

Despite an increased incidence of pediatric stroke, there is often a delay in diagnosis, and cases may still remain under- or misdiagnosed. During the COVID-19 pandemic, neuroscientists should be vigilant about neurological symptoms especially in children. COVID-19 may play a role in the prognosis of ischemic stroke. Therefore, ready-made programs are needed to deal with diseases such as stroke.

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