Children With Croup and SARS-CoV-2 Infection During the Large Outbreak of Omicron

To the Editor:

In children, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) commonly presents with fever, cough or shortness of breath or is sometimes asymptomatic.[1] There have been few case reports about croup caused by SARS-CoV-2 infection, which is a rare symptom, and its characteristics or clinical presentations have not been sufficiently revealed.[2,3] In the current pandemic involving SARS-CoV-2 variants, especially Omicron VOC21NOV-01 (B.1.1.529), we report three cases of Japanese patients with Omicron-induced croup within a short period.

A 3-month-old boy presented to the emergency department with a 1-day history of fever and dyspnea. He was febrile and appeared agitated with tachypnea, inspiratory stridor, and a hoarse cry, as well as severe subcostal retraction and nasal flaring. A nasopharyngeal polymerase chain reaction test was positive for SARS-CoV-2. He was diagnosed with COVID-19 and severe croup. Nebulized epinephrine and oral dexamethasone were administered, but his condition showed little improvement. He was thus admitted and treated with nebulized epinephrine every 3 hours and intravenous dexamethasone. His symptoms gradually improved, and he was discharged on day 4.

We also experienced an 8-month-old boy and a 21-month-old boy who did not respond well to treatments for croup at the emergency department, similar to the previous case. The 8-month-old boy had persistent symptoms lasting 3 days, which eventually improved.

We suggest that the risk of croup is higher with Omicron than it is with other variants. This is supported by recent findings that the possibility of sore throat is higher in patients with Omicron infection than in those with Delta infection, indicating that Omicron may cause severe inflammation in the upper respiratory tract.[4] In vitro research has reported that Omicron infects individuals and quickly replicates in the upper respiratory tract and bronchus, whereas other variants mainly replicate in the alveolar epithelium.[5] These findings are consistent with our suggestion that Omicron infection can induce croup.

From the viewpoint of infection control, we must consider SARS-CoV-2 infection when examining a patient with croup. SARS-CoV-2 can be transmitted via aerosols, and nebulizer use is believed to increase the transmission risk. We have to perform SARS-CoV-2 testing in patients with croup and use airborne precautions for them when nebulized epinephrine is administered during the outbreak of Omicron.

Our cases indicate that patients with Omicron-induced croup may have poor responses to nebulized epinephrine and glucocorticoids and may show symptom improvement after a long time. This is consistent with past cases involving croup caused by other variants.[2,3] Our cases suggest that the number of hospitalizations involving Omicron-induced croup is increasing in the current outbreak, although Omicron is associated with reduced severity and a lower rate of hospitalization compared with other variants.

In conclusion, the risk of croup appears to be higher with Omicron than with other variants, and it might result in a life-threatening condition. The number of patients with Omicron-induced croup will continue to increase as this variant spreads worldwide. It is important to recognize the epidemiology and characteristics of patients with Omicron-induced croup.

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Features of COVID-19 in Children During the Omicron Wave Compared With Previous Waves in Madrid, Spain

To the Editors:

The SARS-CoV-2 variant Omicron (B.1.1.529) replaced other variants in Spain during the sixth wave, accounting for 79%–94% of positive samples in the last 2 weeks of 2021.[1] The information is scarce about Omicron severity in children.

To describe the features of children with COVID-19 during the Omicron wave, we reviewed charts from children with COVID-19 attended at the emergency room of a secondary center in Spain from December 20, 2021, to January 2, 2022. All patients' charts were reviewed 1 week after diagnosis to check complications.

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A.T. conceptualized and designed the study. A.T., A.P.-V., B.I., and A.N. performed the data management. A.T. and D.A.-A. performed the statistical analysis. A.T., D.A.-A., and C.M. drafted the article. All coauthors enrolled participants and participated in the collection of data. All coauthors were involved in the preparation and review of the final article.

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The detection by reverse transcriptase-polymerase chain reaction (RT-PCR) used as target genes ORF1ab and N of the SARS-CoV-2 genome. All samples with a cycle threshold (Ct) <25 were analyzed with a second RT-PCR with probes targeting the gen S mutations consistent with Omicron. This study is part of the study EPICO-AEP.[2]

A total of 1,360 children were attended at the emergency room during the study period. Globally, 94 (6.9%) had a positive RT-PCR for SARS-CoV-2, with a median age of 6.5 years (interquartile range: 1.3–9.7), and 82.9% had fever. Of them, 15 (16.0%) had a Ct <25: 13/15 (86.7%) were identified as Omicron and 2/15 (13.3%) as Delta variant.

Only 2 of 94 (2.1%) patients were hospitalized: a 3-year-old girl with features of bacterial pneumonia and confirmed Omicron variant, and a 40-day-old infant with whooping cough. No patient needed pediatric intensive care unit admission or died. In a study performed by our group during the third wave, caused predominantly by the Alpha variant, 3/75 (4.0%) children with COVID-19 were hospitalized, not differently to the Omicron wave (P = 0.394), and one child needed pediatric intensive care unit admission.

To better describe the profile of children with Omicron, we identified 17 further children with Omicron attended at another center. We compared the features of the 109 ambulatory children attended during the Omicron wave in these 2 centers to 546 ambulatory children attended in previous waves in 35 centers, from March 2020 to October 2021, included in the national COVID-19 EPICO-AEP registry (Table 1).[2] During the Omicron wave, more children presented upper respiratory tract infection, but fewer children had pneumonia. Fever, headache, and diarrhea were more common during the Omicron wave.

Notably, most patients during the Omicron wave were ≤11 years old. Nearly 83% of adolescents ≥12 years old are vaccinated in Spain, which may explain the low proportion of adolescents in our population. Some studies reported that around 1%–2% of children with COVID-19 need hospitalization, likewise our study.[3,4]

This study suggests that children with the Omicron variant do not have a worse outcome than children with previous variants. Omicron in children seemed to have a similar clinical profile but with increased tropism for the upper airway and less tropism for the lungs.

TABLE 1. Comparison Between Features of Ambulatory Children Attended During the Omicron Wave and Previous Waves at the Emergency Rooms

Features	Previous Waves N = 546 (%)	Omicron Wave N = 109 (%)	*P*
Sex (female)	289 (52.9%)	60 (55.0%)	0.686
Age (yrs), median (IQR)	5.7 (1.1–11.7)	6.6 (1.3–9.8)	0.330
Age band (yrs)			**<0.001**
0–4	259 (47.4%)	47 (43.1%)	
5–12	162 (29.7%)	54 (49.5%)	
12 or above	125 (22.9%)	8 (7.3%)	
Comorbidity	99 (18.1%)	12 (11.0%)	0.070
Contact with household confirmed case	240 (44.0%)	33 (30.3%)	**0.008**
Symptoms/signs			
Fever	371 (67.9%)	90 (82.6%)	**0.002**
Cough	264 (48.4%)	61 (56.0%)	0.147
Sore throat	99 (18.1%)	20 (18.3%)	0.957
Runny nose	197 (36.1%)	49 (45.0%)	0.081
Fatigue, malaise	73 (12.2%)	12 (11.0%)	0.728
Wheezing	23 (4.2%)	2 (1.8%)	0.237
Headache	88 (16.1%)	35 (32.1%)	**<0.001**
Myalgia	48 (8.8%)	4 (3.7%)	0.071
Diarrhea	75 (13.7%)	23 (21.1%)	**0.049**
Vomiting	91 (16.7%)	23 (21.1%)	0.265
Syndromic diagnosis*			
Upper respiratory tract infection	195 (37.0%)	73 (67.0%)	**<0.001**
Flu-like	80 (15.2%)	14 (12.8%)	0.532
Fever without a source	84 (15.9%)	5 (4.6%)	**0.002**
Gastroenteritis	40 (7.6%)	7 (6.4%)	0.671
Pneumonia	38 (7.2%)	1 (0.9%)	**0.013**
Asymptomatic	44 (8.3%)	3 (2.8%)	**0.042**
Bronchitis/asthma flare	18 (3.4%)	2 (1.8%)	0.389
Bronchiolitis	2 (0.4%)	0 (0.0%)	0.519

Categorical variables are compared using the χ^2 or Fisher tests, and continuous variables using Wilcoxon rank-sum test. Significant P values (<0.05) are in bold.

*The syndromic diagnosis was not recorded in 19 cases diagnosed in previous waves; percentages and P values are calculated omitting those cases.

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Case of Venous Thromboembolia Under Enoxaparin Prophylaxis After Recovering From Acute Ischemic Stroke in Consequence of COVID-19-Related MIS-C

***To the Editors*:**

Multisystem inflammatory syndrome in children (MIS-C) guidance has been issued by the World Health Organization and by the Centers for Disease Control and Prevention.[1,2] Pediatric acute ischemic stroke and thromboembolic conditions have been reported as rare complications of COVID-19 or MIS-C.[3–5] Venous thromboembolism has not been reported in children with no underlying disease who have undergone enoxaparin prophylaxis after recovery from MIS-C.

This previously healthy 9-year-old boy without any history of head trauma arrived at the hospital obtunded, nonverbal, with a left-sided hemiparesis and left-sided central facial paralysis. He had fever, nausea, vomiting, diarrhea, and tenesmus for 5 days. His parents had been ill with SARS-CoV-2 infection about a month prior.

Body temperature was 38.1°C, oxygen saturation 94%, respiratory rate 45 breaths and heart rate 144 beats per minute, blood pressure 85/45mmHg after norepinephrine, Glasgow coma scale was 13-points, with physical examination notable for left-sided hemiparesis (1/5 muscle strengths) and central facial paralysis, increased patellar deep tendon reflexes and left positive Babinski sign, erythematous plantar areas, and nonpurulent conjunctivitis.

Blood tests revealed a systemic hyperinflammatory state. COVID-19 nucleocapid Ig M and Ig G were positive. Brain magnetic resonance imaging with diffusion-weighted showed that exhibit restricted diffusion at the level of the right temporal lobe and Sylvian cortex (Fig. 1). Transthoracic echocardiogram demonstrated a left ventricular ejection fraction of 51% with global strain and mild mitral valve regurgitation. The thrombophilia panel result was normal. Doppler ultrasonography was negative for deep venous thrombosis.

He was diagnosed with MIS-C based on the World Health Organization and Centers for Disease Control and Prevention criteria and treated with intravenous immunoglobulin, intravenous methylprednisolone, subcutaneous enoxaparin, and oral aspirin.

Progressive resolution of the systemic hyperinflammatory state occurred within 48–72 hours. He was discharged with prophylactic enoxaparin treatment (100 IU/kg-daily) with independence in all activities of daily living end of 14 day. On day 28 outpatient follow-up, the physical examination was normal except for mild left-sided central facial paralysis. After about a week, he was readmitted to the hospital due to swollen right upper limb without pain and tenderness. The linear swelling and reddish discoloration occurred on the median antebrachial vein trace (Fig. 2A). Because of the clinical suspicion of thrombosis, venous doppler ultrasonography was performed and showed absent flow at the level of this vein (Fig. 2B). All other venous system examinations, transthoracic echocardiogram and brain magnetic resonance imaging angiography showed no abnormalities. Blood tests include hyperinflammatory and thrombosis markers were within the normal range. Enoxaparin treatment was readjusted to 100 IU/kg-twice daily.

We describe the first case of MIS-C related acute ischemic stroke with venous thromboembolism while under enoxaparin prophylaxis after recovery from MIS-C in a child with no underlying disease. We suggest that aggressive therapy to halt the cytokine storm and appropriate supportive care while considering differential diagnosis is crucial for reaching positive outcomes in children. It should be kept in mind that pediatric patients treated for MIS-C should be followed closely in terms of thromboembolism risk even if they receive anticoagulant therapy.

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