Toxic epidermal necrolysis following SARS-CoV2 vaccine. A case report

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Case Report

Internal Medicine

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Background
66-year-old female with a history of arterial hypertension of 3 months of diagnosis and colon cancer of 13 years of diagnosis with partial colectomy on two occasions and second-line treatment with imatinib from 2018 to June 2021 with subsequent change to sunitinib in September of 2021 for presenting a recurrence, who received the vaccination schedule against SARS-CoV2 with a third dose from the Pfizer laboratory applied on November 11, 2021. Symptoms began approximately 18 hours after the administration of the vaccine with pain at the application site, after After 24 hours, intense itching was added, lesions on the oral and ocular mucosa made up of ulcers, later he presented multiple red erythematous macules that spread in a cephalo-caudal direction, forming blisters and flaccid blisters of 3 to 25 cm in diameter, some de-epithelialized, forming superficial ulcers. , Nikolsky sign and positive Asboe-Hansen in addition to acute kidney injury. She received treatment with fluid replacement, antihypertensive management, corticosteroids, analgesics, and cleaning of the wounds with antiseptic dressings and hydrocolloid patches in the most extensive lesions, monitoring of the hemodynamic pattern, and evaluation by ophthalmology with the application of antibiotics, steroids, and artificial tears. With the improvement of the clinical picture, progressive weaning of the corticosteroid was carried out and discharge from the intensive care unit was decided. No recurrences were reported after discharge.

Keywords: SARS-CoV2 vaccine, Toxic epidermal necrolysis.

Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) differ primarily in their severity, which is gauged by the proportion of body surface area that is damaged by erosive blistering. Drugs always start the more severe presentation, NET, an immune-mediated skin reaction characterized by significant epidermal detachment of more than 30% of the body surface, although infectious agents can frequently start the milder presentation, SJS. The most frequent triggers are medications. According to estimates, there are between 0.4 and 1.9 cases per million people worldwide each year, with a fatality rate ranging from 14.8% to 348% and an annual incidence of between 0.4 and 1.2 cases per million due to various culpable medicines. [1]

TEN is frequently brought on by medications (such as specific antibiotics and antiepileptics). Although rare, vaccine-induced Stevens-Johnson syndrome (SJS) has been linked to the MMR (measles, mumps, rubella), hantavirus, and meningococcus B vaccinations. Varicella vaccines, Smallpox, anthrax, tetanus, and influenza have all been linked to SJS.[2]
One to three weeks after taking the medicine, patients typically have fever and other flu-like symptoms, followed by uncomfortable erythematous to purpuric skin lesions that have a tendency to consolidate. Erosions, vesiculobullous lesions, and epidermal detachment then appear over a sizable portion of the body surface. Due to the involvement of the mucous membranes, the patient may also have severe conjunctivitis and develop oral and vaginal ulcers.[3]

Case report

A 66-year-old female with a history of recently diagnosed arterial hypertension and colon cancer, 13 years old, diagnosed after partial colectomy surgery on two occasions in 2018 and 2019 and second-line treatment with adjuvant chemotherapy with imatinib from 2018 to June 2021 with subsequent change to sunitinib in September 2021 due to presenting a second relapse. She completed two cycles in a scheme of 4 weeks of application for 2 weeks off, last cycle on November 8, 2021 and who received the vaccination scheme against SARS-CoV2 with a third dose from the Pfizer BioNTech BNT162b2 laboratory applied on November 11, 2021.

Symptoms begin approximately 18 hours after administration of the vaccine with pain at the

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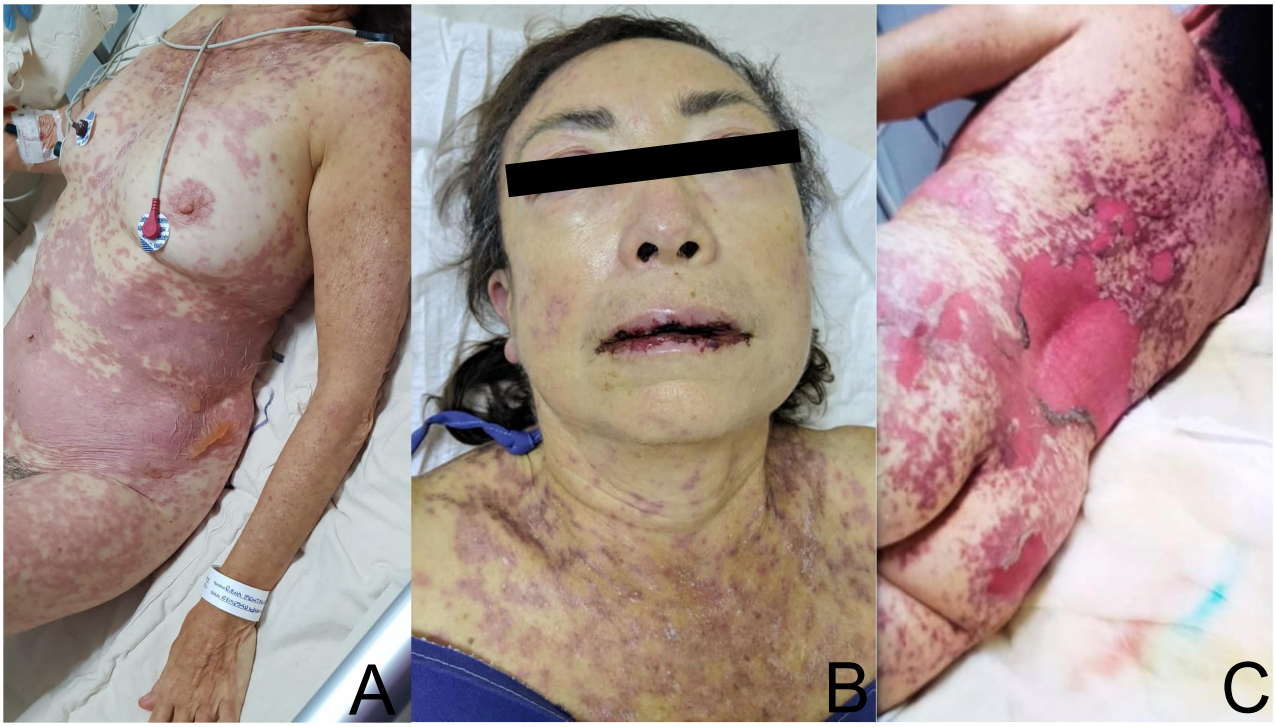

Figure 1. A. Early macular eruption. B. Hemorrhagic crusts and conjunctival erythema and erosion. C. Shedding of large layers of necrotic epidermis and denuded skin.

application site, after 24 hours intense pruritus is added, lesions on the oral and ocular mucosa made up of ulcers, later he presented multiple red erythematous macules that spread in a cephalo-caudal direction. Coming to form blisters and flaccid blisters of 3 to 25 cm in diameter, some de-epithelialized, forming superficial ulcers, positive Nikolsky and Asboe-Hansen sign. (Fig. 1)

Upon admission to hypertensive uncontrolled, laboratories were collected reporting Hb 13 mg/dL, Hct 34.6%, Platelets 267,000/L, Leukocytes 2800/L, ESR 45 mm/h, C-reactive protein 32.53 mg/gL, Urea 103 mg/dL, BUN 48 mg/dL, Creatinine 2.39 mg/dL, Na 135 mg/dL, K 5.4 mEq/dL, Cl 94 mg/dL. The Severity-of- Illness Score for Toxic Epidermal Necrolysis (SCORTEN) score was four on the day of her admission since she was older than 40, had a serum BUN level of >10 mmol/L, more than 10% detached body surface area and history of colon cancer.

Management begins with monitoring of the hemodynamic pattern, fluid replacement, and antihypertensive management, with steroids and intravenous analgesia, as well as cleaning the wounds with antiseptic fomentations and hydrocolloid patches in the most extensive lesions. Ophthalmologists were evaluated due to the conjunctival condition presented with the application of antibiotics, steroids, and artificial tears.

During his stay, he did not present neurological or cardiorespiratory compromise, with improvement of the lesions with drying powders and antiseptic baths, parenteral prophylactic antibiotic and methylprednisolone pulses. After two weeks under surveillance of the intensive care unit, discharge was decided, finding skin lesions in the repair stage with emollients, resolution of AKI III acute kidney injury, recovering baseline values in nitrogen gases as well as corneal injury without repercussions on vision. No recurrences were reported after discharge. (Fig. 2)

Conclusion

A rare, potentially fatal immune-mediated skin reaction known as toxic epidermal necrolysis (TEN) is characterized by severe epidermal detachment of more than 30% of the body surface and blistering. The death rate is estimated to be between 25% and 35%, with an incidence range of 0.4 to 1.9 cases per million people per year.[3] Children and teenagers are the most commonly impacted by Stevens-Johnson syndrome (SJS), whereas premature newborns and the elderly can develop TEN. Elderly patients had a 2.7 times greater prevalence of cutaneous drug responses, including TEN, and TEN mortality is twice as high in the elderly (51% vs. 25%).[4]

TEN and SJS are largely distinguished by their severity, determined by the percentage of body surface area affected by erosive blistering. The more severe presentation, TEN, is always initiated by drugs, but the milder presentation of SJS can often be caused by infectious agents.[5,2]

The most frequent cause of TEN is medication, and symptoms typically appear 8 weeks after exposure, particularly during the first 4 to 28 days. In contrast, post-vaccination adverse reactions

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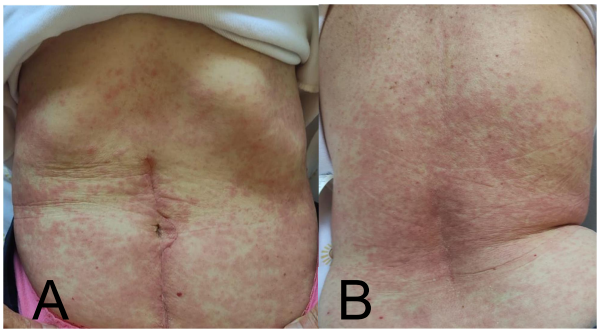

Figure 2. A-B. Post treatment reepithelization

have a shorter timeline, with the rash appearing 1 to 8 days after administration and typically lasting 3 to 5 days. Currently, 3.5 days have passed since immunization on average. In recent years, an incidence of 7.2% of NET cases has been reported, of which 1-2% are caused by vaccines. [6,7]

Acute SJS/TEN is typically thought of as a T-cell mediated, type IV hypersensitivity condition. Affected patients show an exuberant response on reexposure to the offending agent. It has been determined that more than 200 different drugs can contribute to SJS. These medications activate immune cells that release granulysin, which kills skin and mucous membrane cells by dysregulating particular trans-membrane protein pathways, including cytotoxic T cells and natural killer cells. [8]

Mass fatalities from the COVID-19 pandemic have occurred, but work on developing quick, universal vaccines is still ongoing. Urticaria and morbilliform rashes were detected in 414 patients who got the Moderna (83%) or Pfizer-BioNTech (17%) mRNA vaccine, which are unusual skin responses associated with COVID-19 vaccinations. [9]

SJS/TEN is a very uncommon adverse reaction to routine immunization. Additionally, reports of SJS/TEN cases linked to the COVID-19 vaccination are extremely rare. There are few accounts of the vaccine being used again, and the severe variants are associated with advanced age. [10,11]

According to Bakir et al.[12], a 49-year-old female who experienced a TEN after getting the first dosage of the Pfizer COVID-19 vaccination recovered completely after receiving two doses of etanercept. Elboraey et al.[13] described a case of SJS following the delivery of the Pfizer COVID-19 vaccine's second dosage, with recovery occurring following the injection of oral prednisolone. Cases related with the initial dose of the AstraZeneca COVID-19 vaccine, SJS treated with cyclosporine, and a TEN treated with etanercept, according to Dash et al.[14] and Kherlopian A. et al.[15] Mansouri et al. [16,17] presented a serie of 2 cases related to the the administration of Sinopharm COVID-19 vaccine healing completely after the use of oral prednisolone, a SJS and a TEN. Mardani M. et al. [18] reported a case of TEN after the first dose of China National Biotec Group) treated with prednisolone. Padniewski JJ et al. [19] presented a case of SJS following the administration of the first Moderna (Moderna Inc., MRNA 1273) COVID-19 vaccine dose healing with oral prednisolone. Aimo C. et al. [20] reported a SJS case after the administration of the second dose of Vaxvetria (AZD1222) COVID-19 vaccine treated with prednisolone.

According to current case report studies, the age of presentation in adults oscillate between 46-76 years, with 6 of the 9 cases reported being female. The vaccines involved in the presentation of this reaction were Pfizer-BioNTech (BNT 162b1), Astra Zeneca (ChAdOx1 nCoV-19), Sinopharm, (China National Biotec Group), Moderna (Moderna Inc., MRNA 1273), Vaxvetria (AZD1222), being the first three the most commonly associated in the first dose, with the average onset of simptoms between 1-3 days and recovery in 1-3 weeks with no fatal outcomes, the mayority of the case coming to resolution with corticoesteroids.

The most significant complications of TEN treatment include sepsis and organ failure, which require supportive care such as stopping the offending substance, admission to an intensive care or burn unit, fluid and electrolyte replacement, pain control, and temperature control. Numerous immunosuppressive and immunomodulating therapies, such as corticosteroids, IVIG, cyclosporine, and TNF antagonists, have been suggested.[6]

Conclusion

The mainstay of treatment in TEN is early identification and support management in an intensive care unit, so it must be considered of interest to bear in mind the adverse effects caused by the application of any medication; however, since it is an extremely rare adverse reaction, it should not be considered a contraindication to vaccination against SARS CoV2.

Conflicts of interests

We disclose that none of the writers in this scientific study have any potential conflicts of interest.

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