

Clinical course of COVID-19 in a series of patients with chronic arthritis treated with immunosuppressive targeted therapies

Different viral agents are associated with an increased risk of more severe disease course and respiratory complications in immunocompromised patients.¹⁻³ The recent outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) responsible for a severe acute respiratory syndrome (SARS) represents a source of concern for the management of patients with inflammatory rheumatic diseases. Lombardy is the region in Northern Italy with the highest incidence of COVID-19 cases, with more than 33 000 confirmed patients and 1250 requiring admission to the intensive care unit within 1 month. Since the first reports of COVID-19 cases in Italy, we have circulated a survey with a 2-week follow-up contact to patients with chronic arthritis treated with biological disease-modifying antirheumatic drugs (bDMARDs) or targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) followed up at our biological outpatient clinic in Pavia, Lombardy. The survey investigated the patients' health conditions, the presence of contacts with subjects known to be affected by COVID-19 and management of the DMARDs during the first few weeks of pandemic. All patients had provided their informed consent for the use of personal and clinical data for scientific purposes, and no patient refused to participate.

During the first month, we have collected information on 320 patients (female 68%, mean age 55 ± 14 years) treated with bDMARDs or tsDMARDs (57% with rheumatoid arthritis, 43% with spondyloarthritis, 52% treated with tumour necrosis factor inhibitors, 40% with other bDMARDs and 8% with tsDMARDs). As shown in table 1, four were confirmed cases of COVID-19 identified through rhinopharyngeal swabs. Another four patients reported symptoms which were highly suggestive of COVID-19. Five additional patients with reported certain contacts remained asymptomatic at the end of the 2-week observation period.

All patients with confirmed COVID-19 received at least one antibiotic course, and the hospitalised patient also received antiviral therapy and hydroxychloroquine. Overall, five patients were on previous stable treatment with hydroxychloroquine. All patients with symptoms of infection temporarily withdrew the bDMARD or tsDMARD at the time of symptom onset. To date, there have been no significant relapses of the rheumatic disease. None of the patients with a confirmed diagnosis of COVID-19 or with a highly suggestive clinical picture developed severe respiratory complications or died. Only one patient, aged 65, required admission to hospital and low-flow oxygen supplementation for a few days.

Our findings do not allow any conclusions on the incidence rate of SARS-CoV-2 infection in patients with rheumatic diseases, nor on the overall outcome of immunocompromised patients affected by COVID-19. A high level of vigilance and strict follow-up should be maintained on these patients, including the exclusion of superimposed infections. However, our preliminary experience shows that patients with chronic arthritis treated with bDMARDs or tsDMARDs do not seem to be at increased risk of respiratory or life-threatening complications from SARS-CoV-2 compared with the general population.

These findings are not surprising as the severe respiratory complications caused by coronaviruses are thought to be driven by the aberrant inflammatory and cytokine response

Table 1 Clinical characteristics of the patients with confirmed or suspected COVID-19

	Confirmed COVID-19	Clinical picture highly suggestive of COVID-19	Contact with a known COVID-19 patient
Number of patients	4	4	5
Age (years) (mean \pm SD)	58 \pm 5	56 \pm 8	54 \pm 12
Female, n (%)	4 (100)	3 (75)	4 (80)
Comorbidities, n (%)			
Hypertension	1 (25)	2 (50)	1 (20)
Diabetes	0	0	0
Cardiovascular disease	0	0	1 (20)
Other	4 (100)	4 (100)	3 (60)
Smoking, n (%)			
Active	1 (25)	0	0
Previous	2 (50)	3 (75)	1 (20)
Rheumatological diagnosis			
RA, n (%)	3 (75)	3 (75)	5 (100)
SpA/PA,* n (%)	1 (25)	1* (25)	0
Rheumatological treatment, n (%)			
bDMARD			
Adalimumab	0	0	1 (20)
Etanercept	2 (50)	2 (50)	0
Abatacept	1 (25)	1 (25)	0
Tocilizumab	0	0	1 (20)
tsDMARD			
Tofacitinib	1 (25)	0	1 (20)
Baricitinib	0	1 (25)	2 (40)
Concomitant csDMARD			
Methotrexate	2 (50)	1 (25)	3 (60)
Leflunomide	1 (25)	0	1 (20)
Sulfasalazine	0	1 (25)	0
Concomitant hydroxychloroquine	1 (25)	2 (50)	2 (40)
Low-dose glucocorticoids*	2 (50)	2 (50)	2 (40)
Known contact with COVID-19	0	1 (25)	5 (100)
Symptoms, n (%)			
Fever	4 (100)	1 (25)	0
Non-productive cough	3 (75)	2 (50)	0
Sputum production	1 (25)	0	0
Rhinorrhoea	2 (50)	1 (25)	0
Sore throat	0	0	0
Fatigue	4 (100)	2 (50)	0
Myalgia	2 (50)	1 (25)	0
Arthralgia	1 (25)	1 (25)	0
Anosmia/dysgeusia	3 (75)	3 (75)	0
Dyspnoea at rest	1 (25)	0	0
Dyspnoea on exertion	2 (50)	1 (25)	0
Headache	2 (50)	0	0
Diarrhoea	1 (25)	0	0
Nausea/vomiting	0	0	0
Chest X-ray performed	4 (100)	0†	0
Chest X-ray pathological findings	0	0	0
Hospital admission	1 (25)	0	0

*Glucocorticoids \leq 5 mg/day prednisone equivalent.


†Subject to home quarantine.

bDMARD, biological disease-modifying antirheumatic drug; COVID-19, coronavirus disease 2019; csDMARD, conventional synthetic disease-modifying antirheumatic drug; PA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, spondyloarthritis; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

perpetuated by the host immune system.⁴ During different coronavirus outbreaks, such as SARS and Middle East respiratory syndrome, there has been no increased mortality reported in

patients undergoing immunosuppression for organ transplantation, cancer or autoimmune diseases.^{3 5} Accordingly, among 700 patients admitted for severe COVID-19 at our hospital (a referral centre for SARS-CoV-2 infection) during last month, none was receiving bDMARDs or tsDMARDs.

Although continuous surveillance of patients with rheumatic diseases receiving immunosuppressive drugs is warranted, these data can support rheumatologists for the management and counselling of their patients, avoiding the unjustifiable preventive withdrawal of DMARDs, which could lead to an increased risk of relapses and morbidity from the chronic rheumatological condition.

Sara Monti ,¹ Silvia Balduzzi,² Paolo Delvino,³ Elisa Bellis,³ Verdiana Serena Quadrelli,³ Carlomaurizio Montecucco³

¹Rheumatology Department, IRCCS Fondazione Policlinico San Matteo, Pavia, Italy

²Rheumatology Department, IRCCS Policlinico San Matteo, Pavia, Italy

³Rheumatology Department, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Correspondence to Dr Sara Monti, Rheumatology, IRCCS Fondazione Policlinico S Matteo, Pavia 27100, Italy; sara.saramonti@gmail.com

Handling editor Josef S Smolen

Contributors SM and CM contributed to the design of the project interpretation and analysis of the data, and writing of the manuscript. SB, PD, EB and VSQ contributed to the collection of data, interpretation and analysis of the data, and review of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.



OPEN ACCESS

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Monti S, Balduzzi S, Delvino P, *et al.* *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2020-217424

Received 26 March 2020

Accepted 27 March 2020

Ann Rheum Dis 2020;**0**:1–2. doi:10.1136/annrheumdis-2020-217424

ORCID iD

Sara Monti <http://orcid.org/0000-0002-1800-6772>

REFERENCES

- 1 Memoli MJ, Athota R, Reed S, *et al.* The natural history of influenza infection in the severely immunocompromised vs nonimmunocompromised hosts. *Clin Infect Dis* 2014;58:214–24.
- 2 Noreña I, Fernández-Ruiz M, Aguado JM. Viral infections in the biologic therapy era. *Expert Rev Anti Infect Ther* 2018;16:781–91.
- 3 D'Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic. *Liver Transpl* 2020. doi:10.1002/lt.25756
- 4 Shi Y, Wang Y, Shao C, *et al.* COVID-19 infection: the perspectives on immune responses. *Cell Death Differ* 2020;382.
- 5 Hui DS, Azhar EI, Kim Y-J, *et al.* Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. *Lancet Infect Dis* 2018;18:e217–27.