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Case Report
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Stevens Johnson Syndrome from Heterologous COVID-19 Vaccine: A Case Report

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Abstract

Stevens-Johnson syndrome is an acute hypersensitivity reaction which leads to generalized necrosis of the skin and mucous membranes that is often drug induced. Other possible causative factors are bacterial and viral infections. Vaccination induced Stevens Johnson Syndrome is a rare occurrence. In this paper, we reported a case of Stevens Johnson Syndrome in a 62-year-old- male, 1 week after receiving 3rd dose of COVID-19 vaccine. His initial 2 doses were an inactivated form of the COVID-19 virus given 6 months ago. His 3rd dose was an mRNA COVID-19 vaccine. This case demonstrates a rare dermatological complication using heterologous vaccines.

Keywords: Stevens johnson syndrome; COVID-19; Vaccinations; Heterologous

Introduction

Stevens-Johnson Syndrome (SJS) is a rare, acute and life-threatening mucocutaneous disease that is often drug-induced. It is a result of extensive keratinocyte cell death resulting in significant scalded skin appearance. Other rare causes include infections and immunizations. The average mortality rate of Stevens Johnson syndrome in elderly is 1% to 5% and those with very large epidermal detachment has 25% to 35% mortality rates [1]. Stevens Johnson Syndrome is essentially diagnosed clinically. Constitutional symptoms such as fever, malaise, pain in swallowing and joint pains were recorded in the patient's history. Skin manifestations usually present as erythematous purpuric macules which eventually coalesce forming large patches. Most of the time, cases will show oral manifestations described as painful crusts and erosions [2]. In 2019, SARS-CoV-2 caused a pandemic. This led to the emergence of COVID-19 vaccines. Due to its novelty, little is known regarding its side effects. Since the start of vaccinations, many dermatological manifestations have been described. McMahon et.al defined subset of vaccine-related eruption following COVID-19 vaccination [3]. With the current recommendation of having a 3rd dose, heterologous COVID-19 vaccines have been granted emergency use to accelerate vaccine roll-out worldwide, especially in low and middle-income countries [4]. However, the safety profile of using heterologous vaccination has not yet been well elucidated. In this case report, a serious dermatological adverse event after giving booster dose using heterologous vaccination will be discussed.

Case Presentation

Investigation

This is the case of 62-year-old Filipino male a known case of hypertension, diabetes mellitus with chronic obstructive pulmonary disease for years presented with 1 week history of fever and skin lesions. Per patient, he was apparently well until, 1 week after receiving his 3rd dose using mRNA-1273 (mRNA platform, Moderna) COVID-19 vaccine, he experienced multiple erythematous purpuric rashes mostly on the trunk accompanied by fever, pain on swallowing and malaise. He then sought consult with a private physician and was given topical corticosteroids, anti-pyretic and anti-histamines. Only slight relief of symptoms was noted. After 3 days, his skin lesions became more generalized and his eyes were now affected. He went to the emergency room and subsequent admission was advised.

Diagnosis

On physical examination he looked unwell. His vital signs were within normal limits. Cutaneous examination showed generalized brown to hyperpigmented purpuric macules with surrounding erythema with few areas showing bullae, accompanied by tenderness. Mucosal involvement was present in the form of hemorrhagic crusts over the lips, erythema of the buccal mucosa, redness and discharge from the eyes (Figure 1, 2). Patient was also complaining of difficulty of swallowing due to

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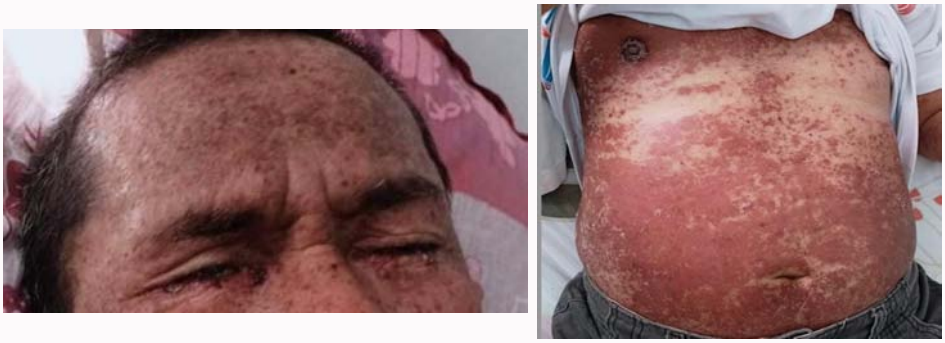

Figure 1: Erythematous macules coalescing into erythematous patches over the trunk and face Hemorrhagic crusting of the eyes.

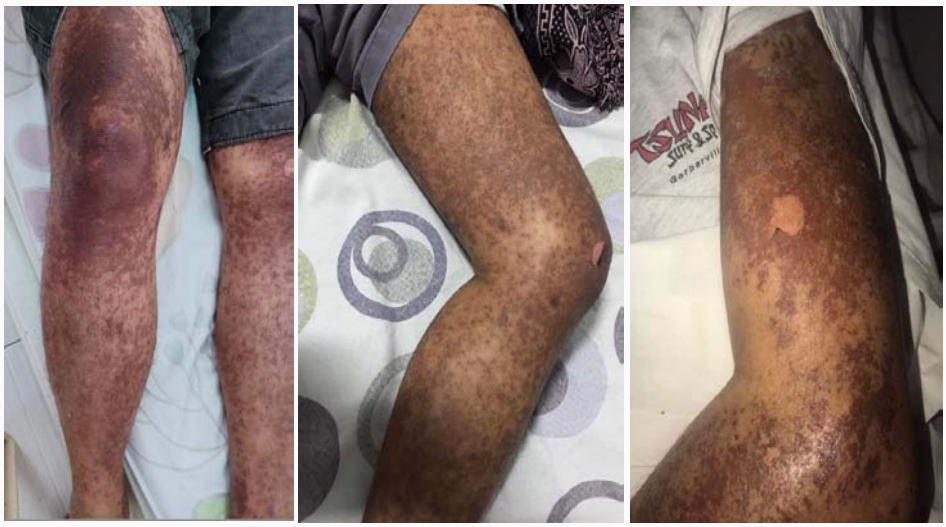

Figure 2: Generalized brown to hyperpigmented macules with surrounding erythema with beginning erosion.

Table 1: Laboratory work ups were requested which include CBC, BUN, creatinine, liver enzymes, electrolytes, HBA1c.

Test	Result	Range
BUN	**83.76 (H)**	17.00-40.00 mg/dL
Creatinine	**2.25 (H)**	0.80-1.30 mg/dL
SGPT	**373.5 (H)**	5.00-45.00 U/L
SGOT	**198.1 (H)**	5.00-35.00 U/L
Sodium	**128.2 (L)**	135.00-155.00 mEq/L
Potassium	4.27	3.50-5.50 mEq/L
Chlorine	101.5	97.00-108.00 mEq/L
HBA1c	4.5%	4.0-6.0%

pain around the oral mucosa but no erosions noted. Stevens Johnson Syndrome was suspected. Detailed drug history was elicited which revealed that for the past 2 years patient had been taking ace inhibitor for his hypertension, sitagliptin for his diabetes and salmeterol fluticasone puff for his chronic obstructive pulmonary disease. Since taking all these medications, there were no side effects noticed. No other recent medications taken that can contribute to the development of skin rashes. He did not report any allergies to medication and food. He denied smoking and drinking alcoholic beverage drink. His initial 2 doses of COVID-19 vaccine were completed 6 months ago, using inactivated whole-virus vaccine (Sinovac). During this time, no adverse event observed. In this case, the diagnosis of Stevens Johnson Syndrome from 3rd dose of COVID-19 vaccine was made based on the timeline, disease course and morphology of the cutaneous findings described as sudden appearance of generalized erythematous purpuric macules coalesced into sheets of necrosed skin with mucosal lesions and constitutional symptoms.

Table 2: Laboratory work ups were requested which include CBC, BUN, creatinine, liver enzymes, electrolytes, HBA1c.

	Results	Normal Values
Hemoglobin	**109.0 (L)**	120.00-160.00 g/L
Hematocrit	0.33	0.37-0.47
RBC	3.77	4.70–6.10 × 10^{12}/L
WBC	9.3	5.00-10.00 × 10^{9}/L
Neutrophils	0.85	0.55-0.65
Lymphocytes	0.09	0.25-0.35
Monocytes	0.06	0.00-0.05
Platelet count	205	150.00-450.00 × 10^{9}/L
MCV	87.5	80.00-96.00 fL
MCH	29.5	27.00-33.00 pg
MCHC	337.0	290.00-370.00 g/dL

Treatment and outcome

On admission, he was placed in an isolated room to avoid infection. Laboratory work ups were requested which include CBC,

BUN, creatinine, liver enzymes, electrolytes, HBA1c (Table 1, 2). He had elevated creatinine and liver enzymes on admission. Serial monitoring was done during his stay in the hospital. Referral to Dermatology and Ophthalmology were immediately placed. He was started on Hydrocortisone 100 mg/IV every 8 h for 5 days and Diphenhydramine/IV. Topical skin care was plain petroleum jelly. Application was instructed to be in a sterile environment. Mouthwash composed of mixed 120 mL Aluminum hydroxide and Magnesium hydroxide, 120 mL diphenhydramine solution, 2% lidocaine solution and 20 mL distilled water was instructed to be gargled three times a day to relieve the pain in the oral mucosa. Ophthalmology immediately treated him with fusidic acid ophthalmic solution and preservative-free hydrating eye drops. Contact precaution was strictly followed. After 5 days, his lesions started to regress as well as his constitutional symptoms. Hydrocortisone/IV was discontinued. Complete resolution of skin lesion was noted after 24 days and his laboratory parameters improved. He was discharged well.

Discussion

Stevens Johnson Syndrome is a rare, severe and potentially fatal delayed-type-four-hypersensitivity reaction. Medications are by far the most common trigger of this condition. In very rare instances, Stevens Johnson Syndrome could be caused by vaccination [3]. Incidence is 1.2 to 6.0 per million person-years for Stevens Johns Syndrome and 0.4 to 1.2 per million person-years for Toxic Epidermal Necrolysis [4]. Diagnosis is essentially clinical. It presents with a prodrome usually recorded as sore throat, fever, malaise and arthralgia proceeded by cutaneous manifestations. Morphology of the skin lesions can initially start as erythematous, dusky red or purpuric macules and have tendency to coalesce. Ninety-percent of the time, erosions of the buccal, ocular and genital mucosa are present [5]. In this case report, our patient experienced mucocutaneous manifestations with fever which clinically fits Stevens Johnson Syndrome 1 week after initiation of 3rd dose of COVID-19 vaccine using mRNA-1273. Per patient, he was able to tolerate his first 2 doses 6 months ago, using inactivated whole virus COVID-19 vaccine. This posts a question for a possible serious adverse effect of having heterologous COVID-19 vaccination. Stevens Johnson syndrome is extremely rare with vaccination. There were few reported cases in the literature and some of the vaccination mentioned to cause Stevens Johnson Syndrome were combined measles, mumps, rubella vaccine and influenza vaccine. Lately there were also cases noted after giving COVID-19 vaccine [6]. COVID-19 vaccines are newly developed vaccines, which were proven to be effective in preventing severe infection. It has two components: Virotropes and excipients. Both can cause severe drug reactions [7]. Different platforms have been used to produce COVID-19 vaccines, and these include nucleic acid (DNA and RNA), viral vector, and protein subunit and whole-virus platforms. These have been widely administered, but challenges have arisen, including vaccine supply shortages, rare adverse events and waning vaccine immunity. Heterologous prime–boost vaccination refers to a scheme in which the booster vaccination and prime vaccination utilize different platforms [8]. Due to large demands, supply became inadequate. Heterologous prime-boost vaccinations were proposed to respond in these challenges most especially in low to middle income countries. However, the immunogenicity and reactogenicity remain largely unclear. To date there are no published data examining the safety of having heterologous COVID-19 vaccines. Although, some reports mentioned that heterologous boost appeared to have increased reactogenicity [9].

Conclusion

There are multiple COVID-19 vaccines that have been approved for emergency use to accelerate vaccine roll-out. Heterologous prime-booster has been implemented most especially in low to middle income countries. However, this should be further studied and investigated with regards to its safety. This case adds to the evidence of a possible rare severe dermatological side effect of having heterologous vaccination.

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