

## Infectious Mononucleosis Complicated With COVID-19

### To the Editors:

Fever of unknown origin in children remains a challenging diagnosis despite advances in modern diagnostic methodologies.<sup>1</sup> Both infectious mononucleosis caused by Epstein-Barr virus (EBV) and coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are generally self-limiting diseases in immunocompetent individuals. However, there are limited reports on color sequential infections caused by these viruses in children. We present a case of a 4-year-old child who presented with fever of unknown origin and was diagnosed with infectious mononucleosis, complicated with COVID-19.

A previously healthy 4-year-old boy presented with a chief complaint of fever that started 7 days before the visit. Accompanying symptoms included slight rhinorrhea and a single event of vomiting. Vital signs of the patient during admission were within normal limits with mild fever (37.8°C). On physical examination, no abnormal findings were noted. Complete blood cell count results were as follows: white blood cells, 5520/μL (segmented neutrophil 28.1%); hemoglobin, 11.5 g/dL; and platelet, 324,000/μL. The peripheral blood smear report revealed mild lymphocytosis with normal morphology and an absence of atypical lymphocytes. Levels of inflammatory markers were within normal limits. After admission, his fever gradually decreased to 38.0°C. However, he depicted a temperature of 39.0°C on hospital day (HD) no. 5. On HD no. 6, the patient showed slightly increased rhinorrhea, and the basal body temperature was gradually increasing up to 38.5°C. As the multiplex polymerase chain reaction (PCR) for other respiratory viruses was negative, although the SARS-CoV-2 nasopharyngeal (NP) PCR tests on HD no. 1 and HD no. 4 were negative, the patient underwent

NP swab test on HD no. 6. The SARS-CoV-2 PCR test was positive. The next day, his fever soared up to 40.4°C. The test for EBV infection (VCA-IgM), which was negative on HD no. 1, was positive on HD no. 8. The patient's fever diminished on HD no. 13 without specific medication, and he was discharged on HD no. 14.

This case depicts a possible combination of the etiologies of fever in the COVID-19 pandemic. Coinfections of other respiratory viruses with COVID-19 have been frequently reported, although the degree varies among literature, and the clinical significance remains unclear.<sup>2</sup> Despite several reports in adults, only 1 case report of COVID-19 and EBV coinfection in children has been published.<sup>3</sup> However, the detection of SARS-CoV-2 was done by an antibody test in the previous case, which implies that COVID-19 could have been a past infection. To our knowledge, this is the first study to report the coinfection of EBV and SARS-CoV-2 in a child. Repeated tests for SARS-CoV-2 in children are sometimes necessary. However, the decision to make timely tests is difficult, especially when the patient has complications of previous NP swab tests. In the present case, as the test result was positive, the caregivers felt reassured that the reworsening fever could be explained. Additionally, because of the test, infection control for COVID-19 was possible.<sup>4</sup> Although the patient recovered perfectly, initially, we faced prognostic uncertainties.<sup>5</sup> In the COVID-19 pandemic, we believe that all possibilities should be considered in managing common and nearly well-known diseases.

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## Among Young Infants With Uncomplicated COVID-19: Should We Broaden Diagnostic Tests for Infectious Causes of Apnea?

### To the Editors:

We read the recent publication by Hobbs et al<sup>1</sup> on the characteristics and complications of COVID-19 in hospitalized infants with interest. The authors reported that the most severe cases were in infants <6 months of age, with respiratory complications being the most frequent. Among all patients (severe and nonsevere), there were no reports of apnea. To the best of our knowledge publications about COVID-19 associated apnea in infants are scarce<sup>2</sup> and published before the delta variant of SARS-CoV-2 became widespread.

Here, we present 5 cases of apnea as the initial manifestation of uncomplicated COVID-19 in young infants treated at our hospital in Croatia (November 2021 to February 2022) (Table 1). The definition of apnea agreed by the American Academy of Pediatrics was used. Except for 1 moderate preterm neonate with intraventricular hemorrhage and another newborn with a small patent foramen ovale, the other infants were healthy with unremarkable prenatal and neonatal medical histories. At the time of admission 4 children appeared well with normal vital signs, although 1 child was hypoxic with physical findings suggestive of bronchiolitis. In all patients, we ruled out other common infectious causes of apnea (normal blood tests, excluded other respiratory viruses and pertussis) and several different diagnoses (cardiac and neurological abnormalities). The association between apnea and COVID-19 was further confirmed by documentation of SARS-CoV-2 infection among

The authors have no funding and conflicts of interest to disclose.

N.K. and G.T. conceived the original idea. N.K. took the lead in writing the article. All other authors (L.S.M., S.R., and G.T.) provided critical feedback and helped in writing the article.

The study was approved by the Ethics Committee of University Hospital for Infectious Diseases Zagreb. All relevant data are within the paper and its Supporting Information files.

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ISSN: 0891-3668/22/4107-e301

DOI: 10.1097/INF.0000000000003536

The authors have no funding and conflicts of interest to disclose.

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ISSN: 0891-3668/22/4107-e301

DOI: 10.1097/INF.0000000000003535

**TABLE 1.** Demographic, Clinical, Diagnostic and Treatment Data of Patients

Case 1	Case 2	Case 3	Case 4	Case 5	
General data					
Gender	Male	Female	Male	Female	
Birth age (wks)	38	39	38	34	
Comorbidities	None	None	None	None	
Age (d)	13	91	23	36	
Date	November 15, 2021	November 18, 2021	November 19, 2021	January 28, 2022	February 2, 2022
Apnea (duration)	November 15–17, 2021	November 18, 2021	November 20–22, 2021	January 28–29, 2022	February 2–March 2, 2022
Fever/cough	+/+	+/+	+/+	+/+	–/–
Diagnostic procedures					
SARS-CoV-2*	+	+	+	+	+
Respiratory viruses†	–	–	–	–	–
BP/BPP‡	–	–	–	–	–
Chest radiograph	Normal	Normal	Normal	Normal	Normal
Cranial ultrasonography	Normal	Not done	Normal	IVH§	Normal
Transthoracic echocardiography	PFO¶	Not done	Normal	Normal	Normal
Treatment (d)					
Oxygen	6	1	1	–	–
Aminophylline	6	–	4	–	–

\*PCR from NP swab.

†Multiplex PCR from NP aspirate for influenza A/B, human metapneumovirus, respiratory syncytial virus, bocavirus, adenovirus, enterovirus, coronaviruses, parainfluenza virus types 1, 2, 3, and 4, parechoviruses and rhinoviruses.

‡PCR from NP aspirate for BP/BPP.

§IVH (grade 2).

¶PFO (3–4mm).

BP/BPP indicates *Bordetella pertussis/parapertussis*; IVH, intraventricular hemorrhage; NP, nasopharyngeal; PCR, polymerase chain reaction; PFO, patent foramen ovale.

patient's family members and rapid clinical improvement with complete recovery with or without methylxanthine treatment.

Apnea in infants can result from prematurity or other underlying conditions. Infants presenting with apnea were previously categorized as “apparent life-threatening events” but in 2016 American Academy of Pediatrics replaced this term to “brief resolved unexplained events” (BRUE) to distinguish benign events from life-threatening and to improve clinical management. However, based on many clinical guidelines and reports, infants with evidence of apnea are excluded from BRUE and should undergo further cardiac, neurologic, gastroenterologic, and hematologic evaluations to establish the underlying disorder.<sup>3,4</sup> Infectious diseases are common causes of apnea in young infants, especially in preterm neonates and infants <2 months of age. Sepsis, central nervous system, or respiratory infections are those which need to be excluded, especially when accompanied by fever or respiratory symptoms. The 2 principal infectious causes of apnea are respiratory syncytial virus and *Bordetella pertussis*; however, other respiratory viruses have also been reported in a small percentage of cases.<sup>3–5</sup> We observed that SARS-CoV-2 can cause apnea in young infants with otherwise asymptomatic or benign COVID-19. We also noticed a cluster of described clinical manifestation during predominant circulation of the delta (until late December 2021) and omicron (from January 2022) variants in the Croatian population. Based on our report, we suggest that testing

for SARS-CoV-2 should be part of the initial evaluation of apnea in infants who were <3 months of age presenting to emergency pediatric departments. Additionally, although the majority of neonatal SARS-CoV-2 infections are mild, caregivers should be aware of this potentially life-threatening complication, especially in very young patients who are discharged or treated in outpatient settings.

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## Kingella kingae Tenosynovitis: No Need for Surgical Management?

### To the Editors:

Infectious tenosynovitis (ITS) caused by *Kingella kingae* have recently been described in young children, commonly

The authors have no funding or conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website ([www.pidj.com](http://www.pidj.com)).

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ISSN: 0891-3668/22/4107-e302

DOI: 10.1097/INF.0000000000003547

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