Glucocorticoid-induced relapse of COVID-19 in a patient with sarcoidosis

The COVID-19 pandemic represents a challenge for rheumatologists: how activity of rheumatological diseases or disease-modifying therapies may affect the outcome of SARS-CoV-2 infection is only beginning to be understood. Gianfrancesco *et al* provided important insights in this regard by evaluating the hospitalisation rate of 600 patients with rheumatological diseases from 40 different countries.[1] They found that glucocorticoid treatment in doses equivalent with prednisolone 10 mg/day or higher was associated with an increased hospitalisation rate.

Here, we describe the case of a 50-year-old man who was diagnosed with Löfgren syndrome in January 2019 presenting with cough, bilateral ankle joint swelling and mediastinal lymphadenopathy. ACE (37.3 U/L, normal range <21.4) and soluble IL-2 receptor (1445 U/mL, normal range <710) were elevated in the serum. The patient was treated with glucocorticoids until October 2019 with complete remission of clinical symptoms and normalisation of laboratory parameters.

On 12 March 2020, the patient had contact with a person who later tested positive for SARS-CoV-2 RNA. One week after the SARS-CoV-2 contact, the patient developed fever (38°C) and dry cough suggesting SARS-CoV-2 infection. In addition, he developed pain in the ankles during night and with exercise. The fever remitted after 4 days, but the joint complaints persisted. SARS-CoV-2 RNA was negative in a combined nasopharyngeal and oral swab 14 days after contact with the patient with COVID-19. Due to persistent pain and swelling in both ankles, the patient re-initiated prednisolone treatment at doses of 20–30 mg/day on 28 March (16 days after the SARS-CoV-2-contact) against medical advice.

On 2 April, 5 days after initiation of prednisolone treatment, the patient presented with painful ankles and slight swelling of the right ankle. Auscultation revealed slight rales in two-thirds of the right lung. Laboratory tests showed an increase of leucocytes to 10 800/µL with 9400 neutrophils/µL and a borderline elevation of ACE in serum (21.9 U/mL, normal range <21.4). C reactive protein and soluble IL2-receptor were normal. Unenhanced CT of the chest showed bilateral, peripheral, ill-defined ground-glass opacities involving mainly the right lower lobe (figure 1). Additional consolidations were present in the right peripheral lung base and to a lesser extent in the left lower lobe. There were no typical findings for alveolar sarcoidosis-like peribronchovascular consolidations.[2] The mediastinal lymph nodes were normal-sized and showed regression compared with previous CT examination from January 2019. Radiologists considered these CT changes as highly suspicious for COVID-19 pneumonia.[3] Also, SARS-CoV-2 RNA was weakly positive in a nasopharyngeal swab (Ct value 37.9), but clearly positive in an oral swab (Ct value 34.7). Prednisolone was discontinued within 2 days and treatment with hydroxychloroquine (HCQ) 400 mg/day orally was initiated.

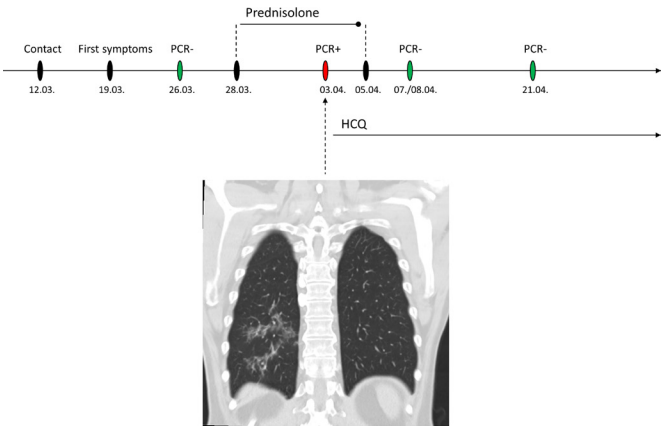

Figure 1 Caption. Timeline of clinical and virological evaluation and CT scan showing mixed pattern of ground-glass opacities and consolidations in right lower lobe with no pleural effusion. HCQ, hydroxychloroquine.

The patient had an uneventful course of infection and could be dismissed 5 days later, after the SARS-CoV2 RNA was negative in the nasopharyngeal and oral swabs.

The patient had experienced a symptomatic SARS-CoV-2 infection with spontaneous clinical improvement. Treatment with prednisolone at doses of 20 to 30 mg/day used for sarcoidosis and initiated 6 days after clinical remission was associated with a virological relapse with detection of SARS-CoV-2 RNA in nasopharyngeal and oral swabs and signs of COVID-19–lung disease in the CT scan. A de novo SARS-2 infection was unlikely due to strict isolation of the patient. Interestingly, COVID-19 was associated with a relapse of symptoms of sarcoidosis with ankle arthritis. Termination of glucocorticoid treatment and potentially also the initiation of HCQ treatment led to viral clearance. While we cannot fully exclude an initial false-negative test, the temporal sequence suggests that glucocorticoid treatment led to relapse of COVID-19, which was terminated after stopping glucocorticoids.

Our case supports previous reports, including the data on patients with rheumatological diseases by Gianfrancesco *et al*, that glucocorticoids may worsen SARS-CoV-2 infection.[1 4] While the data of Gianfrancesco *et al* included 20 patients with sarcoidosis, the authors do not provide information regarding their individual therapy or outcome of COVID-19. In general, the paper does not provide information whether the SARS-CoV-2 infection in rheumatic patients was first, re-infection or relapse. Here, we provide evidence that immunosuppression with glucocorticoids may induce relapse of COVID-19 even after initial clinical improvement. While more specific immunomodulatory therapies may be useful in the treatment of COVID-19,[5] non-selective, broad-spectrum immunosuppression may impair viral clearance and worsen COVID-19.

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