European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences 2020; 24: 12627-12629

Letter to the Editor

COVID-19 in Still's disease

Dear Editor,

Adult-onset Still's disease (AOSD) is a rare autoinflammatory condition of unknown etiology. It is generally characterized by high spiking fever, arthralgia and/or arthritis, transient salmon-like skin rash, leukocytosis, and increased ferritinemia levels. Usually, AOSD is treated with non-steroidal anti-inflammatory drugs, steroids, and immunosuppressive drugs. The presence of high levels of proinflammatory cytokines, such as interleukin (IL) 1β, IL-18, IL-6, and tumor necrosis factor, plays critical roles in AOSD and may serve as therapeutic targets[1]. Recently, Coronavirus disease 2019 (COVID-19) has emerged in China, in December 2019, and it has become a pandemic. Some articles have studied COVID-19 associated with rheumatic diseases, such as lupus, rheumatoid arthritis, inflammatory diseases, and vasculitis[2]. However, to the best of our knowledge, no cases of AOSD with COVID-19 was already described in the literature.

A 49-year-old female patient started in 2012 with recurrent fever (39.4°C), transient rash, sore throat, pericarditis, pleuritis, polyarthritis of wrists, knees, metacarpophalangeal, and proximal interphalangeal joints. Laboratory tests revealed hemoglobin 11.9 g/dL (12-16 g/dL), white blood cell of 12,800 cells/mm^3 (4,000-10,000 cells/mm^3), platelets 798,000/mcL (150,000-450,000/mc/L), AST of 62 U/L (< 32 U/L), ALT of 86 U/L (< 32 U/L), C-reactive protein 44.1 mg/dL (< 5 mg/dL), erythrocyte sedimentation rate of 72 mm/1st hour (< 20 mm/1st hour), acid alpha1-glycoprotein of 279 mg/dL (50-120 mg/dL), and ferritin of 3,465 ng/mL (11-306 ng/mL). Antinuclear antibodies, rheumatoid factor, and anti-CCP were not detected. Tuberculin test was negative. Serology for infectious diseases, such as HIV 1 and 2, HTLV I and II, syphilis, rubella, mononucleosis, hepatitis B and C virus, parvovirus B19, and cytomegalovirus were all negative. A thorax and abdomen computed tomography showed mediastinal lymphadenopathy, pleural and pericardial effusions, and mild splenomegaly. A diagnosis of AOSD was established based on the Yamaguchi et al[3] classification criteria.

She was treated with prednisone and methotrexate 15 mg/week with a good outcome. In June 2020, she was without drugs, and she had fever of 39.2°C, cough with purulent secretion, and dyspnea on efforts. After 3 days, she went to an emergency department (ED); computed tomography showed glass opacities mainly in the peripheral lung area, and also consolidation areas in both lungs with an estimated compromised area of 50%, all symptoms compatible with COVID-19 infection (Figure 1). The peripheral oxygen saturation was 96%. ESR was 50 mm/1st hour, CRP of 7 mg/dL and ferritin 1,250 ng/mL. She collected a nasal swab for PCR-RT COVID-19, which was negative. The ED's physician prescribed azithromycin 500 mg/day and ivermectin 6 mg/day for 5 days, and she was discharged with the orientation of home quarantine. The patient became asymptomatic after 5 days, and SD remained in remission during COVID-19 infection; ferritin was 253 ng/mL. After 3 months, a serology for COVID-19 was positive as follow: IgM 1.31 (nr:< 0.9) and IgG 11.93 (nr:< 0.9), with normal cell blood count, ESR 27 mm/1st hour, AST 18 U/L, ALT 20 U/L, CRP 1.92 mg/L and ferritin of 105.4 ng/mL.

A large retrospective Chinese study evaluated 2,326 subjects with COVID-19 and included 21 patients with rheumatic disease. The comparison between rheumatic patients and the others showed that the presence of respiratory failure was more common in the first group (38% *vs.* 10%, $p<0.001$), and they had similar radiological features of ground-glass opacity, and consol-

Corresponding Author: Jozélio Freire de Carvalho, MD; email: e-mail: jotafc@gmail.com

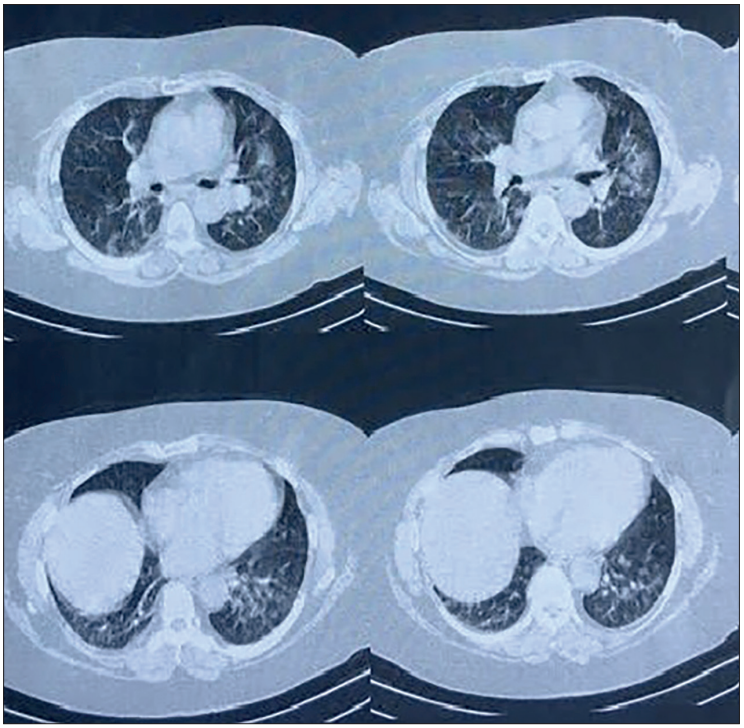

Figure 1. Thorax tomography shows glass opacities mainly in the peripheral lung area, consolidation areas in both lungs with an estimated compromised area of 50%, and is compatible with COVID-19 infection.

idation when compared to the non-rheumatic diseases group[2]. Our patient had precisely these characteristics described in the above study, presenting respiratory features and ground-glass opacities.

Gianfrancesco et al[4] published a large cohort of patients with rheumatic disease and COVID-19, who needed hospitalization. The authors evaluated a total of 600 cases from 40 countries, with 277 (46%) hospitalized, and 55 (9%) died. The factors associated with increased hospitalization risk were prednisone dose ≥10 mg/day (OR 2.05, 95% CI: 1.06 to 3.96). The non-steroidal anti-inflammatory drug, antimalarial, and immunomodulating agents use were not associated with hospitalization. Interestingly, the anti-tumor necrosis factor was associated with reduced hospitalization (OR 0.40, 95% CI: 0.19 to 0.81)[4].

Concerning risk factors for severe COVID-19 in RD patients, a Swiss study[5] evaluated 456 rheumatic and non-rheumatic patients. The authors observed that severe COVID-19 was associated with increased age, male sex, and connective tissue disease.

It is noticed in the literature that clinical and serological features of the phase of cytokine storm in COVID-19 might resemble the typical acute presentation of an AOSD. Some authors even suggested using anakinra, a drug with an excellent therapeutic response in AOSD for the cytokine storm in COVID-19[6]. An interesting review article on COVID-19 and hyperferritinemia was recently published, and the authors reviewed the putative mechanism linked to this serum alteration present in diseases, like macrophage activation syndrome, AOSD, catastrophic antiphospholipid syndrome, and septic shock[7].

Abbreviations

SD: Still's disease; COVID-19: Coronavirus disease 2019.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Data Availability Statement

Not applicable to this article. It is a case report.

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J.F. de Carvalho

Institute for Health Sciences from Federal University of Bahia, Salvador, Bahia, Brazil