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Letter to the Editor

Challenging diagnostics in familial transmission from an asymptomatic COVID-19 carrier: Should we group SARS-CoV-2 samples from households?

Dear Editor in Chief,

By March 8, 2020, 85 cases of coronavirus disease 2019 (COVID-19) had been diagnosed in Denmark and by mid-March an estimated 50% of imported cases were derived from Austria ((SSI, 2020) https://files.ssi.dk/COVID19-overvaagningsrapport-12032020; Correa-Martínez et al., 2020). Between March 3 and March 8, a 49-year-old man went skiing in Ischgl, Austria accompanied by 11 male friends. A few days after returning to Denmark, six travel companions developed symptoms of COVID-19 and tested severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) PCR-positive. In accordance with the Danish guidelines at that time, none of the six asymptomatic individuals was tested. However, one of these, the 49-year-old man, arranged a self-imposed 2-week home quarantine along with his family of four on March 11. Approximately 1 week later, his wife and 18-year-old daughter developed influenza-like symptoms. The following week, the 15-year-old daughter developed ageusia, while the 8-year-old old daughter presented her usual recurrent cough.

The extension of national COVID-19 testing on April 1 led the family to the local test center, where the index person and the daughter presenting ageusia tested SARS-CoV-2 PCR-positive. The wife and two other daughters tested negative. The three negative specimens together with 197 SARS-CoV-2-negative samples from other patients were retested at an external laboratory. All samples remained negative; but the specimens from the wife and youngest daughter were found to be weakly positive. Their initial PCR curves were reassessed and found equally irregular with Ct values of 32 and 35.

Three weeks later, all five displayed a serological SARS-CoV-2 N/S IgG response. The asymptomatic index person and the youngest daughter presented the highest IgG titers (chemiluminescence immunoassay (CLIA), iFlash 1800 Shenzhen YHLO). Comparative testing with the SARS-CoV-2 S1/S2 IgG assay (CLIA, DiaSorin, Liaison) found the index person and three daughters to be positive and the wife just below the cut-off (Table 1).

This family cluster highlights several aspects of the challenges surrounding COVID-19 and SARS-CoV-2 diagnostics. The familial transmission from an asymptomatic carrier who displayed a positive SARS-CoV-2 PCR 4 weeks after becoming infected and a subsequent immunological response. The wife and three daughters, who had mild symptoms of COVID-19, presented diverse and divergent SARS-CoV-2 PCR results, yet displayed an immunological response.

This family case indicates the importance of the duration of infectiousness of an asymptomatic carrier (Chan et al., 2020; Huang et al., 2020). Furthermore, it shows that symptoms and the generation of specific antibodies vary even among closely related

Table 1
Summary of the clinical features and laboratory results of a family of five (father, mother, and three daughters) infected with SARS-CoV-2.

Age (years) and sex	Travel history	Symptoms	Onset of symptoms	Time of oropharyngeal swab (eSwab, Copan)	Altona SARS-CoV-2 PCR (Ct)	In-house SARS-CoV-2 PCR (Ct) (Novo Nordisk, Denmark)	Time of serological testing	iFlash SARS-CoV-2 N/S IgM/IgG (AU/ml)[a]	DiaSorin SARS-CoV-2 S1/S2 IgG (AU/ml)[b]
49 Male	Ischgl, Austria March 3–8	None		April 2	Positive (32)	NA	April 22	Non-reactive/ reactive (108)	Positive (114)
44 Female	None	2–3 days of myalgia, arthralgia, headache, and malaise	Between March 15 and 18	April 2	Negative	Weakly positive (39)	April 22	Non-reactive/ reactive (16)	Negative (9.3)
18 Female	None	2–3 days of myalgia, arthralgia, headache, and malaise	Between March 15 and 18	April 2	Negative	Negative	April 22	Non-reactive/ reactive (32)	Positive (24.1)
15 Female	None	Monosymptomatic ageusia	Between March 22 and 25	April 2	Positive (30)	NA	April 22	Non-reactive/ reactive (52)	Positive (24.6)
8 Female	None	Recurrent cough (known asthmatic bronchitis)		April 2	Negative	Weakly positive (38)	April 22	Non-reactive/ reactive (56)	Positive (55.5)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NA, not applicable; Ct, cycle threshold; N, nucleocapsid protein; S spike protein.
[a] iFlash SARS-CoV-2 N/S IgM/IgG cut-off: ≥12 AU/ml = positive.
[b] DiaSorin SARS-CoV-2 S1/S2 IgG cut-off: ≥15 AU/ml = positive, $12 < x < 15$ AU/ml = equivocal, and ≤12 AU/ml = negative.

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family members, supporting the potential benefit of SARS-CoV-2 detection from a combination of nucleic acid testing and time-related serology (Fafi-kremer et al., 2020; Flodgren, 2020; Okba et al., 2020). Finally, it suggests that COVID-19 diagnostics and containment measures might benefit from grouping samples from households in order to collectively assess results and the potential need for repeat sampling (Winichakoon et al., 2020).

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Informed consent

Oral and written informed consent to describe this family cluster was obtained from the father on behalf of the family.

Conflict of interest

The authors declare that there are no conflicts of interest.

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