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Clinical Letter

Increased Intracranial Pressure in the Setting of Multisystem Inflammatory Syndrome in Children, Associated With COVID-19

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Introduction

Multisystem inflammatory syndrome in children (MIS-C) is now an established sequalae of SARS-CoV-2 infection[1]; however, pediatric neurological manifestations are just beginning to be characterized.[2] We describe two children who presented with MIS-C and were found to have evidence of increased intracranial pressure (ICP).

Patient I

A previously healthy, fully vaccinated nine-year-old boy presented to the emergency department with diplopia and worsening headache following a seven-day febrile illness with abdominal pain. He was diagnosed with MIS-C by the Centers for Disease Control and Prevention diagnostic criteria[3] and admitted. Neurological examination revealed a right abducens palsy without papilledema. Antibodies to SARS-CoV-2 were present, whereas SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) from nasopharyngeal swab was negative. Magnetic resonance imaging and venography of his head were normal. A lumbar puncture (LP) demonstrated an elevated opening pressure (OP) of 34 cm H_2O. The remainder of his cerebrospinal fluid (CSF) studies was within normal limits, including negative SARS-CoV-2 RT-PCR CSF testing. The patient's headache improved after LP, and two days later, his abducens palsy and diplopia resolved. He was treated using our institution's MIS-C protocol,[4] along with acetazolamide, and he was discharged home after his clinical status, laboratory studies, and

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cardiac function had improved. He had no symptoms on two-month follow-up, with normalized laboratory values and cardiac studies.

Patient II

This previously healthy, fully vaccinated six-year-old boy was evaluated for diplopia and was found to have a right abducens palsy and bilateral papilledema. He had been discharged from the hospital the previous day after a week-long admission to treat MIS-C, diagnosed using the Centers for Disease Control and Prevention criteria.[3] During this hospitalization, he demonstrated both SARS-CoV-2 RT-PCR nasopharyngeal swab and antibody positivity, and he required intensive care unit admission for vasopressor support and was treated as suggested by our institution's MIS-C protocol.[4] Before hospital discharge, he had several days of headache and was closing one eye while watching television, which had been attributed to failure to wear his glasses. However, upon re-presentation, and in light of his new focal neurological findings, these observations were reinterpreted as early signs of increased ICP. As such, the patient was readmitted for further evaluation. Magnetic resonance imaging of the brain and orbits was notable for kinking and distention of both optic nerve sheaths with protrusion of the optic discs into the globes, consistent with increased ICP. Despite the papilledema, LP under sedation demonstrated a normal OP of 14 cm H_2O; however, the LP was notably performed one week after the patient had been first observed with symptoms attributable to his abducens palsy. His CSF studies, including SARS-CoV-2 RT-PCR testing, were normal. The following morning, although his papilledema persisted, his diplopia had resolved and he was discharged home on a continued steroid taper. Five months post-presentation, his papilledema has resolved, and he is without recurrence of symptoms.

Discussion

We report two children with increased ICP in the setting of MIS-C. Neither child was obese. At the time that Patient I was noted to have elevated OP on LP, he had not previously taken or received medications known to cause increased ICP. Although Patient II did receive intravenous immunoglobulin and steroids (as part of his MIS-C treatment) before developing his neurological symptoms, his CSF studies were normal, and steroids had only recently been initiated, making these medications unlikely causative factors for his increased ICP. It should be noted that these patients' laboratory studies revealed PCR and antibody positivity to other pathogens. However, there was no consistent infection pattern across the patients aside from SARS-CoV-2, and no other detected pathogen would explain the full constellation of each patient's symptoms. Therefore, it is unlikely that these other pathogens explain the patients' findings of increased ICP; rather, their detection likely reflects either prior or concurrent infection, as has been reported with SARS-CoV-2 infection.[5]

Increased ICP has been noted as the initial manifestation of some systemic inflammatory disorders, including lupus, Sjögren syndrome, and Kawasaki disease.[6-8] We posit that our patients' increased ICP similarly reflects systemic inflammation related to SARS-CoV-2 infection, resulting in central nervous system effects. Given our patients' normal CSF studies, including negative SARS-CoV-2 RT-PCR testing, it is less likely that our patients experienced direct central nervous system infection with SARS-CoV-2.

As more children present with MIS-C, we recommend that practitioners remain vigilant for signs and symptoms of increased ICP in these patients.

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