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Rapid Communication

Single-center experience of patients with interstitial lung diseases during the early days of the COVID-19 pandemic

J. Guiot [a,], M. Henket [a], A.N. Frix [a], M. Delvaux [a], A. Denis [a], L. Giltay [a], M. Thys [b], F. Gester [a], M. Moutschen [c], J.L. Corhay [a], R. Louis [a], on behalf of the COVID-19 clinical investigators of the CHU de Liège[1]*

[a] *Pneumology Department, CHU Liège, Domaine Universitaire Du Sart-Tilman, B35, B4000 Liège, Belgium*
[b] *Department of Medico-economic Information, University Hospital of Liège, Liège, Belgium*
[c] *Department of Infectious Diseases and General Internal Medicine, University Hospital of Liège, Liège, Belgium*

ARTICLE INFO

Article history:
Received 28 May 2020
Received in revised form
6 August 2020
Accepted 19 August 2020
Available online 19 September 2020

Keywords:
COVID-19
Interstitial lung diseases
Lung fibrosis
Clinical epidemiology

ABSTRACT

Introduction: Patients with interstitial lung diseases (ILD) can be suspected to be at risk of experiencing a rapid flare-up due to COVID-19. However, no specific data are currently available for these patients.
Methods: We retrospectively analyzed a cohort of 401 patients with ILD and determined the proportion of patients hospitalized for proven severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and specific symptoms of COVID-19.
Results: We found that 1% of patients (n = 4) were hospitalized (1 in ICU) for COVID-19. In total, 310 of the 401 patients answered the phone call. Only 33 patients (0.08%) experienced specific symptoms of SARS-CoV-2 infection.
Conclusion: Our study did not demonstrate any increased occurrence of severe COVID-19 in ILD patients compared to the global population. Based on our findings, we could not make any conclusion on the incidence rate of SARS-CoV-2 infection in patients with ILDs, or on the overall outcome of immunocompromised patients affected by COVID-19.

1. Brief report

In December 2019, health authorities in Wuhan (China) reported clustered pneumonia cases of unknown etiology. A new coronavirus has been identified as the cause of the epidemic, which has since affected many countries globally. The ongoing outbreak of coronavirus disease (COVID-19) has rapidly spread worldwide, and infections in European countries are steadily increasing. The clinical presentation of patients with COVID-19

* *Corresponding author*. University Hospital of Liège, Domaine universitaire du Sart-Tilman, B35, B4020, Liège, Belgium.
E-mail address: J.Guiot@chuliege.be (J. Guiot).
[1] COVID-19 clinical investigators of the University Hospital of Liège. ANCION A.,BOUQUEGNEAU A., BOVY C., DARCIS G., DEFRAIGNE JO., DUYSINX B., GHUYSEN A., GILBERT A., HEINEN V., LAMBERMONT B., MALAISE O., MARTIN M., MISSET B., MOUTSCHEN M., NGUYEN DANG D., PIAZZA J., SZECEL J., VAILLANT F., VAN CAUWENBERGE H., VON FRENCKELL C., VROONEN L.
https://doi.org/10.1016/j.resinv.2020.08.006

ranges from asymptomatic to severe pulmonary infection. In Belgium, a massive lockdown has been enforced to limit the spread of this pandemic. Presently, more than 51.000 cases have been reported in our country (out of 11.5 million living persons, with 18,8% of the population being over 65 years of age). COVID-19 can induce severe lung injury leading to ARDS (acute respiratory distress syndrome), mainly in older patients, and the global mortality rate in our country is averaging 16% among the infected patients [1]. Patients suffering from interstitial lung diseases (ILDs) can be suspected to be at a high risk of experiencing a rapid flare-up due to COVID-19. This hypothesis is based on the underlying diseases and the median age of such a population (above 60 years). However, it is also based on the risk associated with specific therapies, such as immunosuppressive therapies in connective tissue diseases associated with pulmonary fibrosis (CTD-PF) and anti-fibrotic therapies in idiopathic pulmonary fibrosis (IPF).

To address this hypothesis, we aimed to determine the specific incidence of symptomatic COVID-19 in patients with ILD. We analyzed our database of ILD patients (n = 627) who were followed-up in Liège University Hospital. We excluded patients who did not benefit from regular clinical monitoring as well as patients who died before January 2020. We then investigated whether those patients who were closely followed-up in our ILD center (n = 401) were tested positive for COVID-19 or hospitalized in this context. Moreover, in our clinical phone-based follow-up, we analyzed the proportion of patients who did not experience any specific symptoms of COVID-19 (77% answered). Patients who were not hospitalized were not allowed to be undergo the specific PCR testing, which was solely reserved for the most severe cases during this pandemic. The average age of ILD patients was 64 ± 16 years with a female predominance. This cohort was composed of patients with systemic sclerosis-associated ILD (SSc-ILD), IPF, sarcoidosis, CTD-PF, fibrosing non-specific interstitial pneumonia, and other ILDs (15.7%; 11.2%; 11.6%; 18.5%; 10.3%; and 32.7%, respectively). In our cohort, 37% of the patients were administered specific immunosuppressive therapy (prednisolone >5 mg/day, mycophenolate mofetil, azathioprine, or methotrexate). We compared the four hospitalized PCR-confirmed COVID-19 patients and those with specific symptoms (not hospitalized) to our hospital cohort of patients with a proven severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PCR-positive) (n = 687) without any underlying ILD. Confirmed cases of COVID-19 were identified through rhinopharyngeal swabs.

Different viral agents are associated with an increased risk of a more severe disease course and respiratory complications in immunocompromised patients [2]. Surprisingly, we found that only 4 patients (2 men/2 women) were hospitalized for COVID-19 out of the 401 selected patients, which is in line with the global incidence of the disease [3,4]. Those 4 patients where suffering from SSc-ILD, hypersensitivity pneumonitis, sarcoidosis, and lipidic pneumopathy, respectively. The fourth patient was admitted to the ICU and is now discharged. She was not on any specific background therapy. All the four patients received at least an antibiotic course (amoxicillin + clavulanic acid), empirically associated with hydroxychloroquine. None of them benefited from plasma therapy or anti-viral therapy. As of now, there has been no significant relapse of their underlying ILD. After calling the other ILD outpatients, we found that 33 of them experienced specific symptoms of SARS-CoV-2 infection and met the COVID-19 screening criteria (Table 1) [5]. The symptoms are presented in Table 1 and were mainly cough (67%), dyspnea (58%), rhinorrhea (42%), hyperthermia (48%), and asthenia (51%). Only two of them where tested and recognized as positive for COVID-19.

This observation corroborates with the global incidence of COVID-19. Unsurprisingly, since the severe respiratory

Table 1 – Clinical characteristics of patients with COVID-19 and patients of our ILD cohort.

		All hospitalized with COVID-19 in CHU Liège n = 687	ILD (n = 400)				
			Case 1	Case 2	Case 3	Case 4	Suggestive
		n (%)	SSc-ILD	Sarcoidosis	Chronic HP	Lipidic Pneumopathy	n = 33
	Gender, M (%)	315 (53%)	F	M	M	F	20 (61%)
	Age, Year	58 ± 20	45	37	79	74	60 ± 14
Symptoms	Cough, N (%)	268 (84%)	Yes	Yes	Yes	Yes	22 (67%)
	Dyspnea	162 (51%)	–	Yes	Yes	Yes	19 (58%)
	Chest pain	105 (33%)	–	–	–	–	–
	Rhinorrhea	167 (52%)	Yes	–	–	Yes	14 (42%)
	Diarrhea	99 (31%)	–	–	–	–	5 (15%)
	Hyperthermia	216 (68%)	Yes	Yes	Yes	Yes	16 (48%)
	Asthenia	201 (63%)	–	Yes	Yes	Yes	17 (51%)
	Cephalalgia	202 (64%)	–	Yes	Yes	–	9 (27%)
	Hospitalization	406 (59%)	8 days	5 days	>7 days	>7 days	5 (15%)
	ICU	55 (8%)	–	–	–	6 days	
	Treatment		ECI, Azathioprine CS 10 mg/d	–	CS 5 mg/d	ICS high dose	CS 14 (42%) IS 10 (30%)

The data for symptoms are available for only 318 COVID-19 patients.
ECI: enzyme conversion inhibitor; CS: corticosteroids (Prednisolone); ICS: inhaled corticosteroids; IS: immunosuppressors (Azathioprine, Mycophenolate Mofetil, Ledertrexate); ICU: intensive care unit; ILD: interstitial lung disease; SSc-ILD: systemic sclerosis-associated interstitial lung disease.
All the ILD patients were contacted by phone (at least 2 attempts). In total, 77% of them responded. Patients were suspected to have COVID-19 when they experienced at least one of the COVID-19-specific symptoms of acute onset.

complications caused by the SARS-CoV-2 infection are thought to be driven by the aberrant inflammatory and cytokine responses perpetuated by the host's immune system [6], patients benefiting from immunosuppressive therapy could hypothetically be at a low risk of ARDS. Contrary to this, however, immunosuppressive therapies may lead the patients to an immunocompromised state, which could result in severe infectious diseases with lethal respiratory failure such as pneumocystis pneumonia or cytomegalovirus infection that can increase the risk of non-COVID-19-related severe respiratory failure. We cannot conclude from such a small cohort that ILD patients could be at increased risk of SARS-CoV-2 infection. Nevertheless, the main limitation of this study is the highly preventive intervention of the Belgian government and the awareness of ILD patients that they may be at risk of experiencing a severe form of pulmonary involvement and their consequent containment. Through these observations, it seems essential to maintain active observation of our patients to identify a resurgence of this infection in this specific group of fragile patients. Notably, one study focusing on patients with rheumatoid arthritis [7] implemented these observations. They identified 4 out of 320 patients positive for SARS-CoV-2 infection and 4 with suggestive symptoms but without positive PCR results. Another study on 530 patients identified that 2% of the patients were suspected to be positive [8].

Our findings do not allow us to draw any conclusion regarding the incidence rate of SARS-CoV-2 infection in patients with ILDs, or on the overall outcome of immunocompromised patients affected by COVID-19. By following-up these patients, we could possibly highlight a hypothetical unexpected benefit of certain therapies. For example, immunosuppressive treatments pursued by necessity or anti-fibrotic treatments maintained to reduce the evolution of IPF should be specifically reported within cohorts of patients suffering from COVID-19.

Although continuous surveillance of patients with ILDs receiving immunosuppressive drugs is warranted [9,10], these data can support clinicians in the management and counselling of their patients and in avoiding the unjustifiable preventive withdrawal of immunosuppressive therapy, which could lead to an increased risk of relapses and morbidity linked to uncontrolled chronic ILDs.

Author agreement

We certify that all authors have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

Funding source declaration

There was no specific funding for this specific study.

Permission note

Not applicable.

Conflict of Interest

None.

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