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LETTER TO THE EDITOR

PEDIATRIC PULMONOLOGY WILEY

Prolonged asymptomatic SARS-CoV-2 infection in a child receiving immunosuppressive therapy

To the Editor,

The current coronavirus disease 2019 (COVID-19) pandemic burden is the product of the high infectivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), variable clinical presentation, and high lethality of the disease. Children are relatively spared by the disease, but there is increasing concern regarding their role in the chain of contagion,[1] and little data is available concerning the course of COVID-19 in children receiving immunosuppressive agents. We report a case of familial transmission of SARS-CoV-2 whereby a girl became infected while receiving immunosuppressive therapy; while she did not display any symptom or sign of disease, more than 30 days passed before she eventually tested negative.

Her father, a 46-year-old hospital employee, not involved in patient care, developed fever, cough, and rhinitis on 22nd March. As illustrated in Figure 1, he tested positive for SARS-CoV-2 through polymerase chain reaction amplification on pharyngeal swab on 24th March (Day 1) and was isolated at home; he tested weakly positive 14 days later and negative after 3 weeks. On 24th March his wife began showing flu-like symptoms and tested positive on 28th March (Day 5). She eventually tested negative after 1 month.

The couple's 5-year-old girl was admitted along with her mother and her 38-day-old brother, as he had begun to show symptoms of COVID-19. The infant tested positive for SARS-CoV-2 on 28th March (Day 5) and negative on 16th and 17th April (Days 24-25) and has been previously described.[2]

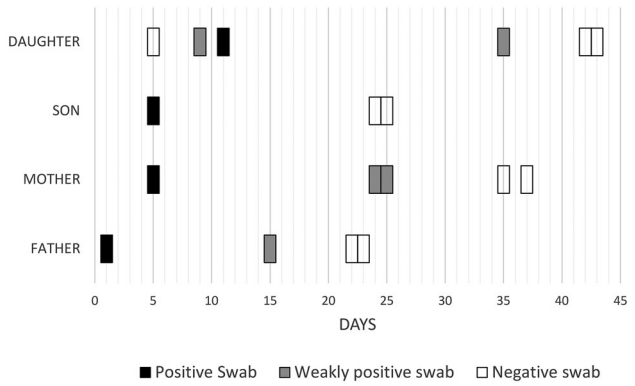

FIGURE 1 Timeline of virus transmission within the household, starting from the first positive swab. Disease resolution was confirmed by two negative swabs for SARS-CoV-2 taken at least 24 hours apart. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

The girl had been diagnosed at the beginning of March with dermatomyositis and placed on a course of high-dose methylprednisolone (25 mg/kg) followed by slow prednisone tapering and methotrexate on 10th March. As recommended by her rheumatologist, she had temporarily suspended her weekly 0.8 mg/kg methotrexate injections upon communication of the father's diagnosis while continuing prednisone at 1.5 mg/kg/d. Her history was otherwise unremarkable. She tested initially negative on 28th March (Day 5), weakly positive on 1st April (Day 9) and subsequently positive on 3rd April (Day 11) always in the absence of signs or symptoms of the disease. Complete blood count was normal, and serum biochemistry was unremarkable, apart from a mild transient increase in liver transaminases (AST 49 U/L, ALT 93 U/L). C-reactive protein was negative and procalcitonin was mildly increased (0.51 ng/mL, normal value <0.5 ng/mL). Urinalysis and pharyngeal swab for *Streptococcus pyogenes* were negative. Given the excellent clinical conditions, no additional investigation was performed. She was discharged home with her brother 14 days after admission to continue strict isolation.

On 27th April (Day 35) she still tested weakly positive; negativity was achieved on 4th May (Day 42) and confirmed on 5th May (Day 43). She has always remained in good clinical conditions without any symptom of COVID-19; serial measurements of body temperature never exceeded 37.2°C. As per rheumatological indication, methotrexate was introduced again (0.8 mg/kg/wk) 20 days after testing positive, while steroid therapy was gradually tapered, down to 1.2 mg/kg/d at the end of the infectious period.

In summary, SARS-CoV-2 infection resolved without symptoms in our 5-year-old patient receiving immunosuppressive therapy. It is possible that prednisone may have partially masked symptoms that would otherwise have been at least mild. Interestingly, the immune suppression did not worsen the disease in our patient, and might on the contrary have been beneficial, as all other members of the family eventually became symptomatic. Furthermore, reintroduction of methotrexate did not modify the clinical picture. Our case further compounds the evidence that COVID-19 may be completely asymptomatic in children, even if receiving immunosuppressive agents, and that SARS-CoV-2 infection in immunosuppressed patients may still have a favorable outcome.[3]

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Her first weakly positive test was confirmed positive after 48 hours, and 31 more days passed before she eventually tested negative. Considering the temporal window between the first weakly positive test and last weakly positive test, the girl may be presumed to have been shedding the virus for at least 26 days; while little evidence is available concerning the contagiousness of children, precaution dictates she may be considered potentially infectious until the first negative swab, that is, 33 days. As such, the potential window for stealthy virus transmission may have well exceeded the 14 days that are usually considered for quarantine and isolation purposes. Indeed, we agree that 14 days may not always be enough for suspected pediatric cases,[4] as asymptomatic children may potentially remain infectious for a long time.

Household members, and especially children with extensive care needs, are at very high risk of infection due to prolonged close contact. Propagation of SARS-CoV-2 among people living together, that may remain asymptomatic, is not entirely accounted for by current World Health Organization (WHO) guidelines,[5] as testing of asymptomatic household contacts at the end of the quarantine period is not mandatory. We could not determine whether our patient was infected by her brother or her parents, but we documented asynchronous household contagion, with a 43-day window between the symptom onset in the first member of the family and the clearance of the virus by the last, asymptomatic, member. Thus, we believe that isolation of the index case and quarantine of household contacts should be grouped, initiated, and terminated at the same time, only when all have been documented to be not infectious; furthermore, children should always be tested along with their caregivers. Without such measures, the combination of asynchronous and asymptomatic SARS-CoV-2 household contagion leading to unwitting or negligent transmission of the virus beyond the initial cluster is a matter of serious concern.

Children receiving immunosuppressive medications are frail; while there is potential concern for worse disease presentation in this population, systemic steroid administration did not worsen the clinical picture of our patient and may on the contrary have contributed to attenuate symptoms, while possibly prolonging virus shedding. Thus, corticosteroids may not necessarily be detrimental for pediatric COVID-19 patients, and could even be beneficial in selected cases. We warrant further investigations regarding the interplay between COVID-19 and immunosuppression in the pediatric population, with respect to both clinical presentation and persistence of virus shedding.

Daniele Canarutto MD[1,2,3]
Paolo Del Barba MD[1]
Marianna Di Frenna MD[1]
Federica Del Tedesco MD[1,2]
Roberta Pajno MD[1]
Maria Pia Guarneri MD[1]
Graziano Barera MD[1,2]

[1]*Pediatric Department, IRCCS Ospedale San Raffaele, Milano, Italy*
[2]*Faculty of Medicine and Surgery, Università Vita Salute San Raffaele, Milano, Italy*
[3]*Pediatric Immunohematology Unit and BMT Program, IRCCS Ospedale San Raffaele, Milano, Italy*

Correspondence
Daniele Canarutto, MD, Università Vita Salute San Raffaele, via Olgettina 58, 20132 Milano, Italy.
Email: canarutto.daniele@hsr.it

ORCID

Daniele Canarutto http://orcid.org/0000-0001-6999-8479

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