

## Case Report



# Stevens-Johnson syndrome related with Comirnaty<sup>®</sup> coronavirus disease 2019 vaccine

João Marcelino <sup>1,\*</sup>, João Vieira <sup>1</sup>, Fátima Ferreira <sup>1</sup>, Irina Didenko <sup>1</sup>, Rute Reis <sup>1</sup>, Rita Silva <sup>1</sup>, Regina Viseu <sup>1,2</sup>, and Elza Tomaz <sup>1</sup>

<sup>1</sup>Immunoallergology Department, Centro Hospitalar de Setúbal E.P.E., Setúbal, Portugal

<sup>2</sup>Laboratório de Imunologia e Biologia Molecular, Centro Hospitalar de Setúbal E.P.E., Setúbal, Portugal

## OPEN ACCESS

Received: May 12, 2022

Accepted: Jul 16, 2022

Published online: Jul 22, 2022

### \*Correspondence to

João Marcelino

Immunoallergology Department, Centro Hospitalar de Setúbal, Rua Camilo Castelo Branco 175, 2910-549 Setúbal, Portugal.

Tel: +351-967872677

Email: jlam\_1987@sapo.pt

Copyright © 2022. Asia Pacific Association of Allergy, Asthma and Clinical Immunology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ORCID iDs

João Marcelino

<https://orcid.org/0000-0001-8462-8847>

João Vieira

<https://orcid.org/0000-0003-3539-249X>

Fátima Ferreira

<https://orcid.org/0000-0003-4141-0594>

Irina Didenko

<https://orcid.org/0000-0002-4466-4680>

Rute Reis

<https://orcid.org/0000-0003-2356-3941>

Rita Silva

<https://orcid.org/0000-0002-8279-4726>

Regina Viseu

<https://orcid.org/0000-0003-1247-2999>

Elza Tomaz

<https://orcid.org/0000-0001-8880-9629>

## ABSTRACT

Stevens-Johnson syndrome is a rare severe delayed-type hypersensitivity reaction. Even though not initially described as a side-effect of the Comirnaty<sup>®</sup> coronavirus disease 2019 (COVID-19) Vaccine, the worldwide public COVID-19 vaccination programs are uncovering this serious adverse event. We present the case of a 44-year-old woman, vaccinated with the 1st dose in July 2021, and the 2nd dose 4 weeks later. Five days after the 2nd dose, a 10 cm, circular, painful, violet/red lesion appeared on the injection site. From then on, multiple, generalized purpuric painful lesions appeared, associated with ulcers on the lips, oral cavity, nasal cavity, vulva, and vagina, oedema of the hands and feet, conjunctival erythema, blurred vision, and malaise. The patient was being treated with lamotrigine and sodium valproate (for 2 years, without interruptions or dose change) which were stopped, and the patient started treatment with systemic corticosteroids. Lymphocyte transformation test were performed and were positive for PEG2000 1 µg/mL (stimulation index [SI], 30.9), and the undiluted Comirnaty<sup>®</sup> vaccine (SI, 32.2). These tests were negative on several vaccinated controls. We can definitively show that sensitization to the vaccine and PEG2000 can occur. A more extensive evaluation and reporting is needed to know the true incidence of this life-threatening condition and possible risk factors; as not only further booster shots of this vaccine will be administered, but also new vaccines with the mRNA technology are likely to be more prevalent in the future.

**Keywords:** Stevens-Johnson syndrome; COVID-19; Comirnaty; PEG2000; Drug allergy; Lymphocyte transformation test

## INTRODUCTION

Stevens-Johnson syndrome is a severe delayed-type hypersensitivity reaction, most commonly triggered by medications. To the author's knowledge, it has never been described as a possible side-effect of the Comirnaty<sup>®</sup> (Pfizer, New York, NY, USA) coronavirus disease 2019 (COVID-19) vaccine in the phase 3 trials. However, due to its rarity, this event may become apparent only in mass vaccination programs.

**Conflict of Interest**

The authors have no financial conflicts of interest.

**Author Contributions**

Conceptualization: João Marcelino, Elza Tomaz. Formal analysis: João Marcelino, Elza Tomaz. Investigation: João Marcelino, Elza Tomaz, João Vieira, Fátima Ferreira, Irina Didenko, Rute Reis, Rita Silva, Regina Viseu. Methodology: João Marcelino, Elza Tomaz, João Vieira, Fátima Ferreira, Irina Didenko, Rute Reis, Rita Silva, Regina Viseu. Project administration: João Marcelino, Elza Tomaz. Writing - original draft: João Marcelino, Elza Tomaz. Writing - review & editing: João Marcelino, Elza Tomaz, João Vieira, Fátima Ferreira, Irina Didenko, Rute Reis, Rita Silva, Regina Viseu.

This report was approved by the corresponding Ethics Committee and the Hospital's Administration (Hospital Administration minute number 26/21). Authorization from patient was also obtained.

**CASE REPORT**

We present the case of a 44-year-old woman, with a history of depression and hypertension. She was under medication with sodium valproate, lamotrigine, paroxetine, and bisoprolol for 2 years (without interruptions or dose change). No other medications or history of acute infections were identified.

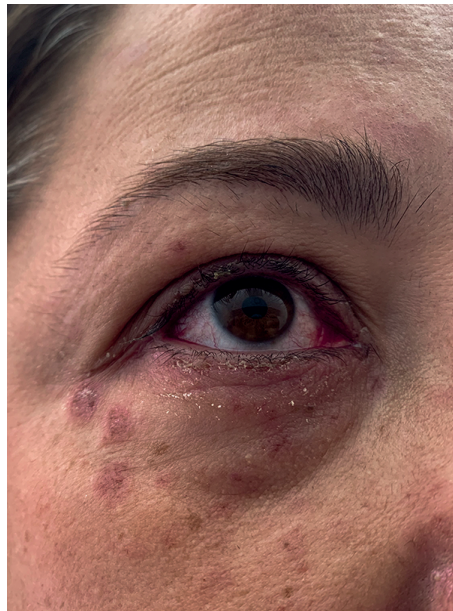
She was vaccinated against the COVID-19 infection with the Comirnaty<sup>®</sup> vaccine: 1st dose (FD8274) was administered in July 2021, with no adverse reaction whatsoever. The 2nd dose (FE4723) was administered 4 weeks later.

Five days after the 2nd dose, a large (10 cm in diameter), circular, itchy, violet/red lesion appeared on the injection site (**Fig. 1**). From the 6th day onward, the lesion darkened and developed a painful burning sensation. Additional macular, oval (of up to 3 cm), purpuric painful lesions spread throughout the body. Two large bullae with clear content appeared on the neck and back. Ulcers appeared on her lips, oral cavity, nasal cavity, vulva, and vagina. There was also oedema of the hands and feet, conjunctival erythema (**Fig. 2**), complaints of blurred vision, and malaise.

She went 3 times to private physicians and was medicated with oral antihistamines and 20-mg prednisolone once a day, without improvement. She was admitted to our emergency department 2 weeks after the symptoms started.



**Fig. 1.** Exuberant purpuric lesion at the injection site of the Comirnaty<sup>®</sup> (Pfizer, New York, NY, USA) vaccine.



**Fig. 2.** Conjunctival hyperaemia.

Lamotrigine and sodium valproate were stopped, and the patient started cetirizine 10 mg twice a day, prednisolone 80 mg/day, ocular dexamethasone, ocular lubrication, and skin emollients. The patient progressively improved and tapering of corticosteroids was started on the 4th day. The patient was discharged after 10 days, and complete symptom resolution was achieved after 1 month.

Serological tests for hepatitis B, hepatitis C, cytomegalovirus, Epstein-Barr virus, herpes 1 and 2, human immunodeficiency virus, parvovirus, mycoplasma, and syphilis were negative. Cutaneous biopsy was performed and was consistent with Stevens-Johnson syndrome.

Two months after discharge, a lymphocyte transformation test was performed, which was positive for the 4 agents tested: lamotrigine 10- $\mu$ g/mL stimulation index of 13.9; sodium valproate 1- $\mu$ g/mL stimulation index of 37.2; PEG2000 1- $\mu$ g/mL stimulation index of 30.9; and Comirnaty<sup>®</sup> vaccine (undiluted) stimulation index 32.2.

Controls for the lymphocyte transformation test were performed, using the blood of vaccinated healthcare workers. All were negative to PEG2000 and the Comirnaty<sup>®</sup> vaccine (stimulation index <2).

Patch testing was performed with lamotrigine 10% pet (chemotechnique), sodium valproate 10% pet, PEG2000 0.1 g/mL aq, and the undiluted Comirnaty<sup>®</sup> vaccine. Readings at 48 hours were negative, and positive only for sodium valproate (++) at 96 hours.

## DISCUSSION

To the authors knowledge, only 2 other reports exist describing Stevens-Johnson syndrome in relation to this vaccine [1, 2]. In one, a patient was also medicated with sodium valproate.

From these reports it is clear that Stevens-Johnson syndrome can arise after the Comirnaty® vaccine. To the author's knowledge, our lymphocyte transformation test is the first one being done in such a case, and it is the first definitive proof that sensitization to the vaccine and PEG2000 can occur. This is highlighted by the fact that our controls showed a negative test and that a second patient with Stevens-Johnson syndrome after the Comirnaty® vaccine, also presented a positive test to PEG2000 and the Comirnaty® vaccine (case not reported here). However, it is still unclear, in the current case, whether this reaction occurs as a response to the vaccine itself, or if the vaccine triggers a reaction to another drug (like sodium valproate), even in the absence of dose change or interruption.

In addition, the publication of this report, and others like this, is highly relevant to: (1) not underrepresent the true incidence of this life-threatening condition caused by such widely used vaccine with so many booster shots still being administered; (2) add information to a better understanding of this syndrome and risk factors associated.

## REFERENCES

1. Mansouri P, Chalangari R, Martits-Chalangari K, Mozafari N. Stevens-Johnson syndrome due to COVID-19 vaccination. Clin Case Rep 2021;9:e05099.  
[PUBMED](#) | [CROSSREF](#)
2. Bakir M, Almeshal H, Alturki R, Obaid S, Almazroo A. Toxic epidermal necrolysis post COVID-19 vaccination - first reported case. Cureus 2021;13:e17215.  
[PUBMED](#) | [CROSSREF](#)