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Short communication

c-ANCA-associated vasculitis with predominant CNS demyelination after COVID-19

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ABSTRACT

COVID-19 infection may trigger the presentation or exacerbation of autoimmune diseases. c-Antineutrophil cytoplasmic antibody (c-ANCA)-associated vasculitis after COVID-19 mainly involves the kidneys and lungs, and is rarely reported. We describe the case of a 13-year-old girl with a history of chronic immunologic thrombocytopenic purpura who presented with transverse myelitis and central nervous system demyelination, and was subsequently diagnosed with c-ANCA-associated vasculitis following COVID-19. The patient’s condition improved after pulse therapy with methylprednisolone and rituximab. To our knowledge, this is the first reported pediatric case of ANCA-associated vasculitis with predominant central nervous system involvement after COVID-19 infection.

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1. Introduction

ANCA-associated vasculitis (AAV) is a pauci-immune small-vessel vasculitis, characterized by neutrophil-mediated vasculitis and granulomatosis [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been shown to trigger the presentation or exacerbation of autoimmune diseases in genetically susceptible patients [2]. AAV has rarely been reported in patients with coronavirus disease 2019 (COVID-19). Renal and pulmonary system involvement are mostly reported in cases of AAV after COVID-19 [3,4]. The central nervous system (CNS) is involved in 15% of AAV cases, and no AAV cases have been reported after COVID-19 infection [5]. We discuss a challenging diagnosis of pediatric AAV with predominant CNS involvement. CNS symptoms in AAV may hinder early diagnosis, causing treatment delays and disease progression, which lead to relapse or even death.

2. Case report

A 13-year-old girl with a history of chronic immune thrombocytopenic purpura was admitted to the pediatric department in June 2021. She presented with walking difficulties and numbness of the lower limbs that had begun 3 weeks prior. Four weeks before her presentation, she was exposed to SARS-CoV-2 through her parents, who had mild COVID-like symptoms. She experienced only mild symptoms of fatigue, myalgia, and low-grade fever. Physical examination revealed a normal Glasgow coma scale score and intact cranial nerves; however, motor strength showed an MRC grade of 4/5 throughout the right lower extremity. Upper motor neuron signs were present in the bilateral lower extremities, with Grade 3+ reflex, positive bilateral Babinski reflex, and decreased sensation in the right lower extremity. Complete blood count as well as renal and hepatic function test results were normal. Magnetic resonance imaging (MRI) of the spine showed thickening of the spinal cord, with hyperintense and diffuse edematous lesions extending from C4 to the cone, with heterogeneous contrast (Fig. 1). A lesion showing nodular contrast at the C5 level was also observed. The MRI of the brain revealed demyelinating lesions in the right capsulo-thalamic, right temporal (Fig. 2), and left cortico-subcortical paramedian hemi-cerebellar white matter, which was enhanced after gadolinium injection. MRI of the lung showed a pulmonary infiltrate (Fig. 3). A nasal swab polymerase chain reaction (PCR) assay for COVID-19 was negative. However, the serology test, utilizing electrochemiluminescence immunoassay, demonstrated a recent COVID-19 infection (total immunoglobulin index = 2.11 [normal < 1.0]). Cerebrospinal fluid analysis showed mild pleocytosis (10 cells/mm\textsuperscript{3} lymphocytes), high protein level (0.59 g/L), and normal glucose level (2.4 mmol/L). Bacterial cultures and a PCR test for COVID-19 were both negative. Serology test results...
for cytomegalovirus, human parvovirus B19, herpes simplex virus, and HIV were also negative. The initial diagnosis was acute CNS demyelination following COVID-19. Pulse steroid therapy was administered for 5 days followed by oral prednisolone. The patient presented with generalized tonic–clonic status epilepticus 2 weeks later, requiring ICU admission. MRI revealed dura mater thickening with focal and diffuse contrast enhancement, cervical and thoracic cord enlargement, swelling with diffuse hyperintensities, and cerebral demyelinating lesions. A whole-body computed tomography (CT) scan revealed bilateral pulmonary infiltrates and nodules with a halo sign, mild hepatomegaly, mild splenomegaly, and multiple retroperitoneal adenomegaly. Blood analysis showed a white blood cell count of 3.0 × 10^9/L and a slightly elevated C-reactive protein level. Cerebrospinal fluid analysis showed slightly elevated leukocyte and protein levels. The renal profile was normal. c-ANCA test results revealed elevated levels with a titer of >1:1000 and a proteinase-3 antibody (PR3) level of 250 (normal < 1.0). Antinuclear antibody, anti-dsDNA, aquaporin-4 antibodies (IFT HEK 293 cells technique), and MOG antibodies (cell-based assay technique), were negative, and serum complement was normal. A few days later, the patient developed diffuse dermatologic manifestations, including palpable purpura and maculopapular exanthema (Fig. 4). The biopsy specimen revealed features of chronic inflammatory leukocytoclastic vasculitis with nonspecific patterns. The patient was treated with pulse intravenous methylprednisolone (1 g/day) for 5 days, followed by oral prednisolone and intravenous rituximab. She underwent physical therapy and rehabilitation, resulting in gradual improvement of neurological symptoms. Repeated MRI showed regression of the demyelinating lesions. A clear reduction in pulmonary nodule size, micronodules, and infiltrates on chest CT (Fig. 5) was also observed. All laboratory markers were within normal limits. Two months after initiation of therapy, the repeated ANCA test results were negative, as were the serum MOG and aquaporin antibody results.

3. Discussion

Our patient presented with transverse myelitis, brain demyelination, and pachymeningitis after COVID-19. She later developed skin

Fig. 1. Magnetic resonance imaging of the spine: T2-weighted sequence shows diffuse thickening of the dura mater and swelling of the spinal cord.

Fig. 2. Magnetic resonance imaging of the brain: FLAIR sequence shows demyelinating lesion.

Fig. 3. Computed tomography of the chest revealed bilateral pulmonary infiltrates and nodules with a halo sign.

Fig. 4. Extensive palpable purpura and maculopapular exanthema.
lesions and pulmonary involvement, and was diagnosed with AAV. CNS involvement has been observed in both AAV and COVID-19 infection [6–8]. Typically, COVID-19 neurological manifestations include stroke, encephalitis, and CNS inflammatory disorders, such as acute disseminated encephalomyelitis, vasculitis, transverse myelitis, acute hemorrhagic necrotizing encephalopathy, multiple sclerosis, Guillain–Barré syndrome, and myasthenia gravis [7]. Only a few case reports of COVID-19-related spinal cord disorders have been described in the literature, including transverse myelitis and acute disseminated encephalomyelitis [8]. In our patient, criteria suggestive of a c-ANCA-associated vasculitis included pulmonary involvement, skin involvement, very high ANCA titer, negativity of other antibodies and infectious work-up, and the improvement of symptoms on rituximab. We can also add the history of chronic immune thrombocytopenic purpura in this patient may increase the risk of other autoimmune diseases and suggests a possible genetic predisposition.

4. Conclusion

The diagnosis of new-onset AAV with predominant CNS involvement can be challenging in COVID-19 patients because of the similarity in symptoms and clinical manifestations of both diseases. Timely diagnosis and treatment are crucial for this life-threatening disease.

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Declaration of Competing Interest

The authors declare that they have no competing interest.

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