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CASE REPORT

Acute disseminated encephalomyelitis associated with SARS-CoV-2 in a 21-month-old: a case report

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Abstract

Introduction: Since its emergence in 2019, SARS-CoV-2 has been responsible for a myriad of symptoms affecting multiple organ systems, including the central nervous system. Although rare, especially in children, cases of acute disseminated encephalomyelitis (ADEM) associated with COVID-19 have also been described. **Case report:** We present the case of a previously healthy 21-month-old girl who presented with altered consciousness and ataxia ten days after SARS-CoV-2 infection was reported. Cranioencephalic MRI revealed hyperintense T2-weighted and hypointense T1-weighted lesions. The remaining imaging, analytical, autoimmune, and serological studies showed no alterations, allowing a diagnosis to be established. Therapy with pulses of prednisolone was initiated with excellent results. **Discussion:** This case report highlights the importance of a high index of suspicion in a child presenting with encephalopathy days to weeks after SARS-CoV-2 infection. A quick diagnosis is vital for early treatment and to improve the clinical course and long-term outcome.

Keywords: ADEM. SARS-CoV-2. Encephalitis.

Encefalomielite aguda disseminada após infeção a SARS-CoV-2 numa criança de 21 meses: um relato de caso

Resumo

Introdução: Desde o seu aparecimento em 2019, a SARS-CoV-2 tem sido responsável por uma miríade de sintomas que afetam múltiplos sistemas de órgãos, incluindo o sistema nervoso central. Embora raros, especialmente em crianças, foram também descritos casos de encefalomielite aguda disseminada (ADEM) associada à COVID-19. **Relato de caso:** Apresentamos o caso de uma criança do sexo feminino de 21 meses, previamente saudável, que se apresentou com alterações do estado de consciência e ataxia dez dias após ter sido notificada a infeção por SARS-CoV-2. A RMN cranioencefálica revelou lesões hiperintensas em T2 e hipointensas em T1. Os restantes estudos imagiológico, analítico, auto-imune e serológico não revelaram alterações, permitindo estabelecer o diagnóstico. Foi iniciada terapêutica com pulsos de prednisolona com excelente melhoria clinica. **Discussão:** O presente caso de caso salienta a importância de um elevado índice de suspeição numa criança que se apresente com encefalopatia dias a semanas após a infeção pela SARS-CoV-2. O rápido diagnóstico é importante para o tratamento precoce e para melhorar o curso clínico e o resultado a longo prazo.

Palavras-chave: Encefalomielite disseminada aguda. SARS-CoV-2. Encefalite

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Keypoints

What is known
- ADEM is a rare inflammatory demyelinating disorder of the central nervous system that usually affects children.
- ADEM is a post-infection disorder and is mostly caused by a virus vancomycin and gentamicin as a first line therapy for LOS.
- The identification of this pathology is vital for early treatment and to improve the clinical course and long-term outcome.

What is added
- Although rare, cases of ADEM associated with COVID-19 have also been described.
- The presentation and course of the disease appear to be similar to classic ADEM, although with a poorer outcome.
- This entity should be considered in a child who has had COVID-19 and presents with encephalopathy.

Introduction

Since its emergence in December 2019, SARS-CoV-2 has been responsible for a myriad of symptoms affecting multiple organ systems. Neurological involvement has been frequently reported, mainly in adults but also in children, ranging from mild symptoms to rare and severe manifestations such as meningoencephalitis, Guillain-Barré syndrome and cerebellitis[1-3]. Data that are currently available show that SARS-CoV-2 has neuroinvasive potential, that its neurotropism is limited, and that it can be neurovirulent in at least a subgroup of patients. This concurs with observations from the clinic, where the impact of SARS-CoV-2-associated central nervous system complications appears limited during the acute phase, but more prominent during the post-acute phase[4]. We report a case of a child with COVID-19-associated acute disseminated encephalomyelitis (ADEM).

Case report

A 21-month-old girl is taken to the emergency department presenting with prostration, drowsiness, and ataxia since that morning, with decreased food intake and generalized abdominal pain since the previous day. The mother reported occasional taking of herbal syrup to sleep but that it had not been administered the night before. She denied the possibility of taking other substances. She had no significant personal or family history. She had a SARS-COV-2 infection ten days before.

On admission, the child was hemodynamically stable, apyretic, awake, but with some periods of decreased responsiveness and obnubilation. She complied with some simple commands but appeared not to distinguish who was around her. Her gait was unbalanced. The remaining physical and neurological examination was unremarkable.

The patient's hematological parameters, renal function, blood glucose, electrolytes, and blood gas analysis were normal. Urine drug screening was negative. Reverse transcription polymerase chain reaction ([rRT]-PCR) for respiratory virus in nasopharyngeal secretions was negative (*Adenovirus, Infuenza A and B, Parainfluenzae 1,2 and 3, Respiratory Syncytial Virus, Methapneumovirus and Coronavirus OC43*). Magnetic resonance imaging (MRI) revealed hyperintense T2 and FLAIR lesions in the posterior left corona radiata as well as faint hypointense signal on T1 images (Fig. 1). MRI of the spinal cord showed no alterations.

Cerebrospinal fluid (CSF) analysis demonstrated 1/mcL erythrocytes, 1/mcL leucocytes, 57 mg/dL glycose, and 19.8 mg/dL proteins. The CSF (rRT)-PCR panel was negative (including *Escherichia coli, Streptococcus pneumoniae, Streptococcus agalactiae, Haemophilus influenzae, Klebsiella pneumoniae, Streptococcus agalactiae, Neisseria meningitidis, Lysteria monocytogenes, Adenovirus, Herpes simplex virus (HSV) 1-2, Human Herpes virus 6, Parechovirus, Varicella Zoster virus, Cytomegalovirus, and Enterovirus*). CSF, blood and urine cultures were negative. Antibody serology tests were negative for *Cytomegalovirus, Epstein Barr virus, HSV 1-2, Adenovirus, Mycoplasma pneumoniae, Borrelia, and Chlamydia pneumoniae*. RT-(rRT)-PCR for SARS-CoV-2 in CSF was negative. The child was started on ceftriaxone, acyclovir, and azithromycin that were suspended after a negative CSF (rRT)-PCR and blood serologies.

Serology testing for SARS-CoV-2 resulted in IgG positive and IgM negative antibodies. The electroencephalogram showed right posterior slow activity. Tests for oligoclonal bands in CSF and serum neuronal autoantibodies (anti-NMDAR, anti-AQP4, and anti-MOG) were negative.

Given the neuroradiological findings, the temporal relationship between SARS-CoV-2 infection and the exclusion of other causes, the diagnosis of COVID-19-associated ADEM was assumed and the child was started on high-dose methylprednisolone (30 mg/kg/day id) for five days followed by tapering for four weeks.

During hospitalization, there was significant clinical improvement, with no abnormalities on neurological examination at the date of discharge. Three months

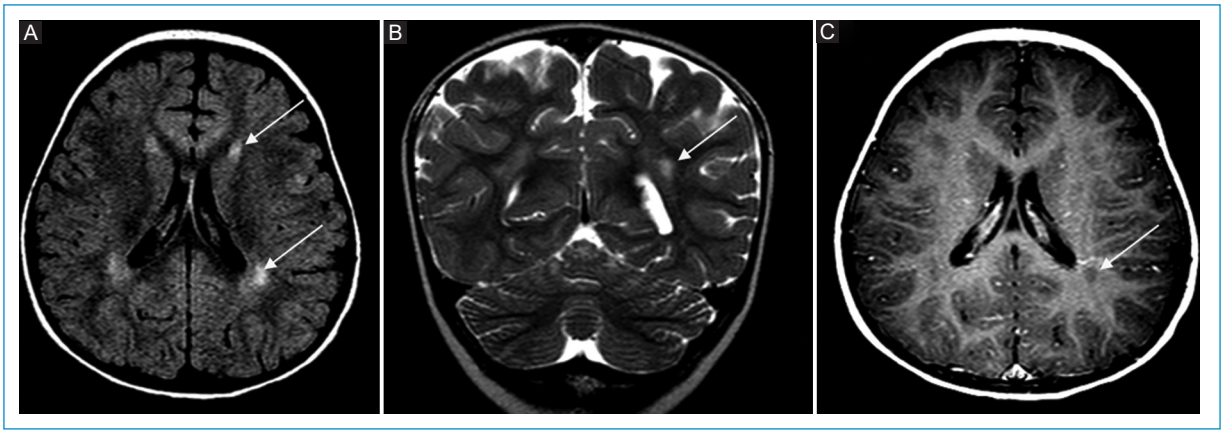

Figure 1: A: T2 FLAIR brain MRI axial image revealing hyperintense lesions in the posterior corona radiata and bilateral frontal periventricular substance. **B:** T2 coronal brain MRI revealing hyperintense lesions in the corona radiata; **C:** T1 axial brain MRI with contrast revealing hypointense lesions with no contrast uptake.

after the episode, the child remains in her usual condition, with no neurological changes and no similar episodes.

Discussion

ADEM is a rare inflammatory demyelinating disorder of the central nervous system that usually affects children and young adults[1,5]. Its etiology is often post-infectious or, more rarely, post-vaccination, with viral agents being a major culprit. Diagnosis can be difficult given the presence of several conditions mimicking ADEM and the lack of specific biomarkers[4,5]. Although rare, cases associated with COVID-19 have also been described. However, our knowledge about this entity is still scarce, since it is still based on case reports[1,6-9]. Despite classic ADEM being more frequent in pediatric age, when associated with COVID-19 it has been more frequently described in adulthood. Although extremely rare, it has also been described in pediatric patients[1,6,7].

ADEM's clinical presentation is heterogeneous. Usually, patients present with prodromal symptoms such as fever, headache, malaise, nausea, and vomiting, followed by the acute phase with encephalopathy, characterized by altered behavior and consciousness, associated with multifocal or focal neurological deficits. Diagnosis is clinical and confirmed with neuroimaging[5].

The clinical and analytical presentation of COVID-19-associated ADEM has been similar to classic ADEM, as in the presented case. However, the time gap between infection and ADEM associated with COVID-19 seems to be greater than in classic ADEM. In the typical presentation of ADEM, acute neurological symptoms develop around seven to 14 days after infection, while in ADEM post-SARS-CoV-2 infection the mean latency period seems to be around 25 days. In the case presented, the latency period was less than that described in the literature. As in the case described, the viral RNA testing for SARS-CoV-2 was negative in almost all the patients reported, reinforcing the immune-mediated character of this pathology. The treatment of classic ADEM is based on nonspecific immunosuppressive therapy, including corticosteroids, and intravenous immunoglobulins and plasma exchange for steroid-resistant patients or with contraindications to steroids[4]. The treatments used in COVID-19-associated ADEM have overlapped those recommended for classic ADEM[1]. The reported case supports this practice, having obtained an excellent clinical outcome in this child. Although the outcome of classic ADEM is usually excellent, with the full resolution of symptoms, ADEM associated with COVID-19 has been described in the literature as being associated with a poorer outcome, with an increased need for ICU, although better in the pediatric age[1,6,7]. The identification of this pathology is vital for early treatment and to improve the clinical course and long-term outcome[5], and pediatricians should consider ADEM in a child who has had COVID-19 and presents with encephalopathy.

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