

Being a rheumatologist and a patient with a rheumatic disease today: A perspective at the time of COVID-19

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The outbreak of the novel 2019-coronavirus (SARS-CoV-2) is a tremendous challenge for rheumatologists and had a great impact in Italy (1). As of the April 3rd, 2020, overall, 119,827 people have been affected with 14,681 deaths, 19,758 recovered and still 81,320 (95%) in mild conditions while 4,068 (5%) in serious or critical conditions (2). The whole rheumatologic community has put utmost efforts in facing the disease. On one side, the direct commitment of a rheumatologist in a COVID-Unit was dependent on the specific mansion of each physician within a hospital. On the other hand, a broader homogeneity across the regions concerned the follow-up of patients with rheumatic diseases. Indeed, given the circumstances, at first local and subsequently national legal briefs were to postpone the non-urgent out-patients rheumatologic visits (Law decree March 9th 2020, n.14 Art.13) especially in order to have the most available to take care of COVID-19 patients. Thus, rheumatologic centers had usually telephonically contacted the patients to investigate circa their status to establish the severity and urgency of their condition when an appointment was already scheduled. Clearly, the challenge was represented by patients waiting for first clinical examination, in these patients a telephone screening may not undoubtedly depict the full scenario. Barriers in terms of available technology and patients' education largely limit the possible solution represented by telemedicine. Notwithstanding and inevitably the fact that rheumatology requires clinical examination and imaging in the evaluation of the patient. Concerning the day-hospital patients, those receiving intravenous treatment were also postponed if conditions allowed. It could be suggested the usage of subcutaneous administration when the same mechanism of the drug is available - with a limited risk for the patients mainly in terms of possible loss of efficacy. Otherwise, treatments were maintained during pandemic. Question was for those therapies that are more immunosuppressive, such as anti-CD20 and cyclophosphamide. There is not unequivocal strategy to be suggested rather individual, considering that often these drugs can be lifesaving. The long-term immunosuppression induced by rituximab may pose the patients at a risk to COVID-19 for an extended period, but no data are available yet. Inpatient consultations were continued, while it would be of interest to estimate the real afflux of rheumatologic patients in emergency rooms and the effective number of rheumatologic patients hospitalized not just because of COVID-19. Indeed, the different allocation of the hospital beds and the fear of some patients to even drive to a hospital may have reduced the effective number of hospitalized patients with rheumatic diseases (RDs).

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Another aspect regards the possibility that our patients with RDs may have an impact from COVID-19 due to their condition. Indeed, viral infections are often associated with disease flares (3) and overall disease worsening (4). Monti et al. (5) reported the first survey on the argument that was performed in Lombardy, the most hardly hit region in Italy, on chronic arthritis patients treated with bDMARDs or tsDMARDs with a 2-week follow-up. They identified 4 confirmed cases of COVID-19, 4 patients with symptoms which were highly suggestive of COVID-19 and 5 additional patients with reported certain contacts who remained asymptomatic. The hospitalized patients received antiviral therapy and hydroxychloroquine, and 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. So far, no relapses of the rheumatic disease were observed in this small cohort, there was neither severe case nor death. This is an important piece to sustain that preventive withdrawal of DMARDs is not recommended in our RDs patients, risking on the other hand disease relapse and morbidity from the chronic RDs. Moreover, to expand this, the Italian Society of Rheumatology (SIR) has launched a registry for the surveillance of COVID-19 patients with RDs.

Meanwhile, to preserve more immunosuppressed patients, the law decree n. 26 of the 17th of March, entitled these patients for leave from work until April 30th. Among these patients were included those using daily prednisone equivalents ≥ 7.5 mg; or using DMARDs (Methotrexate, Leflunomide); anti-TNF, anti-CTLA4; anti-IL-1, IL-6, IL-17, IL-12/23; anti-CD20; JAKi; phosphodiesterase inhibitor; Cyclosporine; Mycophenolate Mofetil, Tacrolimus; Cyclophosphamide or Azathioprine. The broad usage of chloroquine and hydroxychloro-

roquine to treat COVID-19 patients determined also a decline in stocks also for RDs patients chronically treated with these compounds for their condition (6). There are concerns, and also EULAR had to intervene, that the diversion of drug supplies away from people with rheumatic and musculoskeletal diseases may lead to adverse outcomes for this important and sizeable community in Europe and beyond. Manufacturers in Italy are ensuring all the efforts to rapidly upscale output to meet the increasing clinical need. Meanwhile, remote consultation with patients to decide on their treatment with hydroxychloroquine had to be taken, being aware that there is no real substitute of such immunomodulant in most of the cases, but also that temporary suspension or dosage reduction can be individually considered. Finally, we have to keep in mind that for some of our patients this might be an essential treatment, and in the case HCQ will be considered as a prophylactic treatment, all these considerations have to be taken into account. What will come in the future is whether patients with COVID-19 are at risk of developing an autoimmune rheumatic disease. Indeed, environmental factors including viral infections, are triggers of autoimmunity and data on SARS-CoV-2 are just waiting to get out of the box (7).

The last challenge for the rheumatologist regards treatment of COVID-19. Indeed, beside anti-virals, a plethora of drugs, mostly original-

ly developed to treat a rheumatic disease, are now being tested to treat SARS-CoV-2 infection. The Italian Medicine Agency has already approved two trials testing the efficacy and safety of the anti-IL-6 tocilizumab, one the anti-IL-6 sarilumab, one emapalumab and anakinra (8). Since the virus activates the inflammasome, provokes a dysregulated neutrophilic response and its replication might be impaired by microtubule disruption, we recently proposed a trial to evaluate the efficacy of colchicine under the auspices of the Italian Society of Rheumatology (SIR), the Italian Society of Infectious and Tropical Diseases (SIMIT) and the Italian Thoracic Society (AIPO) ("Treatment with COLchicine of patients affected by COVID-19: A Pilot Study - COLVID-19") that was approved by the Italian Medicine Agency (AIFA).

Thus, old and new treatments developed for RDs represent a hope in this giant fight. Nonetheless, we would like to dedicate this paper to all the rheumatologists that have been directly affected and suffered in these hard times.

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