Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

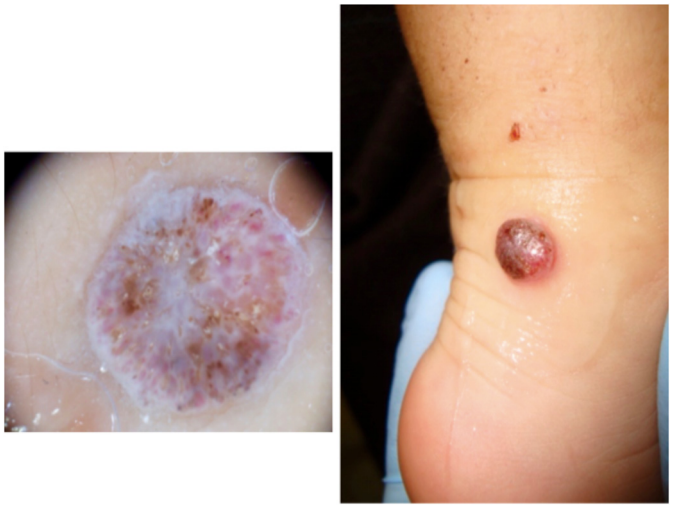

Figure 1 A) Dermoscopy image: pseudovascular lesion. B) Irregular dome-shaped lesion with bright erythematous coloration.

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SARS-CoV-2 PCR negativization in respiratory sample in patients with need for recurring assistance☆

Negativización de PCR a SARS-CoV-2 en muestra respiratoria en pacientes con necesidad de asistencia recurrente

To the editor:

In addition to its impact in terms of morbidity and mortality (especially in adult patients), the SARS-CoV-2/coronavirus disease 2019 (COVID-19) pandemic has threatened to collapse established ongoing care pathways. Thus, the detection of SARS-CoV-2 in patients that require regular contact with the health care system has compelled the development of safe strategies for clinical follow-up and assessment of negative conversion.

We analysed data from patients given a diagnosis of SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) testing of respiratory secretion specimens between March 11 and April 30, 2020 in a tertiary care children's referral hospital in Barcelona (Spain) that underwent repeated PCR tests in nasopharyngeal samples to verify negative conversion. We conducted the study in patients that received ongoing care in day hospitals, with scheduled hospitalizations, etc. To carry out clinical follow-up and monitoring for negative conversion, and after the re-entry of the patient in the usual care pathway, a safe care pathway was created to performed PCR tests at regular intervals, ide-

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Table 1 Data on the negative conversion of the SARS-CoV-2 PCR test based on different variables.

Total patients	Days between positive and negative PCR results (14 patients[a])			Days between onset of symptoms and negative PCR results (12 symptomatic patients[b], 11 included in analysis[a])		
Median	Range	IQR	Median	Range	IQR	
15	13	6-31	11,5-24	18	13-34	15-25

Patient groups	Number of patients	Days between positive and negative PCR results			Days between onset of symptoms and negative PCR results[b]		
Underlying disease		Median	Range	IQR	Median	Range	IQR
Congenital heart disease	6 (40%)	11	6-25	9-13	17 (5 patients)	13-29	13-19
Active blood/solid organ cancer	4 (27%)	21	16-31	17.5-26	21	17-34	18-26.5
Encephalopathy	2 (13%)	13	13-13	NA	13 (1 patient)	NA	NA
Kidney transplant	1 (7%)	56	NA	NA	60	NA	NA
Acute liver failure	1 (7%)	24	NA	NA	25	NA	NA
None (neonate born to mother with COVID-19)	1 (7%)	13	NA	NA	NA	NA	NA

Pharmacological immunosuppression		Median	Range	IQR	Median	Range	IQR
Yes	5 (33.3%)	21 (4 patients[a])	16-31	17.5-26	21 (4 patients)	18-34	18-26.5
No	10 (66.6%)	13	6-25	10.5-13	17 (7 patients)	13-29	13-22

Treatment		Median	Range	IQR	Median	Range	IQR
Patients treated with lopinavir-ritonavir[c]	3 (20%)	12	10-25	11-18.5	19	17-29	18-24
Patients treated with HCQ + azithromycin[d]	5 (33.3%)	13	9-25	10-16	17	13-29	13-17
No specific treatment	9 (60%)	15.5 (8 patients[a])	6-31	13-24	24 (5 patients[a])	13-34	18-25

Age range[e]		Median	Range	IQR	Median	Range	IQR
< 2 years	8 (53%)	13	9-25	12-14	17 (5 patients)	13-29	13-17
≥ 2 years	7 (47%)	21 (6 patients[a])	12-31	14-24	21.5 (6 patients[a])	13-34	18-25

Compatible symptoms		Median	Range	IQR	Median	Range	IQR
Symptomatic	12 (80%)	16 (11 patients[a])	9-31	12.5-24	18 (11 patients[a])	13-34	15-24.5
Asymptomatic	3 (20%)	13	6-13	9.5-13	NA		

HCQ, hydroxychloroquine; IQR, interquartile range; NA, not applicable.

[a] The patient that received the kidney transplant was excluded from these calculations since testing to check for negative conversion was delayed to make it coincide with a scheduled visit far ahead.

[b] Only applies to group of symptomatic patients (12 patients).

[c] Includes 1 patient that only received lopinavir-ritonavir (time to negative conversion, 12 days), 1 given lopinavir-ritonavir combined with HCQ and azithromycin (time to negative conversion, 25 days) and 1 patient given lopinavir-ritonavir, remdesivir, HCQ and azithromycin (time to negative conversion, 16 days).

[d] Includes 2 patients that did not receive any other specific treatment (time to negative conversion, 9 and 13 days), 1 patient that also received tocilizumab (time to negative conversion, 16 days) and the 2 patients included in the previous point.

[e] Four of the 5 patients with solid organ or blood tumours were aged 2 or more years, while the 3 symptomatic patients were aged less than 2 years.

ally weekly but with possible adaptations to current logistics (median days elapsed between tests, 8; interquartile range [IQR], 6-13 days).

Of the total of 25 patients with SARS-CoV-2 infections managed in our hospital during the study period, 15 met the inclusion criteria; the median age was 22 months (range, 1 day-15 years; IQR, 1-148 months), 60% were male. Twelve underwent evaluation due to a clinical presentation compatible with COVID-19 (5 with respiratory symptoms and fever; 4 with respiratory symptoms in absence of fever; 2 with fever without source; 1 with gastrointestinal manifestations and fever), 2 were identified through screening per protocol at admission, and 1 due to the mother having COVID-19. Seven patients (46%) required hospital admission due to COVID-19, of who 3 were admitted to the paediatric intensive care unit. All of them had favourable outcomes. Another 6 (40%) required admission for reasons unrelated to COVID-19, and the remaining 2 did not require hospitalization (13%). As for underlying disease, 6 patients (40%) had congenital heart disease; 4 (27%) active cancer (solid or blood tumours); 2 (13%) encephalopathy; 1 (7%) was a kidney transplant recipient and 1 (7%) had acute liver failure. The remaining patient was a neonate born to a mother with COVID-19 without underlying disease.

Overall, the median time elapsed to negative conversion of the PCR test was 13 days (IQR, 6-31). Eight patients (53%) underwent more than 1 follow-up PCR test until they reached negative conversion, with a maximum of 4 tests in one case. We found a significantly longer time to negative conversion from the initial PCR test to the first negative test in immunosuppressed patients compared to patients with normal immune function (21 vs 13 days; $P = .015$). In symptomatic cases, the median time elapsed from onset of symptoms to the negative test result was 18 days (range, 13-34; IQR, 15-25), which was consistent with the findings of studies in adults[1,2] and somewhat higher compared to recent studies in paediatric patients with non-severe COVID-19 that made no reference to underlying disease.[3] Table 1 presents the times elapsed to negative conversion based on the characteristics of the patients.

In several cases, PCR testing was postponed so it could be performed in visits already scheduled with the patient, which may have led to overestimation of the time to negative conversion. In this regard, the calculation excluded 1 female kidney transplant recipient whose follow-up PCR test was delayed 56 days due to the surgery. On the other hand, due to the reduced sample size, we were unable to analyse differences based on age, severity or treatment, although they may have been relevant.[2] We also did not analyse PCR cycle threshold (Ct) values, although high values could suggest the presence of residual virus, albeit not necessarily associated with infectivity.[4]

Since the actual contagiousness of patients seems to be shorter compared to the duration of viral shedding, follow-up PCR testing for verification of negative conversion could be replaced by quarantine periods in the general population, as recommended by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), although more evidence is required in the paediatric population.[5] However, in the case of immunosuppressed patients or those managed in units for complex or fragile patients, strategies to determine the discontinuation of isolation may still need to include negative conversion verification tests, the use of the Ct or serological testing. More evidence is required on the application of PCR Ct values in paediatric patients and patients with immunosuppression,[4] and we need to continue searching for the right balance between delaying necessary procedures or treatments in children with COVID-19 and maintaining the safety of care pathways.

Our findings may contribute valuable information to help health care institutions that manage similar patients in the adaptation to the current pandemic.

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