Delayed acute bronchiolitis in infants hospitalized for COVID-19

Emilie Grimaud[1], Marie Challiol[1], amille Guilbauld[1], Céline Delestrain[2], Fouad Madhi[3], Julien Ngo[1], Ralph Epaud[1], and Elodie Nattes[1]

[1]Centre Intercommunal de Créteil
[2]Centre Intercommunal de Créteil, Service de Pédiatrie 40 av de Verdun Créteil, FR 94000
[3]Centre intercommunal de Créteil

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To the editor,

Following the online podcast recorded the 31 March 2020 by the International Committee of the American Thoracic Society Pediatrics Assembly and recently published in Pediatric Pulmonology[1], we have interesting discussion with my international colleagues about the likelihood of acute bronchiolitis caused by SARS-CoV-2 infection in absence of RSV co-infection. Here, we report 2 cases of COVID-19 in infants < 3 months old admitted to our paediatric unit. The infants presented fever and neurological symptoms and after a short period, acute bronchiolitis.

Case 1 : A term-born boy with unremarkable history was admitted to the emergency department with poorly tolerated high fever (38.8°C) and rhinitis. The parents, who had no history of asthma or allergy, showed clinical signs suggesting SARS-CoV-2 infection. RT-PCR for SARS-CoV-2 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 x10^9/L; normally 4-6x10^9/L) without modification of biological inflammatory parameters, as assessed by normal levels of C-reactive protein (CRP) and procalcitonin (PCT). 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 respiratory syncytial virus (RSV) and influenza virus (IV). 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 hr, that was stopped with a positive RT-PCR test for SARS-CoV-2 and negative blood culture. Favourable 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 polypnea, shortness of breath, wheezing and hypoxia (SpO2$<$ 92 %). Lung ultrasonography revealed signs of interstitial syndrome with thickened and irregular pleural line associated with confluent B lines and small multifocal subpleural consolidations. RT-PCR for RSV and IV remained negative. Treatment associated supplemental oxygen and enteral nutrition for 6 days. A second episode of acute bronchiolitis occurred 1 month later, but a RT-PCR test for SARS-CoV-2 was negative. The chest X-ray was normal. The child remained hospitalized for 5 days with enteral nutrition support but did not require oxygen supplementation. Long-term treatment with inhaled daily corticosteroids (fluticasone) was introduced.

Case 2 : A term-born eutrophic male with otherwise unremarkable neonatal history was referred for poorly tolerated high fever at age 2 months. Both parents had clinical signs of COVID-19 but were not tested (a member of the family had a positive test). The neurologic examination revealed lethargia and hypotonia in

the child; the respiratory condition and clinical examination findings including hemodynamics were normal. The first blood test showed lymphopenia (lymphocyte count: 1.86 x10^9/L; normally 4-6x10^9/L)without modification of biological inflammatory parameters. Cytobacteriological examination of urine and blood culture were 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 any antibiotics. On day 3 after admission, the respiratory condition progressively worsened, with retraction, wheezing, increased respiratory rate at 80/min and hypoxia (SpO2 $<$ 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 was returned to the emergency department 2 weeks later with a non-severe wheezing episode and was discharged at home.

These 2 cases of COVID-19 in infants hospitalized for poorly tolerated high fever and neurological symptoms in whom acute bronchiolitis developed at a delay of 2 to 8 days suggest that SARS-CoV-2 infection may cause acute bronchiolitis in absence of viral co-infection such as RSV. Pneumonia is the most common diagnosis among symptomatic children with COVID-19[1]. High-resolution CT 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 IV 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, previous study of virus repartition in positive respiratory samples from infants with acute bronchiolitis detected close to a 5% frequency of coronaviruses OC43 and 229E[2]. Moreover, a recent experimental model of COVID-19 in ferrets showed lung lesions compatible with bronchiolitis[3]. 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 presumably due to SARS-CoV-2 infection. RSV as well as rhinovirus bronchiolitis is a risk factor for recurrent wheezing and asthma[4,5],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.

References

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