Neurologic manifestations in an infant with COVID-19

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The authors report no relevant disclosures.
Introduction:
Currently, there are over 1.9 million confirmed cases of Coronavirus disease 2019 (COVID-19) globally with over 590,000 cases in the United States\(^1\). The number of COVID-19 positive children in the United States is unknown. A report summarizing 72,314 COVID-19 cases from the Chinese Center for Disease Control and Prevention noted 416 COVID-19 positive children under 10 \(^2\). An observational study at Wuhan Children’s Hospital noted 31 COVID-19 positive children under 1 year with the youngest confirmed case in a 1 day old \(^3\). Cases were largely characterized by upper respiratory tract infection or pneumonia, fever, cough and pharyngeal erythema\(^3\). Concomitant neurological problems have been reported amongst COVID-19 positive adult patients\(^4\).

We report the case of a COVID-19 positive 6-week-old who presented with fever, cough, and two brief 10-15 second episodes of upward gaze and bilateral leg stiffening.

Case:
A 6-week-old term male infant presented for evaluation after one day of cough, fever, and brief episodes of sustained upward gaze associated with bilateral leg stiffening. The initial episode occurred following a diaper change. There was no shaking, breathing change or pallor during this episode. There was no association with feeding. The infant had two siblings with cough and fever at the time of presentation, both diagnosed with streptococcal pharyngitis. On arrival to the emergency room, vital signs were notable for fever of 38.4° C and mild hypertension (114/57). Exam was notable for a mottled appearance and bilateral overlapping fourth and fifth toes. The anterior fontanel was soft and non-bulging and neurologic exam was unremarkable. However, the patient had a witnessed episode of sustained upward gaze associated with bilateral leg stiffening and decreased responsiveness lasting ten seconds with subsequent return to baseline and no hypoxia or vital signs change.
The patient was born at 39 weeks via uncomplicated normal spontaneous vaginal delivery, weighing 3.91kg. Family history was notable for simple febrile seizures in a developmentally normal sibling. There was no family history of epilepsy.

Laboratory data were notable for leukopenia of 5.07 x10^3 white blood cells (wbcs)/µL (normal 8.14-14.99 x 10^3) with a normal differential and elevated procalcitonin of 0.21 ng/mL. (normal <0.08ng/mL). Electrolytes were normal. Respiratory pathogen polymerase chain reaction panel (PCR) was positive for rhinovirus/enterovirus. SARS-CoV-2 Real-Time Reverse Transcriptase (rRT)-PCR was positive. A chest radiograph was not performed. A lumbar puncture had an unremarkable cerebrospinal fluid (CSF) profile with one red blood cell and two wbcs/µL, glucose of 50 mg/dL, serum glucose of 84 mg/dL, and protein of 40mg/dL. Meningitis/Encephalitis PCR panel was negative. CSF culture showed no cells nor organisms. Standard CSF testing does not detect COVID-19.

The patient was connected to long-term electroencephalogram (EEG) monitoring which showed an excess of temporal sharp transients for age and intermittent vertex delta slowing with normal sleep-wake cycling. Magnetic resonance imaging (MRI) of the brain with and without contrast to rule out a corresponding structural lesion was normal. Given the abnormal EEG findings and unexplained clinical events, further CSF, nasopharyngeal swab, serum, plasma, and anal swab testing was performed using high throughput sequencing and quantitative rRT-PCR, after obtaining parental consent (see supplementary e-Methods; https://doi.org/10.5061/dryad.v41ns1rsc)

rRT-PCR nasopharyngeal swab testing was positive for SARS-CoV-2 RNA (~2X10^6 copies/ml). Anal
swab testing showed low levels of viral RNA (~200 copies/ml). SARS-CoV-2 RNA was not detected in CSF, serum, nor plasma. High throughput sequencing showed SARS-CoV-2 RNA and rhinovirus-C sequences in nasopharyngeal and anal swab samples. *Moraxella* and *Corynebacterium*, common nasal flora, were detected in the nasopharyngeal swab (see supplementary e-Results; https://doi.org/10.5061/dryad.v41ns1rsc).

The patient was discharged home one day after admission without further fevers or events on follow-up one week later.

**Discussion:**

The acute events reported in this case were characterized by sustained upward gaze, dystonic bilateral leg extension and altered responsiveness in the setting of COVID-19 and Rhinovirus. While there was a strong initial suspicion for seizures, no events were captured on subsequent EEG to confirm this.

Infections, specifically pertussis and respiratory syncytial virus (RSV), have been diagnosed in up to 18% of infants with acute events, previously termed apparent life-threatening events. Most febrile seizures occur in the setting of viral infections; most commonly adenovirus, followed by influenza, rhinovirus and RSV with coronavirus OC43 commonly detected in children under 12 months old.

Our patient had COVID-19 in addition to rhinovirus confirmed on high throughput sequencing. Interestingly, a study of coronavirus positive infants in the first 6 months of life noted a 27% coinfection rate with rhinovirus. There are reports of other pediatric co-infections with COVID-19.
Despite the reports that children generally seem to have mild infection, this case report highlights the possibility of rare but important neurologic manifestations of COVID-19 in children. Additionally, recognition of common co-infections will be important in guiding ongoing clinical evaluation and management of COVID-19 positive children.

Appendix 1. Authors

<table>
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References:

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