






## Clinical Notes

## Seizure in children with severe acute respiratory syndrome coronavirus 2 Omicron variant infection

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After the World Health Organization designated the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant from South Africa as variant of concern on November 24, 2021, it spread quickly around the globe, including Japan.<sup>1</sup> During the Omicron surge, several reports described seizures in children with coronavirus disease 2019 (COVID-19), which was an unusual manifestation compared with the previous variants.<sup>1,2</sup>

Our hospital, Tokyo Metropolitan Children's Medical Center, is one of the largest tertiary children's hospitals in Japan, located in the Tama area of Tokyo, where approximately 500 000 children live. We have around 32 000 emergency visits annually, and 1% of them present with a febrile seizure. Recently, we experienced five consecutive cases of prolonged seizures admitted to our hospital, later revealed to be COVID-19 caused by the Omicron variant. All five patients were febrile at presentation and were admitted to our hospital from late January to mid-February 2022, during which period the Omicron variant prevailed over the Delta variant in Japan. The genome sequence of SARS-CoV-2 revealed Omicron variant, BA.1, for all five cases. The background and seizure characteristics of patients are shown in Table 1. Additional clinical and laboratory information is provided in Table S1. We describe in-depth case histories of case 4, who had several comorbidities.

A 9-year-old boy diagnosed with COVID-19 developed convulsions. His seizure stopped after he received intramuscular diazepam 0.25 mg/kg and intravenous midazolam 0.05 mg/kg at the local hospital. He was transferred to our hospital for further monitoring. Upon arrival, subcostal and intercostal retractions with prominent stridor were observed. His glasgo coma scale score was E1V2M5. Due to respiratory instability, he was intubated and admitted to a pediatric intensive care

unit. As he was on anticoagulation for a mechanical mitral valve, we opted not to perform a lumbar puncture. His head computed tomography (CT) scan revealed a cystic encephalomalacia on the right parietal lobe, which implied an old ischemic stroke. There was no cerebral edema on the head CT. As he had bilateral pulmonary infiltrates on his chest radiograph and required mechanical ventilation, remdesivir and dexamethasone were started for the treatment of COVID-19 pneumonia. He was placed on synchronous intermittent mandatory ventilation with pressure support mode with respiratory rate 18/min, peak inflation pressure 22 cmH<sub>2</sub>O, pressure support 5 cmH<sub>2</sub>O, peak end-expiratory pressure 8 cmH<sub>2</sub>O, and a fraction of inspired oxygen (F<sub>I</sub>O<sub>2</sub>) 0.5. His partial pressure of arterial oxygen / F<sub>I</sub>O<sub>2</sub> was 450 at the time of admission. Although intermittent spikes and waves were observed in Fp2 on continuous electroencephalography, other abnormal patterns including diffuse, high-voltage, slow-wave, electrical storm, or absence of spindle waves were not observed. He had no clinically apparent seizure afterward. He was extubated on day 4 of hospitalization. After confirming that his neurological status was normalized, he was discharged home on day 12 of hospitalization.

Prematurity of brain development in young children is thought to lead to a predisposition to febrile seizures triggered by common viral illnesses of childhood. A report from South Africa suggested that febrile seizures might be a common complication of the Omicron variant in children.<sup>1</sup> Febrile seizures usually occur in pediatric patients of 6 to 60 months old.<sup>3</sup> In the present case report, all patients were older than this age range. Swedish researchers have also reported two pediatric cases of febrile seizures at the atypical ages of 3 months and 14 years.<sup>2</sup> The influenza virus is also known to cause febrile seizure in older children, which was considered to be related to the high prevalence of influenza virus infections among school-aged children compared with preschool-aged children.<sup>4</sup> During the COVID-19 reemergence with the Omicron variant in Japan, children were infected widely regardless of age. Age distribution of infections may not

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**Table 1** Clinical and laboratory features of five cases

	Case 1	Case 2	Case 3	Case 4	Case 5
Day of admission	1/27/2022	1/31/2022	2/14/2022	2/15/2022	2/16/2022
<b>Background</b>					
Age	7 years	8 years	6 years	9 years	10 years
Sex	Female	Female	Male	Male	Female
History of FS	No	Yes, 2 times	Yes, 4 times	No	Yes, 4 times
Final episode of FS	NA	6 years	2 years	NA	8 years
Family history of FS (first relative)	No	No	No	NA	Yes
Neurodevelopmental abnormality	No	No	No	Yes	No
Other comorbidities	No	No	No	Severe mitral stenosis, mitral valve replacement, sick sinus syndrome, periventricular leukomalacia	No
Contact with COVID-19 patients	No	Yes	No	Yes	Yes
<b>Seizure characteristics</b>					
Fever duration before seizure onset	5 h	4 h	3 h	10 h	NA
Seizure duration	40 min	2 h	30 min	1 h	25 min
Seizure pattern	Tonic-clonic seizure	Tonic seizure	Tonic seizure	NA	Clonic seizure
Focal neurological signs	No	No	No	No	No
Use of anticonvulsant	No	Midazolam 0.2 mg/kg, Fosphenytoin 22.5 mg/kg	No	IM diazepam 0.5 mg/kg, Midazolam 0.05 mg/kg	No
Postictal period of unconsciousness	3 h	NA	1 h	NA	1 h
Use of antipyretics before seizures	3 h before	No	No	NA	No

FS, febrile seizure; IM, intramuscular; NA, not available.

explain the atypical age of presentation observed in seizure caused by the Omicron variant. Cases 2 and 5 had a previous history of older-onset febrile seizure, which suggests that they had a lower seizure threshold than usual.

Four of our five patients presented with status epilepticus lasting for more than 30 min. Two of them required mechanical ventilation to secure and support respiration. This was different from the report from South Africa, in which the majority of admitted patients were simple febrile seizures, characterized by a short duration of the seizure.<sup>1</sup> Genetic predisposition may explain this observation because the risk of status epilepticus is known to be higher in Asians than in other races.<sup>5</sup> As case 2 and case 4 were sedated for mechanical ventilation, it is difficult to exclude encephalopathy as a cause of seizure in these patients.

The present case report described the first Asian cases of seizures developed in children who were microbiologically diagnosed with Omicron variant BA.1 infection. Unlike previous variants, the Omicron variant may manifest with febrile seizures in older children. In Japan, the SARS-CoV-2 mRNA vaccine for patients aged 5–11 years started at the end of February 2022. There is global controversy regarding vaccinating this age group because COVID-19 seldom progresses to severe disease in this pediatric population. However, seizure prevention may be a potential benefit of vaccination in this

age group. The Omicron variant disease burden among children should be closely evaluated in future studies, especially for neurologic complications.

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## Disclosures

The authors declare no conflict of interest.

## Author contributions

K.I. conceptualized this report. Y.H., O.S., Y.I. and Y.H. critically reviewed the manuscript. All authors approved the final manuscript.

## Informed consent

Informed consent was obtained from all patients or their parents.

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## Supporting Information

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**Table S1.** Clinical and laboratory features of 5 cases.