Abstract
Anti-N-methyl-D-aspartate receptor encephalitis is a clinical condition characterized by sudden changes in the level of consciousness, behavior, or mood; new onset seizures; abnormal movements; and autonomic instability [1]. Viral infections constitute its most frequent precipitating factor in children [2, 3]. The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with various neurological complications attributed to neural infection, vascular complications, or the inflammatory reaction. Four adult cases of SARS-CoV-2-associated anti-NMDAR encephalitis and only one young child have been reported to date [4–7].

We present a pediatric case with anti-NMDAR encephalitis and SARS-CoV-2 infection confirmed by viral PCR.

Case presentation
A 7-year old boy was admitted to our hospital because he had experienced unsteady gait for the prior 4 days. He had no complaints of headache, fever, or antecedent infection. Medical and family histories were unremarkable. A general physical examination was normal. He had ataxia and wide-based gait. Deep tendon reflexes could not be elicited. On the
second day, he developed somnolence and seizures, and levetiracetam was started (Fig. 1). Peripheral blood biochemistry and erythrocyte sedimentation rate were normal; C-reactive protein (CRP) was 20 mg/L (0–5 mg/L); absolute lymphocyte count was 700/mm$^3$ (2.25–8.89/mm$^3$) (Fig. 2). Brain magnetic resonance imaging (MRI) was normal. Cerebrospinal fluid (CSF) analysis was normal for protein, glucose, lactate, and pyruvate levels and IgG index; no cells or oligoclonal bands were observed, and serology for Epstein-Barr virus (EBV), Herpes simplex virus type 1 and type 2 (HSV-1 and -2), and Borrelia burgdorferi was negative. Treatment was started for possible encephalitis with acyclovir, ceftriaxone, and clarithromycin. CSF bacterial culture and PCR for HSV-1 and HSV-2 were negative. On the third day of admission, the SARS-CoV-2 rtPCR test from the throat swab was reported to be positive. The patient had no fever or respiratory symptoms, but lymphopenia persisted. Awake and sleep EEGs were encephalopathic with widespread delta waves (Fig. 3). Persistent lymphopenia and increasing creatinine and CRP levels prompted the use of plasmapheresis and intravenous immune human globulin (IVIg) to the treatment, with no significant benefit. On the 8th day of admission, choreiform movements in the hands and feet, tongue protrusion, bruxism, lip smacking, agitation, catatonia, echolalia, and tachycardia were observed. A test of the CSF for anti-NMDAR IgG was positive. Three courses of plasmapheresis were performed in the first hospital week. The patient’s lymphopenia and creatinine values started to normalize and methylprednisolone 30 mg/kg/day for 5 days followed by 20 mg/kg for 2 days, and IVIg 2 g/kg over 5 days were applied, followed by prednisolone 2 mg/kg p.o. His level of consciousness, oral intake, and involuntary movements gradually improved within 2 weeks after beginning prednisolone. A focal seizure occurred on day 26 in hospital: a second brain MRI was normal and clobazam and topiramate were added. The patient was discharged ambulating but mildly ataxic, with the plan of slow oral prednisolone taper, anti-epileptic treatment, and repeat IVIg if necessary.

**Discussion**

As of when this written, over 37 million COVID-19 cases and one million deaths have been reported globally (WHO COVID-19 Dashboard). The neurological complications are explained by various pathogenic mechanisms: direct...
viral injury, systemic inflammatory response syndrome, para- and post-infectious inflammatory or immune-mediated reactions triggered by virus, in particular cross-reacting antibodies against host antigens [8–11]. Monti et al. [6] reported a 50-year-old patient with status epilepticus, anti-NMDAR antibody, and COVID-19 rtPCR positivity but no respiratory or systemic symptoms; Panariello et al. [4] described a 23-year-old boy with acute psychosis due to anti-NMDAR encephalitis, also with no respiratory system involvement. Younger patients with anti-NMDAR encephalitis and COVID-19 positivity were reported by Burr et al. [5] and Moideen et al. [7] in 23 months and 17-year-old patients, respectively, the latter with acute psychosis. Our patient, unlike those in other reports, manifested with acute ataxia, only to become encephalopathic over days.

The NR1A subunit of the NMDAR, the target of the autoantibodies, is expressed in the neocortex, hippocampus, and also cerebellum in humans [12, 13]. The expression level of the NMDAR is subject to age-dependent changes; its function and response to exogenous factors such as stress or steroids can also change during development, which can explain different clinical manifestations of anti-NMDAR encephalitis according to age and developmental status [14].

The diagnosis of autoimmune encephalitis was strongly considered at our patient’s initial presentation. The marked lymphopenia precluded steroid treatment and IVIg was started first along with an antiviral drug and antibiotics. Lymphopenia is a well-known finding in Covid-19 infection [15]. Lymphocyte counts started to increase and pulse steroid treatment was started on the 10th day of admission, resulting in more rapid clinical improvement. Despite a few days’ delay, our patient’s diagnosis and treatment beginning within 4 days of symptoms can still be considered as relatively early. Although his clinical picture worsened in the first week, the normal MRI findings at admission and follow-up and prompt response to treatment also support timely diagnosis and intervention in this case.

We believe this report can serve as an example of pediatric autoimmune encephalitis associated with COVID-19 and contribute to the clinical perspective, management, and treatment of neurological complications observed during the pandemic.

Acknowledgements I would like to thank to Prof. Dr. Cetin Okuyaz and Prof. Dr. Ilknur Erol for their support during the follow-up process of this case.

Declarations

Ethics approval and consent to participate The presentation of the case was approved by the guardians of the patient. Informed consent was obtained.

Conflict of interest The authors declare that they have no conflict of interest to disclose. There is no funding support available for this study.

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