COVID-19 Infection in an Immunosuppressed Patient with Arthritis

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The outbreak of coronavirus disease-2019 (COVID-19), first identified in December 2019 in China, has spread worldwide and is considered a pandemic outbreak representing a substantial global healthcare challenge. The disease is induced by infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

COVID-19 morbidity and mortality have been linked to old age and co-morbidities such as hypertension, diabetes mellitus, and obesity, as well as heart, liver, or kidney failure. Patients with these co-morbidities have poorer outcome, more often resulting in hospitalization and higher likelihood for non-invasive and invasive ventilation [1,2]. Despite the lack of concrete evidence, rheumatologic patients with autoimmune or autoinflammatory diseases, which are treated with synthetic or biological disease modified anti rheumatic drugs (DMARD), are considered a high-risk population for COVID-19 infection. Until now, only a few reports on patients with rheumatic conditions who developed COVID-19 related disease have been reported [3,4].

PATIENT DESCRIPTION

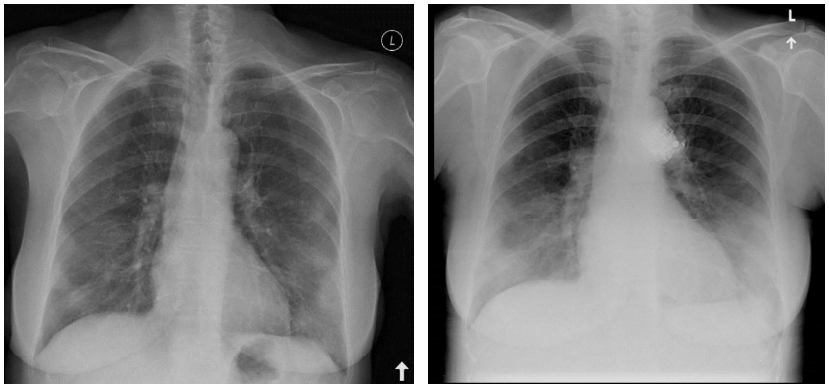
We report the case of a 63-year-old woman with psoriatic arthritis and Behçet's disease who was diagnosed with COVID-19 infection. The patient had a long-time history of recurrent oral and genital ulcers and positive pathergy tests compatible with Behçet's disease and a strong family history of psoriasis. At the age of 40 years, she developed oligoarthritis with eventual ankylosis of the left wrist, dactylitis, and unilateral sacroiliitis. Tests for rheumatoid factor, anti-citrullinated peptide antibody (ACPA) and anti-nuclear antibodies were negative. For the past 6 years she has been treated with oral methotrexate 7.5 mg/week and subcutaneous adalimumab injections (40 mg every 2 weeks) with significant amelioration of the arthritis and Behçet's disease manifestations. Co-morbidities were hyperlipidemia, treated with statins, and gastritis, treated with proton-pump inhibitors.

On 17 March 2020, the patient was referred to the emergency department with high fever, malaise, cough, and progressive shortness of breath, which had been present for 10 days. The patient reported contact with a friend, who returned from abroad, 5 days prior to the occurrence of fever. She had been treated with azithromycin and amoxicillin for 3 days without any improvement. The last adalimumab injection was administered 2 weeks before her symptoms started. Methotrexate was discontinued when the fever started.

The physical examination revealed tachypnea (24 respiration/min with O_2 saturation of 90–91% at room air, tachycardia (pulse 110/min), fever 39°C, and bilateral lung crackles. There were no signs of active arthritis, skin rash, or aphthae. The nasopharyngeal swab was positive for SARS-CoV-2 by real-time reverse transcription PCR test. The blood tests revealed thrombocytopenia of 94000/µl, hemoglobin 12.8 g/dl, mild leukopenia (leukocytes 4780/µl), high sensitivity C-reactive protein (CRP) of 2.3 mg/dl (normal < 0.5 mg/dl), AST 68 U/L (normal < 31 U/L), and LDH 640U/L (normal < 480U/L). The other liver function tests, the levels of urea, creatinine, creatine phosphokinase, fibrinogen, and procalcitonin were within normal limits. A chest X-ray showed bilateral infiltrates in the lower lung fields [Figure 1]. The patient was hospitalized and treated with intravenous ceftriaxone (1 G/day), oral levofloxacin (500 mg/day) hydroxychloroquine (600 mg/day), and nasal oxygen supplementation. The patient continued to present with high fever for several more days, and was hypoxic (pO_2 58 mmHg, O_2 saturation of 90%) despite the supplementary nasal oxygen.

The repeated blood tests revealed lymphopenia of 700/µl without leukopenia, and normal platelet count (208000/µl). The hemoglobin decreased to 11.1 g/dl, high sensitivity CRP level raised to 33 mg/dl, LDH 948U/L, elevated transaminases (AST 204U/L, ALT 103U/L), GGT 93U/L (normal < 36 U/L), high D-dimer (1850 ng/ml, normal < 500 ng/ml), myoglobin 89 ng/ml (normal < 58 ng/ml), ferritin 1233 ng/ml (normal < 150 ng/ml), and fibrinogen (1042 mg%, normal < 800 mg%). The levels of urea, creatinine, alkaline phosphatase, triglyceride, cholesterol, troponin, and creatine phosphokinase were normal. The oxygen saturation improved and gradually normalized after using optiflow (high-flow nasal cannula administrating air/oxygen blends). Within a week, the fever, dyspnea, and cough resolved. There was some residual fatigue. The patient was discharged

Figure 1. Chest X-ray



[A] at admission, bilateral peripheral lower lobe opacities;

[B] after several days, bilateral multilobar consolidation

after 13 days of hospitalization, following two consecutive negative tests for SARS-CoV-2. Three weeks later, she was feeling well, without any sequelae. She renewed adalimumab and methotrexate.

COMMENT

Despite the wide list of bad prognostic factors (lymphopenia; high levels CRP, ferritin, and D-dimers; hypoxia; and bilateral pulmonary infiltrates) and the immunomodulatory treatment (synthetic and biological DMARDs) our patient recovered from the COVID-19 infection without need for invasive ventilation and without any complication.

Accumulating evidence suggests that a subgroup of patients with severe COVID-19 infection develop a cytokine storm syndrome [5]. High levels of inflammatory cytokines, including tumor necrosis factor-α and interleukin-6 (major mediators of acute and chronic systemic inflammatory responses) have been observed in patients with COVID-19, and these correlate with disease severity [5].

In cases of hyperactivation of the immune system, particularly when lung and other vital organs are involved, immunosuppression might be considered as a therapeutic option, supporting the intricacy of the interaction among the virus and the immunological response depending on every single individual capacity. Prophylactic discontinuation of immunosupressive treatment during the pandemic, in otherwise stable patients, will lead to the rheumatic disease exacerbation and the need for steroids and may increase the risk of complications and even mortality. Although immunosuppressive agents are formally contraindicated in patients with active infections, they may show benefit in certain subgroups of COVID-19 associated severe acute respiratory distress syndrome or cytokine release syndrome, and may even prevent the severe complications.

CONCLUSIONS

Our case report is in line with the findings reported by Haberman et al. [4] that baseline use of biologics is not associated with worse Covid-19 outcomes. We assume that the chronic immunomodulatory treatment with methotrexate and adalimumab in our patient might have alleviated the clinical course and prevented the development of the cytokine release syndrome.

We are aware of the limitations of a single-case observations, and more data regarding the role of immunomodulatory treatment should be obtained.

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Capsule

Smothering fecal-oral coronavirus spread

Diarrhea is a common symptom in patients with coronavirus disease-2019 (COVID-19). **Zang** et al. used organoid cultures of cells from the epithelial lining of human small and large intestine as an in vitro model system with which to study viral entry and replication in enterocytes. Mature enterocytes expressing the viral receptor were susceptible to productive infection, which was also stimulated by the expression of a protease involved in viral entry. A subset of patients with COVID-19 shed high amounts of viral RNA in feces, but experiments with simulated human colonic fluid suggested that any shed virus would be rapidly inactivated during transit through the colon.

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