Ann Ig 2021; 33(3): 297-298. doi: 10.7416/ai.2021.2433

LETTERS

Two nasal swabs may not be enough to exclude SARS-CoV-2 infection in symptomatic patients

Due soli tamponi nasali potrebbero essere insufficienti per escludere un'infezione da SARS-CoV-2 in pazienti sintomatici

Dear Editor:

The spread of COVID-19 (COronaVIrus Disease 2019), due to SARS-CoV-2 (Severe Acute Respiratory Syndrome CoronaVirus 2) has taken on dramatic pandemic proportions, affecting over 100 countries in a matter of weeks. Italy has had 237,828 confirmed cases according to the Istituto Superiore di Sanità as of May 13, and 34,448 deaths (1).

Strategies to contain viral transmission include active tracing and isolation of confirmed/suspected cases, and their contacts. In the hospital setting, an early and correct diagnosis is crucial, since infected but undiagnosed individuals may spread the virus to both the patients and the Healthcare Workers (HCWs).

As of May 13 2020, 128 cases of COVID-19 were admitted to the Infectious Diseases Unit of the University Hospital (Ospedali Riuniti) of Foggia, Italy, with various degrees of disease severity. The mean time elapsed from symptoms onset to hospital admission was 6 days.

At admission, nasopharyngeal swabs were collected for RT PCR test for SARS-CoV-2. In patients tested negative, but with clinical conditions still highly suspected for COVID-19, a second specimen was collected 24/48 hours apart.

RT-PCR test for SARS-CoV-2 from nasopharyngeal swabs was performed according to the manufacturer's instructions. Viral RNA was extracted within 2 hours from each sample using the STARMag 96 X 4 Universal Cartridge kit with the Microlab NIMBUS IVD instrument (Seegene Inc. Seoul, Korea). Amplification and detection of target genes (N, E and RdRP) were carried out using the commercially available kit AllplexTM 2019-nCoV Assay (Seegene Inc. Seoul, Korea) with the CFX96TM instrument (Bio-Rad, Hercules, CA). Results interpretation was made with the Seegene Viewer software.

Table 1 - Clinical characteristics of the three patients at baseline.

		Patient A	Patient B	Patient C
Age yrs		75	85	93
Sex		Male	Male	Male
Fever		Yes	Yes	Yes
Dyspnea		No	Yes	Yes
Admission (n° days from onset)		6	1	1
Chest X-ray	Consolidation	Yes	Yes	Yes
	Interstitial disease	Yes	Yes	Yes
WBC (x10^9 cells per L, normal range 3.9-9.9)		3.7	12.8	14.8
Lymph (x10^9 cells per L, normal range 1,1-3.6)		0.5	2.0	1.9
CRP (mg/L, normal range 0.0-0.5)		45.4	147.4	108.9
D-dimers (ng/ml, normal range 0.00-0.5)		45.282	4.787	3.420
Po2 (mmhg)		57	66	69
P/f ratio		203	212	246

In 110/128 cases (85.9%), SARS-Cov-2 was detected in the first swab, while in 15 cases (11.7%) the virus was detected from the second swab, taken after 24/48 hours, for a total of virus recovery of 125/128, or 97.6%.

In the three remaining cases (2.4%), diagnosis of COVID-19 was more complicated, since more than two nasopharyngeal swabs were needed to obtain an etiological diagnosis. Table 1 shows the baseline clinical characteristics of the 3 patients.

All the three patients, although symptomatic, were tested negative for Sars-Cov2 in nasopharyngeal swabs at days 10th and 12th (patient A) and days 2nd and 5th (patients B and C) after the onset of symptoms. Only a third swab analysis performed later, showed a positive result in the three patients.

At the admission, all these patients, received a ventilatory support, none of them required ICU transfer. Blood and sputum cultures and nasopharyngeal swabs for common respiratory pathogens were negative.

Our observations support recently published data (2) indicating that only two nasal swabs may not be enough to exclude a SARS-CoV-2 infection in patients with clinical and radiological interstizial and/or ground glass lung involvement. To minimize the risk of transmission of SARS-CoV2 to other patients and to HCWs, the nasal swabs should be repeated several times. Alternatively, other clinical specimens (feces, sputum) (3, 4) or serology or high resolution CT scan could be useful, in order to early detect the virus before viral detection in the nasal swab.

The existence of patients with repeated SARS-CoV-2 negative nasopharyngeal swabs is of great interest because these misdiagnosed cases can contribute to the spread of the virus in the hospital setting.

Author's contribution

Jose Ramon Fiore planned and supervised the study and and the manuscript writing, Maria D'Errico, Irene Bottalico, Marianna Rizzo and Laura Montemurro did clinically care the patients and collected the clinical and laboratory data, Giuseppina Faleo and Mariantonietta Di Stefano renned the laboratory tests, Sergio Lo Caputo and Teresa Santantonio contributed to the analysis of the data and the manuscript writing.
All the authors read and approved the final version of the manuscript.

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References

1. Ministry of Health, Italy. COVID-19. La Situazione in Italia. 3 luglio 2020. Available on: http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioContenutiNuovoCoronavirus.jsp?area=nuovoCoronavirus&id=5351&lingua=italiano&menu=vuoto [Last accessed: 2020, July 21.
2. Lee TH, Lin RJ, Lin RTP, et al.; National Centre for Infectious Diseases COVID-19 Outbreak Research Team. Testing for SARS-CoV-2: Can We Stop at Two? Clin Infect Dis 2020; **71**(16): 2246-8. doi: 10.1093/cid/ciaa459.
3. Feng H, Liu Y, Lv M, Zhong J. A case report of COVID-19 with false negative RT-PCR test: necessity of chest CT. Jpn J Radiol 2020; **38**(5): 409-10. https://doi.org/10.1007/s11604-020-00967-9.
4. Chen D, Jiang X, Hong Y, et al. Can Chest CT Features Distinguish Patients With Negative From Those With Positive Initial RT-PCR Results for Coronavirus Disease (COVID-19)? AJR Am J Roentgenol 2020; ***5***: 1-5. doi:10.2214/AJR.20.23012.

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