Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Encephalitis and transverse myelitis associated with Covid-19 infection, a case report

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Introduction

Covid-19 infection was rarely reported to be associated with severe manifestations in children [1]. Neurological complications of Covid-19 are not yet fully understood but some reports in adults included autoimmune encephalitis, autoimmune epilepsy, Guillain Barre syndrome [2]. In children, a few neurological complications were reported including mainly headache and loss of smell [3]. However, a few cases of more serious complications such as seizures and encephalitis were reported with a wide variation in presentation and outcome [1, 4–9]. The pathophysiology of encephalitis with Covid-19 is not clear with a possibility of direct viral invasion, autoimmune or vascular process [8]. We are reporting a case of a child who developed encephalitis and transverse myelitis confirmed by MRI in the context of Covid-19 infection.

Case description

A previously healthy 2-year-old male, vaccinated and developmentally up to age, presented with fever and mild cough in the context of positive Covid-19 infection. He has a history of febrile seizure one year ago, Central Nervous System (CNS) infection was ruled out at that time, and he continued to be seizure free and developing well. Prior to presentation, he developed generalized tonic clinic seizure at home for 5 min followed by another seizure while being transferred by ambulance to the emergency department (ED) and a third seizure in the ED. In the ED, the child was febrile, seizure was aborted by Midazolam, and he went into post ictal state with decreased level of consciousness and was intubated accordingly. Head computed tomography was normal, and he was started empirically on Ceftriaxone, Vancomycin and Acyclovir to cover for possible CNS infection. He was admitted to the Pediatrics Intensive Care Unit (PICU) for further care.

In the PICU, he was extubated on the second day. Lumbar puncture was performed and showed one white blood cell/μl, 285 red blood cells/μl, glucose of 3.4 mmol/l (serum glucose: 3.9 mmol/l), protein of 0.76 gm/l, culture and PCR from the CSF for common organisms were negative including (*Streptococcus pneumoniae, Streptococcus agalactiae, Haemophilus influenzae, Neisseria meningitidis, Listeria monocytogenes, enterovirus, human parechovirus, HSV 1 and 2, varicella zoster virus, CMV, human herpesvirus 6, Cryptococcus neoformans, and Cryptococcus gattii*). Covid-19 PCR from CSF was negative. White blood cells count was 3.9 × 10^3/ul (low) with lymphopenia 1.4 10^3/ul. Renal and liver function tests were normal, Serum c-reactive protein was 22 mg/l. He had no respiratory symptoms except for mild cough and his chest x ray (CXR) was normal.

The child had no seizures in the PICU yet he was very irritable with inability to sit or turn in bed and no clear speech. On exam, he had weakness of the upper and lower extremities that was more prominent on the left side, intact cranial nerves, hyperreflexia, and no apparent sensory deficit. Electroencephalography showed no subclinical seizure activity. MRI of the brain and spine showed Evidence of bilateral

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considerably symmetrical small punctate foci of microhemorrhages, diffusion restriction and T2WI/FLAIR hyperintensity seen along bilateral periventricular region, centrum semiovale, bilateral cerebellar hemispheres and vermis, thalamus more prominent on the right site, with scattered foci seen in the left precentral gyrus, right frontal, temporal and occipital juxtacortical region with subtle abnormal post-contrast enhancement noted. Evaluation of the spinal cord shows longitudinally extensive transverse myelitis between the level of C3 C7 involving mainly the central part of the spinal cord without any obvious contrast enhancement.

The child was treated with Intravenous Immunoglobulins 2 gs/kg over 2 days in addition to Methylprednisolone 30 mg/kg for 5 days then decreased to 2 mg/kg and weaned gradually.

He received 5 sessions of plasmapheresis, after which he showed clinical improvement. The child improved after 10 days in the PICU, he regained his motor power gradually and was able to walk independently, talk and interact with his parents. He was discharged home in stable condition with complete recovery of his neurological symptoms.

Discussion

Since the rise of COVID-19 very few cases have been reported in the pediatric population of COVID-19 induced encephalitis. Due to the scarce number of cases and few reports being published no diagnostic criteria has been set and no clear management guidelines are available, thus each institute follows its own protocols.

Although the ability of SARS-CoV-2 to invade cells by using the ACE2 receptor has been proven, the exact process by which it causes brain damage is yet to be well understood.

It has been hypothesized that like in other neuro-invasive human viruses, coronavirus could retrogradely propagate through the olfactory nerve or peripheral lung nerves to reach the CNS or through the vascular system entering the CNS using ACE2 receptors expressed in brain vessels. An indirect mechanism through which SARS-CoV2 might leak into the CNS is by crossing a permeable BBB affected by systematically produced Cytokines [13].

Many etiologies have been proven to cause focal inflammation and injury involving the spinal cord, also known as transverse myelitis. It has been well established that TM can be a sequel of viral as well as bacterial infections [10].

Past reports from 2003 suggest that certain coronavirus genotypes are known to have neurotropic features and may lead to Guillain-Barre, encephalomyelitis, and seizures [11].

A case reported by Zhao and colleagues back in 2020 described a 66-year-old gentleman who presented with symptoms suggestive of Guillain-Barre in the context of positive COVID-19 PCR and no preceding respiratory symptoms thus suggesting a para-infectious process [12].

It is yet to be cleared whether TM occurs as a direct effect of the virus on neuronal cells or as a result of a post infectious immune process.

It is worth highlighting that our patient did not at any point during his hospital stay meet the laboratory or clinical criteria of multisystem inflammatory disease in children (MISC), he also did not complain of any major symptoms suggestive of respiratory affection, he rather presented with signs and symptoms of CNS involvement thus suggesting no correlation between the severity of respiratory symptoms and degree of CNS involvement. Moreover, the patient's acute presentation with CNS symptoms in the absence of significant respiratory involvement further supports the process being a Para infectious etiology rather than a post infectious immune mediated process.

The above reported case is one of the few in pediatric population which presented with clinical and radiological evidence of both encephalitis as well as transverse myelitis, early aggressive management with IVIG, pulse steroids and plasmapheresis allowed for complete recovery with no long-term disability.

In conclusion, we would like to emphasize on the importance of keeping a low threshold of suspicion for COVID related CNS affection despite mild or absent respiratory involvement in order to achieve early recognition and aggressive management thus allowing for the best possible outcome.

Declaration of Competing Interest

All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version. This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue. The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

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