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CASE REPORT

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Adult-onset Still's disease after SARS-Cov-2 infection

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Abstract

Adult-onset Still's disease (AOSD) is an uncommon inflammatory disorder. AOSD and SARS-Cov-2 infection share clinical and laboratory features, including systemic inflammation. A 19-year-old woman had prolonged fever for 3 weeks, joint pain, and biological inflammatory syndrome. Post COVID-19 AOSD was diagnosed. SARS-Cov-2 infection induces many inflammatory diseases including AOSD.

KEYWORDS

adult-onset, autoimmune diseases, hyperferritinemia, SARS-CoV-2, Still's disease

1 | INTRODUCTION

Adult-onset Still's disease (AOSD) is a rare inflammatory disorder characterized by a fever of more than 39°C, transient skin rash, leukocytosis, arthralgia, arthritis, or a combination of these symptoms. The Yamaguchi criteria for the diagnosis of AOSD require the presence of at least five criteria including at least two major criteria. Minor criteria are sore throat, lymphadenopathy, hepatomegaly or splenomegaly, abnormal liver function tests, and negative tests for antinuclear antibodies and rheumatoid factor.

Other rheumatic diseases, infections, and malignancies need to be excluded to make the diagnosis.[1]

Coronavirus-19 (COVID-19) emerged in late 2019 and was declared by the world health organization a pandemic in March 2020.[2]

AOSD and COVID-19 share several clinical and laboratory features, including systemic inflammation, unremitting fever, high serum ferritin, and potentially a cytokine storm syndrome.[3]

De Carvalho was the first to report a case of AOSD post-COVID-19.[4]

We herein report a challenging case of AOSD in a patient with a post-SARS-Cov-2 infection.

2 | CASE REPORT

A 19-year-old woman with no medical history was admitted to the internal medicine department in August 2021 with a history of fever, sore throat, multiple joint pain, and body rash mainly on the forearms for 3 weeks. Eight weeks before her admission, she was diagnosed with COVID-19 infection. Symptoms included headache, anosmia, ageusia, and fatigue without dyspnea. Three weeks after recovery the patient had a high temperature reaching 38.2–39.7°C, and an evanescent maculopapular rash on both arms and legs with arthralgia, myalgia, headache, and sore throat. Physical examination revealed fever and arthritis of both ankles and the right knee. Blood analysis

TABLE 1 Summary cases of AOSD post-COVID-19.

Article year	Country	Age/sex	Covid symptoms	Interval	AOSD presentation	Laboratory findings	Treatment	Outcome
Bamidis AD, et al[7] 2021	Germany	29/Female	Sore throat, headache, anosmia, ageusia, shortness of breath, fever, diarrhea, chilblain-like skin eruptions of the toes	Six months	Sore throat, myalgia, arthralgia, fever, lymphadenopathy, evanescent salmon-colored rashes, tachycardia, hypotension, pericardial and pleural effusion	↑ CRP, Leukocytosis 21.39 $\times 10^9$/L, Ferritin = 1771.8 ng/mL, ↑liver enzymes	Intravenous prednisolone + anakinra	Improved
Alshablan A, et al. 2021	Saudi Arabia	27/ Male	Not precised	Eight weeks	Sore throat, Fever, joint pain, body rash on the forearms	↑CRP Leukocytosis 25.9 $\times 10^9$/L Ferritin = 1750 ng/mL ↑ liver enzymes	Intravenous prednisolone	Improved
Current case 2021	Tunisia	19/Female	Headache, anosmia, ageusia, generalized weakness	Eight weeks	Sore throat, fever, joint pain, arthritis, body rash mainly on the forearms, myalgia, headache	↑CRP Leukocytosis 18 $\times 10^9$/L Ferritin = 25,000 ng/dL ↑ liver enzymes	Oral prednisolone	Improved

Abbreviation: CRP, C-reactive protein.

showed leukocytosis (18,000/mm^3) with neutrophilia (15,000/mm^3), anemia (hemoglobin = 10.2 g/dL), no thrombocytopenia and normal prothrombin time (83%) elevated serum C-reactive protein (303 mg/L), elevated serum ferritin (>25,000 ng/dL), and elevated liver enzymes (aspartate aminotransferase = 13 UI/L and alanine aminotransferase = 30 UI/L). Renal function was within normal limits. Nasopharyngeal swap for SARS-CoV-2 polymerase chain reaction was negative. The transthoracic echocardiogram showed no abnormalities. Blood and urine analysis revealed no evidence of bacterial or fungal infection. Antinuclear antibodies and rheumatoid factor were negative. Chest and abdomen computed tomography found hepatomegaly (155 mm) without splenomegaly. Infectious endocarditis was ruled out since hemocultures were negative and the transthoracic cardiac echography was normal. The hemophagocytic lymphohistiocytosis syndrome probability was 1%–3%.

Adult Still's disease was suspected, and the patient fulfilled all major and minor criteria of the Yamaguchi classification. Glycosylated ferritinemia was low (13%) supporting the diagnosis. A treatment regimen of prednisolone at the dose of 1 mg/kg/day was started. Three days later, the patient improved clinically with a resolution of joint pain and fever, and the inflammatory markers declined.

3 | DISCUSSION

AOSD is a rare multisystemic inflammatory disorder. Its incidence is about 0.16 cases per 100,000 people and has gender incidence equality.[5]

Infectious causes, malignancies, and other connective tissue diseases must be ruled out before establishing the diagnosis according to Fautrel or Yamaguchi criteria.[6]

Yamaguchi criteria have a sensitivity of 96.2% and a specificity of 92.1%.

No infectious, neoplastic, or autoimmune etiology was identified during etiologic investigations.

The patient's symptoms upon presentation, 2 months after COVID-19 infection, raised suspicion for AOSD, and she had all 4 of the major criteria and 3 of the minor criteria. Her nasopharyngeal SARS-CoV-2 swab was negative at the moment of diagnosis.

To our knowledge, there have been three other published cases of AOSD post-COVID-19 infection.[7,8]

The cases are resumed in Table 1.

The mechanism by which COVID-19 infection could trigger AOSD is unknown.[3,4] Interestingly, both diseases share clinical features, and they have probably common pathogenic pathways. IL-1 seems to have a central role in AOSD. IL-1 leads to an intense innate immune response by activating neutrophils, macrophages, and mast cells. It drives to aberrant production of several proinflammatory cytokines (IL-6, IL-8, IL-17, IL-18, and TNF).[9] Targeting IL-1 is considered an efficient treatment for AOSD, and there is evidence of a similar role for IL-1 in COVID-19 hyperinflammation. Interestingly, data obtained from the single-cell analysis revealed IL1-1β-positive monocytes in the peripheral blood of patients with severe COVID-19.[10] A recent study has demonstrated that treatment with Anakinra reduces significantly hyperinflammation, acute respiratory distress syndrome, and mortality in patients with severe COVID-19.[11,12]

The treatment of AOSD depends also on glucocorticoid therapy.[13] Our patient showed a favorable response in just a few days without the need for an IL-1 inhibitor.

4 | CONCLUSION

It was noticed that COVID-19 can induce many inflammatory diseases including AOSD. The mechanism is not completely understood but it suggests the participation of cytokines in the inflammatory response. The common role of IL-1 in the pathogenesis of COVID-19 and AOSD explains their close similarities.

AUTHOR CONTRIBUTIONS

Tayssir Ben Achour: Methodology; writing – original draft. **Wiem Ben Elhaj:** Writing – original draft. **maysam jridi:** Writing – review and editing. **Ines Naceur:** Methodology. **Monia Smiti:** Validation. **Imed Ben Ghorbel:** Supervision. **Mounir Lamloum:** Visualization. **Fatma Said:** Visualization. **Mohamed Habib Houman:** Supervision.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data are available on request from the authors.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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