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Research letter

Does bronchoscopy help the diagnosis in Covid-19 infection?

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Research letter

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To the editor:

Dear Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the agent responsible for the recent Coronavirus Disease 2019 (COVID-19) pandemic. This virus is predominantly spread through large droplets. The clinical features of COVID-19 are varied, ranging from asymptomatic to acute respiratory distress syndrome and multi-organ dysfunction. The diagnosis of COVID-19 is mainly based on typical symptoms, history of exposure to an infected person and bilateral involvement on chest radiographs, and it is confirmed by a positive nucleic acid test for SARS-CoV-2 from numerous types of specimens including oropharyngeal (OP) and nasopharyngeal (NP) swabs, anal swabs, stool, urine and broncho-alveolar lavage fluid (BALF). Reverse-transcriptase-polymerase-chain-reaction (RT-PCR) that targets the RdRP, N, or E genes is the most common method for SARS-CoV-2 detection. OP and NP swabs are the most frequently used samples, but it has been demonstrated that their sensitivity is limited, 32% and 63% respectively while BALF is reported to be positive in 93% of patients. However the role of bronchoscopy in ruling out suspected COVID-19 patients is under debate. According to several guidelines, bronchoscopy is relatively contraindicated mainly because of its high risk of spreading the infection to the staff involved in the procedure. It is primarily recommended in immunocompromised patients, if there is the strong suspicion of superinfection or mucus plugging, or in life saving conditions, and it is not strictly recommended in the COVID-19 diagnostic algorithm. Nevertheless, some cases of negative OP and NP swabs in which BALF tested positive for SARS-CoV-2 by RT-PCR were reported.

There are two main problems in negative swab patients with CT scans and clinical picture suggestive for COVID-19: firstly, according to the sensitivity of the swabs, misdiagnosing a SARS-CoV-2 positive patient may be a great risk for public health, secondly, an alternative diagnosis may be required for patients’ appropriate treatment.
Here we report our experience from a COVID-19 hospital in Rome, Italy, where patients with typical symptoms of the disease, suggestive CT scans and three NP/OP negative swabs performed on consecutive days and IgG and IgM serology negative for SARS-CoV-2 underwent bronchoscopy with BAL to define the diagnostic issue.

In the period between March 13th and April 30th 2020, 28 patients (age 65 ±16yrs, 16 male and 12 female) with the described characteristics, discussed by the multidisciplinary clinical-radiological team, underwent bronchoscopy with BAL. All the patients performed a non-enhanced chest CT scan in supine position, from the apexes to the bases of the lungs during inspiratory breath-hold, with a 128-slice scanner. Two Radiologists independently evaluated the axial images with a visual score. CT manifestations were characterized by a predominant ground glass pattern (68%) mixed with consolidations (32%), mainly peripheral (26%) or combined peripheral and central distributions (72%), bilateral (83%) and lower lung zones (93%) being mostly involved. Lymphadenopathy and pleural effusion were rarely founded (0% and 4%). According to several recent reports regarding CT findings in COVID-19 patients, these results were suggestive of COVID-19 in all considered cases.

BALF was analyzed for SARS-Cov2 by RT-PCR and for routinely microbiological examination. In the BALF, the RT-PCR for SARS-Cov2 was negative for all three detectable genes in all 28 patients. Microbiological examination was negative in 15 patients (53,6%). Of the other 13 patients, 6 had galactomannans greater than 0.8, 1 patient between 0.5 and 0.8, 4 patients were positive at microbiological culture for Candida Albicans, 2 patient for Pneumocystis jiroveci, 1 patient for Candida glabrata, 1 patient for Streptococcus pneumoniae, 2 patients for Staphylococcus epidermidis, 1 patient for Klebsiella pneumoniae, 1 patient for Enterococcus faecium. The final diagnosis was pneumonia in 22 patients (no specific agent in 11 patients, 5 of which were immunocompromised; specific agent in 11 patients, 4 of which were immunocompromised), heart failure in 3 patients, exacerbation of
interstitial lung disease in 2 patients and an acute respiratory distress syndrome in 1 patient. Antibiotic therapy was modified in 13 patients according to the microbiological findings.

In these pandemic times, the low sensitivity of RT-PCR can miss many diagnoses of COVID-19, representing a far too high risk for infection transmission. On the other hand, even if CT scan has a higher sensitivity (97%), its lower specificity (25%)\(^2\) makes alternative diagnosis more likely and bronchoscopy with BALF is the recommend procedure to rule out any doubts.

Our findings suggest that three negative swabs done in three different days and a negative serology are sufficient to rule out COVID-19, even in patients with highly suggestive CT scans and clinical features compatible with the disease. Differently than other reports\(^7,8\), we performed three OP/NP swabs and serology tests before performing the bronchoscopy, instead of just one or two OP/NP swabs. This conduct allowed to detect some patients who resulted positive at the third swab or at serology, avoiding unnecessary procedures, therefore reducing the risk of transmission to healthcare workers.

Bronchoscopies were performed with disposable devices and with the recommended personal protective equipment\(^6\). Even if our results are very reassuring about the safety of this procedure in patients with three negative swabs and negative serology, the risk for the staff still remains high and we strongly suggest to maintain all the recommended precaution to minimize the risk of possible disease transmission.

Interestingly, BALF was positive for other pathogens in 46% of patients, reinforcing its role in finding alternative diagnoses.

In conclusion, our findings demonstrate that three negative swabs along with negative antibodies, despite a suggestive CT scan, can safely rule out the SARS-CoV-2 infection in suspected patients, hence to proceed in alternative diagnosis process.
Bronchoscopy should not be used for the confirmation of SARS-CoV-2 infection alone, but it can be very useful in resolving diagnostic complexity.
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Authorship

1) Drafting the article or revising it critically for important intellectual content: JO, EP, FC, FMG, AG, MC, GLS, MF, PR.
2) Visual scoring was performed independently by two Radiologists: GS and MC.
3) Final approval of the version to be published: JO, EP, FC, FMG, AG, MC, GLS, MF, PR.
4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: JO, EP, FC, FMG, AG, MC, GLS, MF, PR.

Conflict of interests

JO, EP, FC, FMG, AG, MC, GLS, MF, PR, all authors declare that they do not have conflict of interest to this manuscript.
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