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COVID-19 croup: solitary infections and a coinfection case – Author Reply to a Letter

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Thank you for sharing your institution’s recent data and experience with a case of croup who was seen in your emergency department (ED), admitted on oxygen after dexamethasone treatment, and was found to be co-infected with both SARS-CoV-2 and enterovirus. I am glad your patient had a swift recovery. In our three reported cases of croup associated with SARS-CoV-2 infection over a two-month period, all three patients were positive for a single virus and had a negative viral panel (Biofire® FilmArray Respiratory Panel) (CR) for nineteen other viruses, including the ones most commonly associated with croup.[1] Two other case reports have also described solitary infection of SARS-CoV-2 associated with presentations of croup;[2] your description is the first case of croup that we are aware of that had a SARS-CoV-2 infection with a second virus. Other solitary and co-infection cases of croup will likely be reported in the literature as the pandemic progresses.

From your description, sixteen patients presented to your ED in 2020 with croup and only the aforementioned patient tested positive for SARS-CoV-2. To help understand this data more fully, it would be helpful to know when you had SARS-CoV-2 added to your multiplex RT-PCR viral testing platform and exclude any of the 16 cases that were done before that time. Our hospital’s multiplex RT-PCR panel added the SARS-CoV-2 to their panel in April 2020. It would also be helpful to know how many of the remaining cases were tested at all with your multiplex viral panel, as most of the cases were probably discharged and might not have been tested. Prior studies on patients with croup suggest approximately 80% of cases are positive for a virus.[4, 5] If your positivity rates for these cases that you did perform viral testing on were significantly lower, this potentially could be an issue with inadequate sampling collection.

Given the novelty of the SARS-CoV-2 virus, multi-center studies will need to be performed to determine the true rate of co-infection with other viruses. Regarding the three studies you cited, you mentioned that “most often, co-infections were found” and that “single infections [with coronaviruses] are rare.”[4-6] In three those studies, co-infections were relatively infrequent, found in 19% (6 of 31 coronavirus infections in Sung JY, et al.), 100% (1 of 1 cases in Miller EK, et al.), and 0 to 100% (unknown number of 3

coronavirus infections in Rihkanen, et al.; Personal Communication) of cases; in aggregate, these studies showed co-infection in only 7 to 10 (20 to 29%) of the 35 cases.[4-6]

After excluding any of the 16 cases that were diagnosed during a time without SARS-CoV-2 PCR testing capacity or not tested for SARS-CoV-2 infection, how many of the remaining patients were admitted to the hospital? Admissions for croup are a relatively infrequent event in our hospital and historically elsewhere as well.[7]. In a recent large database study, reviewing the NEDS and NHAMCS databases over an eight year period, there were 2.8 million ED visits for croup, of which only 3% were admitted to the hospital and their data showed a significant decreasing trend in admission rates over time over the study period ($p < 0.001$).[8]. How many of the remaining patients were admitted with an oxygen requirement? In two recent studies, with a total of 1096 admitted patients for croup, only 14 (1.3%) of the 1096 children had an oxygen requirement.[9, 10] While your patient thankfully had a brief (12 hour) inpatient admission, his need for both an admission and his oxygen requirement do place him at the higher severity end of the spectrum of croup disease when compared to these aforementioned studies. Our three cases were also atypical in their need for admission and other interventions. As mentioned in our paper, there might have been other cases of croup in our ED that were milder in severity and subsequently not tested for SARS-CoV-2 infection.

The absence of reported croup symptoms with SARS-CoV-2 infections in children in the three studies you cited is noteworthy.[11-13]. This could have been influenced by the retrospective nature of their study designs in that their symptom screening tools for recording data might not have included stridor or barking cough. Additionally, most patients with croup have mild symptoms and are discharged without being tested for any virus. Our three cases were tested primarily due to their need for admission, which prompted viral testing due to infectious control reasons for bed placement. It is also possible that SARS-CoV-2 infection associated with croup is a relatively rare presentation compared to the more common pediatric presentation of a flu-like illness. Multi-centered or database studies will likely be required to further characterize the nature of this association. Given the pandemic nature of this virus, we certainly hope that this emerging association of SARS-CoV-2 infection and severe cases of croup is a rare one.

Declarations of Interest: None

Contributor CRediT Author Statement: **April Venn:** Conceptualization, investigation, writing-review & editing. **James Schmidt:** Conceptualization, investigation, writing-review & editing. **Paul Mullan:** Conceptualization, investigation, writing-original draft, writing-review & editing, supervision. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Patient consent from parents was obtained from all three cases in this case series. In addition, parents have reviewed the reports for accuracy and have provided verbatim follow-up outcome quotes in descriptions of each case.

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