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.

Journal of Cystic Fibrosis 19 (2020) e16–e17

Contents lists available at ScienceDirect

Journal of Cystic Fibrosis

journal homepage: www.elsevier.com/locate/jcf

Letter to the Editor

COVID-19 in lung-transplanted and cystic fibrosis patients: Be careful

Dear Editors,

Elderly patients and those with comorbidities are at higher risk of presenting a severe SARS-CoV-2 infection [1]. Although the disease has yet to be well-described among cystic fibrosis and lung-transplanted patients, these patients are probably at major risk of presenting a severe disease. We report the case of a SARS-CoV-2 infection in a lung-transplanted patient for cystic fibrosis characterized by several singularities.

A 35 years-old man, lung-transplanted 8 years ago for cystic fibrosis, was admitted for fever and dyspnea. His wife had suffered from rhinopharyngitis for a few days when he began to complain of asthenia, myalgia, and headache. Two days later, he became feverish at 38.5 °C and dyspneic (FEV-1 decreased at 85% of his baseline value). On admission, the patient presented with dyspnea, fever, and diarrhea but without pharyngitis. The physical examination revealed fine crackles of the lung bases with no cardiac abnormality and oxygen saturation of 90% in ambient air. Biological tests were normal except a C-Reactive Protein level of 126 mg/L (N < 5 mg/L) and a natremia at 131 mmol/L (N: 135–145 mmol/L). A SARS-CoV-2 RT-PCR (Allplex nCov 2019 assay, Seegene, Seoul, South Korea) performed on a nasopharyngeal sample was negative. A chest computed tomography revealed ground-glass opacities of both basal pulmonary parenchyma. He was hospitalized, piperacillin-tazobactam combination and oxygen therapy (5l/min) started. As the presentation was evocative of SARS-CoV-2 infection a second nasopharyngeal swab was sampled on day 2. A multiplex RT-PCR for respiratory pathogens (FilmArray RP, BioMérieux, Marcy-l'Etoile, France) was positive for a rhinovirus while the SARS-CoV-2 RT-PCR (Seegene) remained negative. On day 3, the patient respiratory function worsened and he was transferred to an intensive care unit and placed on mechanical ventilation. A broncho-alveolar liquid was immediately sampled. The SARS-CoV-2 RT-PCR was strongly positive, with cycle thresholds (CT) less than 25 for all viral targets: *N* gene (CT = 20.91), *E* gene (CT = 17.14) and *RdRP* gene (CT = 19.32). Bacterial culture identified 10^3 CFU/mL of oropharyngeal flora.

SARS-CoV-2 infection has been so far poorly reported from lung-transplanted and cystic fibrosis patients. The present case highlights at least 3 findings: (i) a non-specific presentation of the disease at its early stage; (ii) a possibly lower sensitivity of the RT-PCR performed on nasopharyngeal swabs in patients who present with primarily pulmonary symptoms; (iii) the identification of another respiratory pathogen should not exclude a SARS-CoV-2 infection, at least in patients presenting severe pathology.

Clinical presentation of SARS-CoV-2 might be variable with a wide range of clinical symptoms and complaints [1]. Therefore, particular attention is required for lung-transplanted and cystic fibrosis patients. A delayed diagnosis might increase the spread of the virus and induce a suboptimal medical management. In the present case, the SARS-CoV-2 RT-PCR were performed on 3 successive samples a day apart. Several factors associated with false-negative SARS-CoV-2 RT-PCR results were previously reported [2,3]. However, it is unlikely that nasopharyngeal swabs were not optimally performed as the 2 swabs were sampled by 2 different trained-operators. Furthermore, the hypothesis has been raised after the first negative result and particular attention was taken for the second swabbing. Alternatively, it is possible that the patient was hospitalized for a rhinovirus infection and then he acquired a SARS-CoV-2 infection. However, he had been placed on respiratory isolation at admission and the incubation period of the disease range from 2 days to 11 days [4]. Furthermore, rhinovirus is rarely associated with severe disease in lung-transplanted patients and his wife presented mild disease, with exclusively pharyngeal symptoms, that could be attributed to either rhinovirus or SARS-CoV-2. Finally, in a previous report including 205 patients, only 5 (63%) of 8 nasal swabs performed from SARS-CoV-2 infected patients were positive while the rate of positivity was 93% (14 of 15 samples) for bronchoalveolar lavage [5]. However, the author reports a lower CT for nasal swabs and they did not compare nasal swabs and bronchoalveolar lavage performed in the same patients. And, as few nasal swabs were performed one could wonder if negative swabs were accurately sampled.

In conclusion, lung-transplanted and cystic fibrosis patients might be at major risk of developing a severe SARS-CoV-2 infection. To date, the presentation of the disease is unknown in these patients. A wide screening is probably needed in symptomatic patients, including those presenting minor symptoms. We aware of performing microbiological analysis on respiratory deep samples in patients with mainly pulmonary disease. Furthermore, the recovery of another pathogen should not exclude a SARS-CoV-2 infection. In the pandemic context, all these findings would help to improve the rapid identification of SARS-CoV-2-infected patients and therefore their medical management but also the implementation of specific infection prevention and control measures.

Declaration of Competing Interest

The authors state they have no conflict of interest to declare.

Acknowledgments

Members of the Sars-Cov-2 Foch Hospital study group: Emilie Catherinot, Colas Tcherakian, Louis-Jean Couderc, Charlotte Roy and Antoine Roux (service de pneumologie et transplantation pulmonaire), Benjamin Zuber and Mathilde Neuville (service de réanimation), Morgan Le Guen (service d'anesthésie), Mathilde Roumier, Antoine Bizard, David Zucman, Mathieu Groh, Yoland Schoindre,

https://doi.org/10.1016/j.jcf.2020.03.021

David Khau and Romain Paule (Service de médecine interne), Philippe Grenier, Anne-Laure Brun and François Mellot (service d'imagerie médicale), Anne Verrat and Etienne Imhaus (service des urgences), Marianne Asso-Bonnet, Emilie Jolly, Marion Lecuru, Tiffany Pascreau and Laurence Mazaux (Service de biologie clinique)

References

[1] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Articles clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China : a retrospective cohort study. Lancet 2020;6736:1–9. https://doi.org/10.1016/S0140-6736(20)30566-3.

[2] Li D, Wang D, Dong J, Wang N, Huang H, Xu H, et al. False-negative results of real-time reverse-transcriptase polymerase chain reaction for severe acute respiratory syndrome coronavirus 2: role of deep-learning-based CT diagnosis and insights from two cases. Korean J Radiol 2020;21:505. https://doi.org/10.3348/kjr.2020.0146.

[3] Lippi G, Simundic A-M, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clin Chem Lab Med 2020;0. https://doi.org/10.1515/cclm-2020-0285.

[4] Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. Euro Surveill 2020;25. https://doi.org/10.2807/1560-7917.ES.2020.25.5.2000062.

[5] Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020. https://doi.org/10.1001/jama.2020.3786.

Eric Farfour* on behalf of the
Service de biologie Clinique, Hôpital Foch, Suresnes, France

Clément Picard, Laurence Beaumont
Service de pneumologie et transplantation pulmonaire, Hôpital Foch, Suresnes, France

Philippe Lesprit
Service de biologie Clinique, Hôpital Foch, Suresnes, France

Marie-Christine Ballester
Service des urgences, Hôpital Foch, Suresnes, France

Felix Ackermann
Service de médecine interne, Hôpital Foch, Suresnes, France

Richard Galliot
Service de réanimation médicale, Hôpital Foch, Suresnes, France

Sylvie Colin de Verdiere
Service de pneumologie et transplantation pulmonaire, Hôpital Foch, Suresnes, France
Université Versailles-Saint Quentin en Yvelines, France

Charles Cerf
Service de réanimation médicale, Hôpital Foch, Suresnes, France

Marc Vasse
Service de biologie Clinique, Hôpital Foch, Suresnes, France

*Corresponding author at: Service de biologie Clinique, Hôpital Foch, Suresnes, France
E-mail addresses: ericf6598@yahoo.fr, e.farfour@hopital-foch.org (E. Farfour)

Revised 27 March 2020