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Short Clinical Case

Multisystem inflammatory syndrome in an adult following COVID-19

ARTICLE INFO

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Pediatric multisystem inflammatory disease

1. Introduction

Since March 2020, a newly recognized condition associated with COVID-19 that shares features with Kawasaki disease has been described in the pediatric population. Following SARS-CoV-2 infection, a subset of children has developed multisystem symptoms including fever, elevated inflammatory cytokines, cutaneous manifestations, and cardiovascular shock without severe respiratory illness [1]. A symptom-free interval of 1-2 months between SARS-CoV-2 infection and multisystemic manifestations has been reported. Early on, the emergent nature of the pandemic and the difficulty to prove recent infection with SARS-CoV-2 led to a range of criteria used for diagnosis, which could potentially be one of three disorders: pediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS), multisystem inflammatory syndrome in children (MIS-C), or Kawasaki-like syndrome [2]. Since June 2020, a similar condition has also been reported as a rare complication of COVID-19 in adults (MIS-A) [3] but only a small number of cases have been described [3–9].

The immunopathogenic mechanisms of MIS-C and MIS-A are not fully elucidated, potentially representing post-infectious processes that are seemingly initiated by the adaptive immune response. Of note, MIS-C and MIS-A occur in the absence of viral replication and with a singular cytokine profile with elevated levels of IL-10 and TNF-α compared to severe COVID-19 [1]. To improve the understanding and clinical management of these conditions, there is an urgent need to describe more cases, especially in adults.

2. Case report

A 24-year-old female patient was referred to our department for fever, myalgia, headache, trismus, torticollis, and chest pain in January 2021. Symptom onset occurred 5 weeks after SARS-CoV-2 infection with usual symptoms (fever, headache, anosmia). SARS-CoV-2 PCR from nasopharyngeal swabs was positive at that time. A one-month symptom-free interval occurred after SARS-CoV-2 infection. Upon admission, the patient was febrile with minimal respiratory symptoms. The physical examination showed complete trismus, fleeting rash involving the face and trunk, and cracked lips

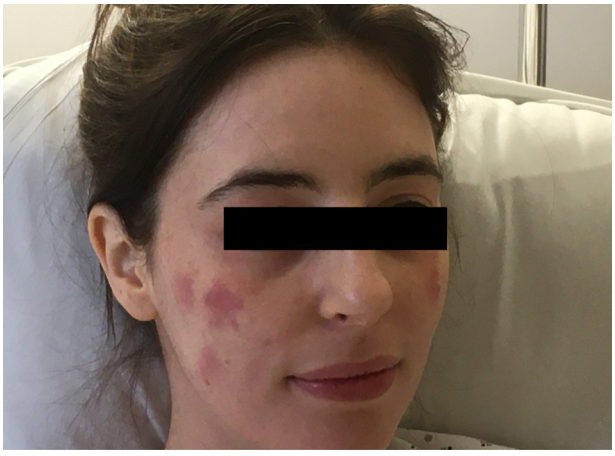

Fig. 1. MIS-A-associated facial rash.

(Fig. 1). There was no sign of cardiac decompensation. Ear nose and throat examination was normal.

Initial laboratory evaluation showed elevated C-Reactive Protein (CRP) (159 mg/L) and lymphopenia (0.8 G/L) without other hematological disorders (Fig. 2). Liver and kidney tests as well as troponin level were normal. NT-pro brain natriuretic peptide (BNP) was elevated at 1,550 pg/mL (0–300 pg/mL). Head, neck, and chest scans were normal. SARS-CoV-2 serology was negative. Blood cultures were negative. Serology for HIV, Epstein Barr virus, and cytomegalovirus were negative. Autoimmune markers such as antinuclear antibodies, antineutrophil cytoplasmic antibodies, and rheumatoid factor were negative. Still's disease was excluded because of the low ferritin level, as well as secondary hemophagocytic lymphohistiocytosis/macrophage activation syndrome because there was no cytopenia and no organomegaly.

Daily methylprednisolone (1 mg/kg) was started immediately. As the patient was allergic to aspirin, she received preventive anticoagulation instead. Her general condition and the trismus rapidly improved after infusion of methylprednisolone. However, after two days of slowly decreasing CRP and NT-pro BNP levels, improvements became stagnant (Fig. 2). At that time, EKG abnormalities appeared in the form of isoelectric T waves, but the echocardiography remained normal. Methylprednisolone was increased to 2 mg/kg daily and intravenous immunoglobulin (IVIG) was administered at 2 g/kg. Following IVIG infusion, the overall condition of the patient, as well as CRP and BNP levels rapidly improved (Fig. 2), and the EKG was normal. Corticosteroids were gradually reduced and discontinued over 4 weeks. Following steroid withdrawal, the patient experienced clinical relapse including fever, headache, generalized pain, elevation of CRP levels without cardiac manifestations. Corticosteroids were restarted orally at 20 mg/day for 1 month and then progressively tapered. Four months later, the

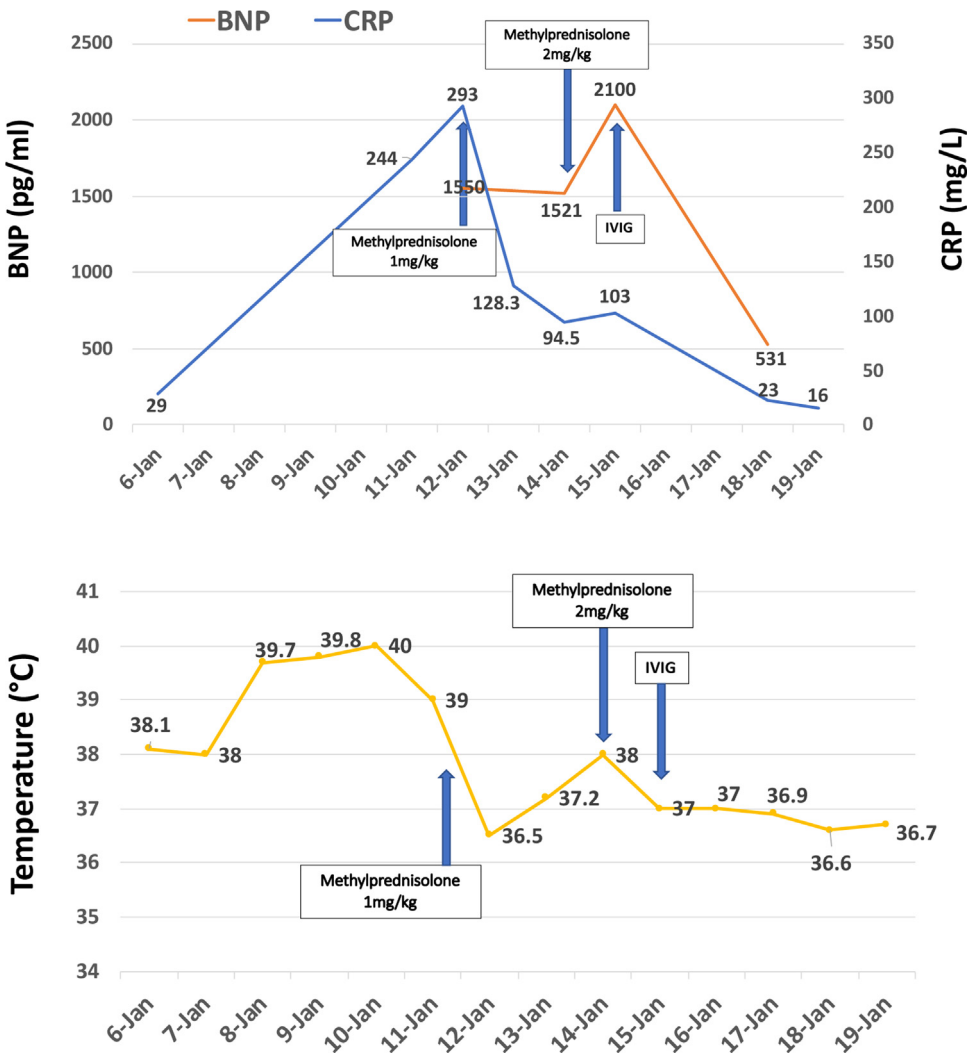

Fig. 2. Clinical parameters following therapeutic intervention.

patient is on a maintenance dose of steroids at 5 mg/day with no sign of relapse.

3. Discussion

This case meets the criteria for MIS-C or PIMS-TS except for age [1,2]. Our patient meets criteria of the Brighton Collaboration Case Definition for multisystem inflammatory syndrome in children and adults (MIS-C/A) [10]. She had no respiratory symptoms in conformity with the case definition, which was meant to discriminate MIS-A from severe COVID-19.

Approximately 40 cases of MIS-A are described in the literature. Clinical presentations are heterogeneous, and age ranged between 21 and 50 years old [3–9]. Like other adult patients in the literature, our patient had no coronary aneurysms [3]. Our patient is the first case with torticollis and trismus. Only one other patient suffered from odynophagia with retropharyngeal and parapharyngeal edema observed on the scan and others presented with neck pain and cervical lymphadenopathy [3].

Initial COVID-19 serology was negative, but this patient was previously positive for COVID-19 by PCR. Nearly all patients who had COVID-19 followed by MIS described in the literature had antibodies against COVID-19, while only one was negative [6], and five others had not been tested [3]. Regardless of age, adult patients with clinical presentation compatible with MIS-A must be tested for COVID-19 antibodies and the MIS-A diagnosis must be considered.

Although standard of care is well defined for pediatric patients, there are no guidelines for the treatment of MIS-A in adults. Among the patients described in the literature, the majority received corticosteroids or IVIG [3–9], a few received tocilizumab, and anticoagulation regimens and aspirin were frequently used [3]. Most treatment plans are derived from pediatric guidelines for MIS-C/Kawasaki diseases. Corticosteroids are considered the cornerstone of therapy. If cardiac involvement is suspected, literature data suggests that IVIG use could be beneficial, but proper use of tocilizumab has yet to be defined. In our experience, initial dosage and tapering of corticosteroids might differ between adults and children. Taken together, MIS-A should be considered as a differential diagnosis in adults with fever and multisystem symptoms during the COVID-19 pandemic. Physicians must be trained to recognize and take care of these patients in order to quickly identify the disorder and rapidly start treatment [4].

4. Conclusion

This is the first case describing febrile trismus associated with post-COVID-19 inflammatory manifestations that was successfully managed with IVIG and corticosteroids. Healthcare workers of adult medical units should be made aware of this diagnosis in order

to rapidly start treatment and to avoid incorrect interpretation of disease presentation.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article and that this report does not contain any personal information that could lead to their identification.

Disclosure of interest

The authors declare that they have no competing interest.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

Consent to participate

Written informed consent was obtained from the patient for publication of this case report.

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Comparison of the first and second waves of coronavirus disease in Toulouse, France

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We conducted a retrospective Covid-clinic-Toul cohort study at Toulouse university hospital, in southern France (2800 beds, tertiary hospital covering an area of about 3 million inhabitants) and selected hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia from September 1st, 2020 to October 31st, 2020. We compared their demographics, clinical, biological and radiological features, as well as unfavorable outcome (admission in an intensive care unit, mechanical ventilation, death) at Day 14 after admission to those of hospitalized patients during the 1st wave (March 11, 2020 to April 20, 2020). Like many other European countries, France faced a second wave of Coronavirus 2019 (COVID-19) pandemic from September to November 2020 [1]. A number of studies have compared the epidemiological and clinical features of hospitalized patients with COVID-19 during the first and second wave, mostly in Italy [2–6]. In addition, a few studies have assessed whether the characteristics and outcomes of hospitalized patients with COVID-19 changed in the second phase of the epidemic due to the evolution of healthcare system organization, patient demographics, and/or progress