

# Delayed acute bronchiolitis in infants hospitalized for COVID-19

To the Editor,

Following the online podcast recorded the 31 March 2020 by the International Committee of the American Thoracic Society Pediatrics Assembly that was recently published in *Pediatric Pulmonology*,<sup>1</sup> we had an interesting discussion with our international colleagues about the likelihood of acute bronchiolitis caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the absence of respiratory syncytial virus (RSV) coinfection. Here we report two cases of coronavirus disease 2019 (COVID-19) in infants less than 3 months old admitted to our paediatric unit. The infants presented with fever and neurological symptoms and after a short period, acute bronchiolitis.

## 2 | CASE 1

A term-born boy with an unremarkable history was admitted to the emergency department with poorly tolerated high fever (38.8°C) and rhinitis. The parents showed clinical signs suggesting SARS-CoV-2 infection. Reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 performed on a nasopharyngeal swab was positive for the father and the grandfather, who was hospitalized in the intensive care unit. Neurologic examination of the infant revealed lethargy and hypotonia with a bulging anterior fontanelle. The respiratory condition and clinical examination findings including hemodynamics were normal. The first blood test showed isolated lymphopenia (lymphocyte count:  $1.56 \times 10^9/L$ ; normally:  $4-6 \times 10^9/L$ ) without modification of biological inflammatory parameters, as assessed by normal levels of C-reactive protein and procalcitonin. Spinal fluid analysis, cytobacteriological urine analysis, and blood culture were negative. RT-PCR of a nasopharyngeal swab was positive for SARS-CoV-2 but negative for RSV and influenza virus (it was not performed in the cerebrospinal fluid). The patient received fluid volume expansion (20 mL/Kg of 0.9% sodium chloride solution) together with antibiotic treatment (cefotaxime, amoxicillin, and gentamicin at meningeal doses) for 24 hours that was stopped following a positive RT-PCR test for SARS-CoV-2 and a negative blood culture. A favorable clinical outcome was obtained shortly thereafter, allowing the infant to return home 2 days later.

Ten days later, the child returned with acute bronchiolitis. Respiratory symptoms included tachypnea, shortness of breath, wheezing, and hypoxia ( $SpO_2 < 92\%$ ). Lung ultrasonography revealed signs of an interstitial process with a thickened and irregular pleural

line associated with confluent B lines and small multifocal subpleural consolidations. RT-PCR for RSV and influenza virus remained negative. Treatment included supplemental oxygen and nasogastric tube feeding for 6 days. A second episode of acute bronchiolitis occurred 1 month later, but an RT-PCR test for SARS-CoV-2 was negative. Because of the infant's history, a chest X-ray was performed and returned normal. The child remained hospitalized for 5 days with nasogastric tube feeding but did not require oxygen supplementation. Long-term treatment with inhaled daily corticosteroids (fluticasone) was introduced.

## 3 | CASE 2

A term eutrophic male with otherwise unremarkable neonatal history was referred for poorly tolerated high fever at age 2 months. He received first hexavalent vaccination 48 hours before. Both parents had clinical signs of COVID-19 but were not tested. The neurologic examination was normal but mild hypotonia was noted. The respiratory and clinical examination findings including hemodynamics were normal. The first blood test showed lymphopenia (lymphocyte count:  $1.86 \times 10^9/L$ ; normally:  $4-6 \times 10^9/L$ ) without modification of biological inflammatory parameters. Cytobacteriological examination of urine and blood culture was negative and spinal fluid analysis was not performed. RT-PCR testing of a nasopharyngeal swab was positive for SARS-CoV-2 but negative for RSV and IV. The patient did not receive antibiotics. On day 3 after admission, the respiratory condition progressively worsened, with retractions, wheezing, increased respiratory rate at 80/minute, and hypoxia ( $SpO_2 < 92\%$ ) requiring supplemental oxygen together with enteral nutrition for 3 days. The chest X-ray was normal, and no lung ultrasonography was performed. The infant returned to the emergency department 2 weeks later with a nonsevere wheezing episode and was discharged at home.

These two cases of COVID-19 in infants hospitalized for poorly tolerated high fever and neurological symptoms in whom acute bronchiolitis developed following a delay of 2 to 8 days suggest that SARS-CoV-2 infection may cause acute bronchiolitis in the absence of a viral coinfection such as RSV. Pneumonia is the most common respiratory illness among symptomatic children with COVID-19.<sup>1</sup> High-resolution computed tomography scan usually shows ground-glass opacities or bilateral lung consolidations, especially in the periphery, and lung ultrasonography, as in our case 1, reveals signs of lung involvement. In contrast, to the best of our knowledge, acute

bronchiolitis due to SARS-CoV-2 infection has never been reported. The wheezing episodes described in our patients were likely due to SARS-CoV-2 infection for the following reasons: first, RT-PCR tests for RSV and influenza virus were always negative in both children, and second, the epidemic season for both viruses was over and the lockdown in France was still active at the time of the cases. Finally, a previous study of virus speciation in positive respiratory samples from infants with acute bronchiolitis detected close to a 5% frequency of coronaviruses OC43 and 229E.<sup>2</sup> Moreover, a recent experimental model of COVID-19 in ferrets showed lung lesions compatible with bronchiolitis.<sup>3</sup> Our patients showed bronchiolitis symptoms several days after those of COVID-19, which may explain the lack of wheezing episodes reported in the literature. Case 2 was diagnosed with recurrent wheezing possibly due to SARS-CoV-2 infection. RSV as well as rhinovirus bronchiolitis is a risk factor for recurrent wheezing and asthma,<sup>4,5</sup> but little is known about the long-term impact of SARS-CoV-2 infection in lung function trajectory, which emphasizes the need to follow these children. Whether the infection in symptomatic or asymptomatic infants may predispose to recurrent wheezing or asthma remains to be determined.

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#### REFERENCES

1. Yilmaz O, Gochicoa-Rangel L, Blau H, et al. Brief report: international perspectives on the pediatric COVID-19 experience. *Pediatr Pulmonol*. 2020;55(7):1598-1600.
2. Legrand L, Vabret A, Dina J, et al. Epidemiological and phylogenetic study of human metapneumovirus infections during three consecutive outbreaks in Normandy, France. *J Med Virol*. 2011;83(3): 517-524.
3. Kim YI, Kim SG, Kim SM, et al. Infection and rapid transmission of SARS-CoV-2 in Ferrets. *Cell Host Microbe*. 2020;27(5): 704-709.e2.
4. Jackson DJ, Gangnon RE, Evans MD, et al. Wheezing rhinovirus illnesses in early life predict asthma development in high-risk children. *Am J Respir Crit Care Med*. 2008;178(7):667-672.
5. Sigurs N, Bjarnason R, Sigurbergsson F, Kjellman B. Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7. *Am J Respir Crit Care Med*. 2000;161(5): 1501-1507.