



## Case report

## Multisystem Inflammatory Syndrome after Ad26.COV2.S vaccination

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## ABSTRACT

**Background:** The multisystem inflammatory syndrome (MIS) is a rare and sometime life-threatening post-infectious complication of coronavirus disease 2019 (Covid-19) in children and adults. To date, only a very few reports have associated such systemic reaction with SARS-CoV-2 vaccination.

**Case report:** we describe a case that resembled MIS, in a 46-year-old White man, 12 days after vaccination with Ad26. COV2. S vaccine (Johnson & Johnson/Janssen), a recombinant adenovirus serotype 26 vector encoding the SARS-CoV-2 spike glycoprotein. The patient experienced high grade fever, cutaneous rash, severe weakness, pericardial effusion and raised inflammatory markers, which met the criteria for definition of MIS. The symptoms improved with steroidal therapy.

**Conclusions:** Our case suggests that MIS could occur after SARS-CoV-2 vaccination.

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## Introduction

The multisystem inflammatory syndrome (MIS) is a rare and sometime life-threatening post-infectious complication of coronavirus disease 2019 (Covid-19) in children [1]. It is characterized by fever, laboratory evidence of inflammation and multisystem organ involvement [1]. The syndrome is being increasingly described in adults with recent Covid-19, some of whom had also received severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination [2,3]. The United States Centers for Diseases Control and Prevention is eagerly collecting data on this serious condition [4]. To date, such systemic reaction has been associated with vaccination against SARS-CoV-2 alone in a very few reports [5–8]. We describe a case that resembled MIS, after vaccination with Ad26. COV2. S vaccine (Johnson & Johnson/Janssen), a recombinant adenovirus serotype 26 vector encoding the SARS-CoV-2 spike glycoprotein.

## Case report

A 46-year-old White man with an unremarkable medical history presented to the emergency department with a 7-day history of sore-

throat, mild cough, weakness, erythematous non-itchy cutaneous rash and high grade fever. The patient had received the Ad26. COV2. S vaccine 12 days before symptom onset. His family physician had prescribed oral amoxicillin-clavulanate, and then ceftriaxone, ciprofloxacin and low dose prednisone. Because of the lack of clinical improvement the patient was admitted to the hospital. SARS-CoV-2 RNA was not detected on reverse transcriptase-polymerase-chain-reaction assay of a sample obtained with a nasopharyngeal swab. The result remained negative on day 5 and 10. The initial evaluation showed normal blood pressure (120/70 mm Hg), high body temperature (39.2 °C), leukocytosis (24.000/mm<sup>3</sup> [reference range, 4.000–11.000]) with lymphopenia, elevation in c-reactive protein (228 mg/L [reference value, < 5]), ferritin (22,363 ng/ml [reference range, 11–307]), D-dimer (23 mg per liter [reference value, < 0.5]) alanine-amino transferase (292 U/L [reference range 5–50]) and procalcitonin (13.97 ng/ml [reference value < 0.09]). The patient received fluids, 40 mg intravenous hydrocortisone, and then was transferred to internal medicine department. During the in-hospital stay an extensive evaluation for infectious and auto-immune diseases was unsuccessful. The echocardiography demonstrated a moderate pericardial effusion, whereas computed tomographic imaging of thorax and abdomen was unremarkable. Antibodies against SARS-CoV-2 spike glycoprotein were strongly positive, due to vaccination. However, antibodies against nucleocapsid were negative, thereby almost certainly excluding previous Covid-19. Prednisone at the dose of 75 mg per day (1 mg/Kg of body weight) orally was started and the patient progressively improved. At the time of this report He is going well.

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**Table 1**

Criteria for definition of definitive cases of Multisystem Inflammatory Syndrome in adults (from ref. 9).

Age > 21 years
<b>AND</b> Fever ≥ 3 consecutive days
<b>AND</b>
2 or more of the following clinical features:
- Mucocutaneous (rash, erythema or cracking of the lips/mouth/pharynx, bilateral non-exudate conjunctivitis, erythema/edema of the hands and feet)
-Gastrointestinal (abdominal pain, vomiting, diarrhea)
- Shock/Hypotension
- Neurologic (altered mental status, headache, weakness, paresthesias, lethargy)
<b>AND</b>
Laboratory evidence of inflammation including any of the following:
- Elevate CRP, ESR, or procalcitonin
<b>AND</b>
2 or more measures of disease activity:
-Elevate BNP or NT-ProBNP or troponin
- Neutrophilia, lymphopenia, or thrombocytopenia
- Evidence of cardiac involvement by echocardiography or physical stigmata of heart failure
- EKG changes consistent with myocarditis or myo-pericarditis
<b>AND</b>
Laboratory confirmed SARS-CoV-2 infection
OR Personal history of confirmed COVID-19 within 12 weeks
OR Close contact with known COVID-19 case within 12 weeks
OR Following SARS-CoV-2 vaccination

## Discussion

MIS is a known rare complication of COVID-19 in children [1]. The syndrome has also been identified in adults with recent COVID-19 infection [2–4]. Working criteria for definition of MIS have been published [9], and the features of our patient met the definition of definitive cases (Table 1).

However, in this case no precedent COVID-19 infection was identified, and the symptoms onset 12 days after SARS-CoV-2 vaccination strongly suggest a cause-effect relationship. Interestingly enough, albeit our patient needed hospitalization, he never appeared severely ill, differently from most cases of COVID-19 or vaccine-related MIS in children and adults [1–3,5–8]. In ours and in the other vaccine-related MIS, steroidal therapy and/or immunoglobulins proved to be efficacious, and no deaths were recorded. The mechanism by which the SARS-CoV-2 causes MIS is largely unknown to date [9]. One possibility is an aberrant interferon response leading to hyperinflammation [10]. Indeed, when cytokine profiles of severe COVID-19 were compared with MIS in children, patients in both groups had high interferon levels [11]. Differently from severe COVID-19, MIS in children is characterized by lower viral loads at presentation, as well as lower anti-S IgM, supporting the idea of a post-infectious phenomenon [11]. Several elements in MIS-Children patients suggest an endothelial dysfunction and microangiopathy, including a tendency to higher values of soluble complement components. This finding correlate with higher cytokine levels, suggesting that endothelial dysfunction may contribute to perpetuating inflammation [11]. In the case we present, the vaccine might have mimicked the effect of SARS-CoV-2. It is known indeed that vaccines can occasionally induce an acute autoimmune disease [12]. In conclusion, our case suggests that MIS could occur after SARS-CoV-2 vaccination. While this vaccination remains an absolute priority, clinicians should be aware of potential, albeit rare, side-effects of vaccines.

## Ethics approval

This case report has obtained approval from the head of the Internal Medicine unit at the Department of Internal Medicine of the Azienda Ospedaliera di Cosenza (Italy).

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request

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## Conflict of Interest

Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

## CRediT authorship contribution statement

Bova C: Conception and design of study, drafting the manuscript. Vigna E, Gentile M: Review of the manuscript for important intellectual content.

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