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## COVID-19: Fever syndrome and neurological symptoms in a neonate<sup>☆</sup>



## COVID-19: Síndrome febril y clínica neurológica en neonato

Dear Editor:

Coronavirus disease 2019 (COVID 19), caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in Wuhan, China, in late 2019. Since then, it has spread and caused a global pandemic. From the time of its detection to early April 2020, one million cases have been reported worldwide, including 100 000 in Spain.<sup>1</sup>

The first published paediatric studies with data of case series in China described an incidence in children ranging from 0.8% to 2% of the total reported cases, with a milder disease course compared to adults and a predominance of respiratory symptoms.<sup>1</sup>

We present one case of infection by coronavirus with an atypical course.

The patient was a male infant aged 26 days with an unremarkable history who was brought to the emergency department after experiencing 2 paroxysmal episodes, the first one with upward rolling of the eyes and generalised hypertonia lasting several minutes and associated with feeding, with the newborn requiring stimulation to end the episode. The second episode manifested with generalised hypertonia and facial cyanosis of several minutes' duration during sleep. There were no abnormal movements. On arrival to the emergency department, the infant was free of paroxysm, and presented with a fever of 12 hours' duration with nasal discharge and vomiting. The infant was exclusively breastfed, had adequate weight, had no history of gastro-oesophageal reflux and had normal bowel activity.

There was a relevant family history (living in close quarters with multiple symptomatic household members).

The findings of the physical examination were normal save for a mild hypertonia of the limbs and irritability, with no clonus, and mildly increased deep tendon reflexes with normal tone and normal alertness. Energetic crying.

Blood tests, blood, urine and stool cultures, a nasal wash respiratory virus panel and cerebrospinal fluid analysis were performed at admission. Due to the epidemiological

circumstances, a nasopharyngeal swab sample was tested for SARS-CoV-2. The complete blood count revealed a normal white blood cell count with lymphocytes on the lower range of normal (lymphocytes, 2100/ $\mu$ L). The platelet and red blood cell counts were normal. The results of the comprehensive metabolic panel were normal (liver and kidney function and electrolyte levels). We found elevated serum levels of creatine kinase (CPK, 380 U/L) and lactate dehydrogenase (LDH, 390 U/L). There were no coagulation abnormalities except for a mildly elevated level of fibrinogen (418 mg/dL). The C-reactive protein test was negative, as was the urine toxicology test.

During his hospital stay, the patient had fever the first 24 h (peak, 38.8 °C) associated with irritability and watery stools. Given this picture, viral antigen tests were ordered, the results of which were negative. The workup was completed with a cranial ultrasound examination that revealed no abnormalities. The patient was placed under continuous monitoring with amplitude-integrated electroencephalography (EEG) for 36 h, which revealed a continuous background patters with sleep-wake cycles in the absence of electrical and clinical seizures.

Given the presence of fever associated with neurologic manifestations, empirical antibiotic therapy was initiated until the cultures yielded negative results. The blood, urine, CSF and stool cultures were negative and the stool was negative for respiratory syncytial virus and influenza A and B virus. The polymerase chain reaction (PCR) test for detection of SARS-CoV-2 was positive.

The patient remained hospitalised for 6 days. He was isolated with implementation of droplet and contact precautions in a negative pressure room, and visits were restricted per the current protocol. The outcome was favourable, and the patient was afebrile since day 2. There was no evidence of convulsive seizures. The findings of the neurologic examination were age appropriate. The infant was discharged with recommendations of maintaining isolation at home, with a plan that included follow-up by telephone and an appointment for a clinical evaluation and an electroencephalogram in the paediatric neurology department.

We have described the case of a patient presenting with fever and neurologic manifestations. In the current epidemiological context, infants aged less than 3 months presenting with fever of unknown origin should be screened for coronavirus. As for the neurologic manifestations, we did not find references in the literature associating these symptoms with SARS-CoV-2. However, studies on other coronavirus types demonstrate that these respiratory viruses have neurotropic properties. There have been descriptions of patients with convulsions, febrile seizures, decreased level of consciousness, encephalomyelitis and encephalitis.<sup>2</sup>

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A prospective study in children aged less than 6 years that assessed the association between human coronaviruses (HCoVs) with febrile seizures, bronchiolitis and gastroenteritis concluded that there was a higher proportion of patients with febrile seizures that tested positive for HCoVs compared to patients with other presentations. However, the pathogenesis of febrile seizures is not directly related to the neuroinvasiveness of these viruses,<sup>3</sup> so further research is required to elucidate their role in the aetiology of seizures.

We ought to highlight that in most cases published in the literature the child had close contact with a symptomatic individual, mainly in the family home,<sup>4</sup> as was the case of our patient.<sup>5</sup>

As recommended by paediatrics scientific societies,<sup>5</sup> it is essential to include the SARS-CoV-2 PCR test in the workup of infants aged less than 3 months.

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## Cutaneous manifestations in the current pandemic of coronavirus infection disease (COVID 2019)<sup>☆</sup>

### Manifestaciones cutáneas en contexto del brote actual de enfermedad por coronavirus 2019

Dear Editor:

Infection by novel coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2), first identified in 2019 in Wuhan, China, is the aetiological agent of the coronavirus disease 2019 (COVID-19).<sup>1</sup> At present, it has spread to become a global pandemic that, according to the World Health Organization, affects more than one and a half million people throughout the world.<sup>2</sup> When the COVID-19 outbreak was first described, there were only exceptional cases in the paediatric population, but as the outbreak spread the number of reported cases in children has grown, with most affected patients having mild or no symptoms.<sup>3</sup>

The most frequent manifestations include fever, dry cough, sore throat, headache, asthenia, myalgia and respiratory distress. To date, cutaneous manifestations in association with COVID-19 have only been described in adults.<sup>3,4</sup> Given the scarce information on these symptoms in the paediatric population, we present the cases of



2 paediatric patients with infection by SARS-CoV-2 with cutaneous manifestations.

The first case corresponded to a boy aged 6 years admitted to hospital for evaluation of cholestatic liver disease of unknown aetiology. At 2 weeks, after the patient developed a low-grade fever and a worsening of the markers for cholestasis and cytolytic hepatitis, he was tested for SARS-CoV-2 and turned out positive. Forty-eight hours later, the patient developed an erythematous, confluent, nonpruritic maculopapular rash with onset in the trunk and neck that gradually spread to the cheeks and upper and lower extremities, reaching the palms of the hands (Fig. 1). The cutaneous manifestations lasted a total of 5 days and resolved with no complications and without specific treatment. Improvement in the rash was associated with improvement in laboratory markers (bilirubin, transaminases and coagulation parameters). In light of the worsening of liver disease associated with the positive PCR result for SARS-CoV-2 in a nasopharyngeal swab sample, we performed a PCR test on a liver biopsy sample obtained in the initial evaluation of the patient, which was negative. During hospitalization, the patient did not exhibit any other manifestations related to infection by coronavirus.

The second case corresponded to a girl aged 2 months brought to the emergency department due to a low-grade fever and acute urticaria, apparently pruritic, of 4 days' duration. The rash was initially located in the face and upper extremities and spread in a few hours to the trunk and lower extremities (Fig. 2). The palms and soles were not affected. The patient had no angioedema in the fingers, toes, lips or tongue.

The most relevant epidemiological feature of the history was cohabitation with 2 individuals with confirmed COVID-19, which prompted performance of a SARS-CoV-2 PCR test

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