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CASE REPORT

Ischemic stroke in childhood associated with COVID-19.

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Abstract

This case report deals with an ischemic stroke in a 2-year-and-5-month-old child associated with COVID-19. The patient, initially presenting with paresis and facial paralysis, tested positive for the coronavirus. Additional examinations suggest an acute vascular event without apparent risk factors. The discussion highlights the potential relationship between COVID-19 and pediatric ischemic stroke. The case aims to contribute to the understanding of the possible link between COVID-19 and stroke in children, addressing diagnosis, treatment, and potential underlying mechanisms of this association.

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INTRODUCTION

Stroke in children is defined as an acute episode of sudden occlusion or rupture of cerebral vessels resulting in focal brain dysfunction and clinical neurological deficit lasting more than 24 hours with changes in imaging tests. Data suggest that stroke is slightly more common than brain tumors in this group of patients, with an incidence of 2 to 13 per 100,000 children per year. Despite efforts to increase awareness of stroke in children, the condition is often overlooked as a cause of symptoms by healthcare professionals and families.[1] Delayed diagnosis is one of the issues seen in the care of children with stroke. Ischemic stroke (55%) occurs due to arterial or venous embolism or thrombosis, while lacunar stroke or hemorrhagic stroke (45%) is caused by intracerebral hemorrhage (80%) (vascular malformation) or subarachnoid hemorrhage (20%). Unlike adults, in whom ischemic stroke predominates, children are more susceptible to hemorrhage. Stroke is among the ten leading causes of death in children, causing 10-20% of deaths in this age group. It is a medical emergency that might require surgery, in which time-dependent therapies have proven successful. Patients with acute stroke require emergency care.[2]

According to the International Pediatric Stroke Study (IPSS), pediatric stroke is divided into three types:

1. Perinatal: from the 20th week of gestational age to the 28th day of life.

2. Pediatric: from the age of 28 days to 18 years

3. Presumed perinatal (associated with hemiparetic cerebral palsy)

Significant differences are observed between perinatal and pediatric stroke. Incidence is higher in the perinatal period, and recurrence in pediatric cases is similar to that of adults: 25% may experience stroke recurrence when previously treated and 50% when not. Although perinatal stroke is more frequent, recurrence is low (1 to 2%).

Risk factors are different between adults and children. Current evidence supports the idea that the pathogenesis of stroke in children is multifactorial. There is often a combination of inherited risk factors increasing susceptibility to stroke and acquired ones that may trigger a stroke.[3] A wide range of underlying systemic factors have been linked to stroke in children, including heart disease, sickle cell anemia, coagulation disorders, vascular malformations, arteriopathies, systemic vasculitis, acute infections, chronic infections, genetic and metabolic diseases, lymphomas and other types of cancer, head and neck trauma, inherited coagulopathies and thrombophilia, and drug use. The underlying causes cannot be identified in approximately a third of the cases.[4]

Most children with coronavirus infection present mild to moderate symptoms. However, reports of serious complications include post-COVID stroke, of which healthcare professionals, parents, and caregivers should be aware to expedite diagnosis and treatment.[5]

CASE REPORT

A white male infant aged 2 years and 5 months was brought to the emergency room with left arm paresis, left facial paralysis, sialorrhea, and a runny nose. According to his family, the symptoms had been active for one day. The mother claimed they had first gone to another healthcare service, where the infant was placed on observation and had two skull computed tomography (CT) scans performed, one at admission and another 24 hours later.

Since a neurologist was unavailable, the infant was referred to our service. A third skull CT scan was performed 72 hours after the onset of symptoms, showing a hypodense area in the internal capsule area in the region of the right middle cerebral artery (MCA). A neurosurgeon assessed the patient and prescribed expectant management. The mother denied having prodromal symptoms of flu or illnesses in the family.

The patient is a full-term newborn with an uneventful vaginal delivery and Rh incompatibility at birth. The mother received immunoglobulin, and hospitalization was not required. The patient was diagnosed with wheezing with no other comorbidities. The mother reported that the patient had two older, healthy siblings and denied a history of thrombosis or miscarriage, stroke in young people in the family, allergies, or previous hospitalizations. She reported giving the infant salbutamol to manage acute episodes of asthma.

On physical examination, the child weighed 14.150 kg and had a height of 87 cm. He was in good general condition, acyanotic, hydrated, afebrile, awake, and oriented. He presented neurological symptoms and responded to the examiner with simple sentences. His pupils were photoreactive, and he had preserved extrinsic eye movements with complete left hemiparesis. He had difficulty walking, lifting his left leg, and showing the teeth on the left of his mouth when smiling. He had no trouble frowning. Physical examination revealed no other alterations. Interview and physical examination findings were consistent with a sudden ischemic internal capsule stroke in the territory of the right MCA that occurred between the 8th and the 9th of April with an unclear etiology (the patient tested positive for COVID). Transient cerebral arteriopathy, cardioembolic stroke, inflammatory arteritis, and vasculitis were also considered.

ADDITIONAL TESTS

- On April 9th, skull CT scans showed no alterations.
- On April 10th, contrast-enhanced CT scans of the skull revealed cortico-subcortical hypodensity in the right internal capsule region, notably in the head of the caudate nucleus, slightly pushing other structures in

the area, causing a decrease in the size of the frontal horn of the right lateral ventricle. No signs of acute hemorrhage were seen. The findings suggest a recent ischemic vascular event in the middle cerebral artery territory. No areas of abnormal contrast enhancement were evident.

- On April 11th, the patient tested positive for SARS-Cov-2 infection, negative for influenza in a rapid test, and negative for respiratory syncytial virus (RSV). His CSF was clear and colorless, with a protein level of 27, a glucose level of 65.7, a leukocyte count of 4, and a red blood cell count of 0. Other test results were as follows: C4 28; C3 121; antistreptolysin O <100; IgM 115; IgG 733; IgA 46; CK 23; CK-MB 18; CRP <1; Troponin T 7.64. The ECG showed a sinus rhythm without changes
- On April 12th, toxoplasma IgG and IgM were nonreactive; TSH 0.85; free T4 1.73; CMV IgG nonreactive and IgM reactive; treponemal test nonreactive; BT 0.64; C4 28.0; C3 121.0; Streptolysin O <100.0; Fibrinogen 250.23; D-Dimer 190; ACANE nonreactive; CMV PCR negative; Infectious mononucleosis nonreactive; Hep B nonreactive; Hep C nonreactive; Hep A IgG R and IgM nonreactive; HIV nonreactive.

TRANSTHORACIC ECHOCARDIOGRAM WITH COLOR DOPPLER SEQUENTIAL SEGMENTAL ANALYSIS - CONCLUSION: PATENT FORAMEN OVALE, WITHOUT HEMODYNAMIC REPERCUSSIONS.

CERVICAL AND INTRACRANIAL ARTERY COMPUTED TOMOGRAPHY ANGIOGRAPHY.

Analysis: The image shows hypodensity in the right internal capsule region affecting the middle third of the basal ganglia, with a slight expansile effect. There are no signs of acute hemorrhage. A mild parietal irregularity and reduced caliber in the M1 segment of the right middle cerebral artery were seen compared to the contralateral artery. Flow is preserved. There were no other alterations in the test. **Conclusion**: The patient suffered a recent ischemic stroke in the right internal capsule. A mild parietal irregularity and reduced caliber in the M1 segment of the right middle cerebral artery were observed compared to the contralateral artery. Flow is preserved.

DISCUSSION

Although children appear less affected during the acute stage of the disease, complications may occur after COVID-19, such as multisystem inflammatory syndrome in children (MIS-C), immune-mediated neurological complications, and immune-mediated conditions.

The clinical manifestations of patients with COVID vary considerably, from asymptomatic infection to death.[6] According to an initial study conducted in Wuhan, China, although most of the symptoms caused by COVID-19 were respiratory, 2.3% of 214 hospitalized patients had ischemic stroke.[7] The cause of the association between ischemic stroke and COVID-19 is still unclear, but previous studies have suggested that inflammatory cytokine storms may trigger a hypercoagulable state and endothelial damage.[8] Several studies have described the different mechanisms by which SARS-CoV-2 can cause neurological disorders and strokes. Many of these mechanisms focus on angiotensin-converting enzyme-2 (ACE-2), the binding site of SARS-CoV-2, and its role in triggering a series of events that lead to vasoconstriction, hypertension, and thrombotic imbalance. Other authors suggested that immune-mediated mechanisms and cytokine overexpression, a hypercoagulable state, and thromboembolism are potential causes of stroke.[9,10] COVID-19 is closely related to ischemic stroke and factors that can potentially cause stroke.

Since SARS-CoV-2 cannot always be found in cerebrospinal fluid (CSF), most authors consider the diagnosis presumed when patients present with clinical neurological signs and positive serology for COVID-19.[10]

Our patient had an acute vascular event without other risk factors. After he tested positive for COVID-19, the patient was kept in isolation. He improved from the neuromotor deficits and runny nose. Laboratory and imaging tests were performed to investigate the etiology and rule out other causes. The main hypothesis was ischemic stroke due to transient cerebral arteriopathy with an etiology associated with COVID-19.

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