Case Report

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Stevens–Johnson syndrome associated with pancytopenia: a case report

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Introduction and importance: Stevens–Johnson syndrome (SJS) is a rare and unusual hypersensitivity reaction to certain drugs like allopurinol, commonly used for treating gout. SJS is recognized by extensive necrosis and detachment of skin and mucus membranes. Pancytopenia, characterized by decreased levels of red blood cells, white blood cells and platelets, is an exceedingly rare occurrence in the rare disorder SJS.

Case presentation: The authors present a 61-year-old male who exhibited symptoms of fever and rash for 5 days accompanied by pancytopenia and liver injury.

Clinical discussion: The abdomen and bilateral lower extremities exhibited several well-defined dusky-colored hyperpigmented macular lesions. Initially, these lesions were small, tender, erythematous, and raised, later transitioning to a dark red. Multiple distinct ulcerations were present on the lips and buccal cavity. Additionally, there was denudation of the skin with bleeding observed between the toes of both legs. The causality was assessed as a definite adverse drug reaction according to the Naranjo and ALDEN algorithm. The patient received treatment consisting of intravenous steroid along with prophylactics antibiotics. The individual's pancytopenia was resolved without requiring any blood cells or plasma or platelet concentrate transfusion.

Conclusion: The exact pathophysiology of SJS associated with pancytopenia has not yet been fully elucidated. The authors' study hypothesized that the cause of pancytopenia in SJS could be either the direct cytotoxicity of drugs or immune-mediated damage to the bone marrow cells. Additional studies are necessary to establish the precise pathophysiology of the condition. Moreover, our study also indicates that pancytopenia can resolve in SJS without the need for blood cells or plasma or platelet concentrate transfusion. Once more, further studies are required to establish precise management strategies for managing SJS associated with pancytopenia.

Keywords: allopurinol, hypersensitivity, pancytopenia, severe cutaneous adverse reaction, Stevens–Johnson syndrome

HIGHLIGHTS

- Pancytopenia is an exceedingly rare occurrence in the rare disorder Stevens–Johnson syndrome (SJS). The exact pathophysiology of SJS associated with pancytopenia has not yet been fully elucidated.
- Our study hypothesized that the cause of pancytopenia in SJS could be either the direct cytotoxicity of drugs or immune-mediated damage to the bone marrow cells. Additional studies are necessary to establish the precise pathophysiology of the condition.
- Moreover, our study also indicates that pancytopenia can resolve in SJS without the need for blood cells or plasma or platelet concentrate transfusion. Once more, further studies are required to establish precise management strategies for managing SJS associated with pancytopenia.

Introduction

Stevens–Johnson syndrome(SJS) is an infrequent hypersensitivity reaction to some medications identified by widespread necrosis and detachment of skin and mucus membranes[1,2]. The incidence of SJS associated with drug use is 1.8 per 10^6 persons per year[3]. Allopurinol is frequently associated with SJS or toxic epidermal necrolysis (TEN)[4]. Hematological abnormalities such as pancytopenia are seldom reported in the rare condition SJS[5,6]. We present a 61-year-old with SJS and pancytopenia. The exact pathophysiology of SJS associated with pancytopenia has not yet been fully elucidated.

Case presentation

A 61-year-old male presented with chief complaints of rash with fever for 5 days. The rash first manifested on the extensor surface of lower limbs, then extended to the abdomen followed by the extensor surfaces of upper limbs, and eventually appeared on the

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face and scalp within a span of 48 h. The patient had recently been diagnosed with gout characterized by an elevated level of uric acid identified during a routine blood test. As a result, patient started allopurinol treatment and experienced rash and fever on 28th day of administration. Upon further inquiry, it was revealed that the patient had no history of herbal medicine consumption, alcohol use, or insect bites. The patient had no history of similar illness in the past. There were no other medications the patient had been taking except for amlodipine for hypertension. There was no notable family history reported. The highest recorded temperature was 103°F, accompanied by chills and rigor, which were alleviated by antipyretic medication.

During general examination, the patient appeared pale and unwell. His blood pressure was recorded as 120/80 mmHg, with a pulse rate of 120 beats per min, regular rhythm, respiratory rate of 22 breaths per min, and a temperature of 98°F. Additionally, bilateral eye congestion was observed. During the local examination, multiple well-defined dusky-colored hyperpigmented macular lesions were present over the abdomen (Fig. 1) and bilateral lower extremities. Initially, the lesions were small, multiple, tender, erythematous, raised, later transitioning to dark red. Multiple well-defined ulcerations were noted on the lips and buccal cavity (Fig. 2). Furthermore, denudation of skin with bleeding was also observed between the toes of both legs (Fig. 3). No blisters, vesicles, or pus formation were observed in the lesions. Nikolsky's sign was present. The extent of body surface area involvement was calculated to be 7% of the total body surface area at the time of presentation. Systemic examination was unremarkable.

The patient's blood work revealed a hemoglobin level of 10.2 g/dl, a white blood cell count of 3800/mm3, a red blood cell count of 2.5 million/mm^3 and a low platelet count of 81 000/mm^3 on his first day of admission. Liver function tests (LFT) showed a total bilirubin of 1.5 mg/dl, direct bilirubin of 0.5 mg/dl, aspartate aminotransferase (AST) of 172 U/l, and alanine aminotransferase (ALT) of 131 U/l. The serum uric acid level was 8.3 mg/dl. Renal function tests (RFT) revealed a blood urea level of 60 mg/dl and a creatinine level of 1.6 mg/dl. Routine urine examination showed 6–8 red blood cells (RBCs) per high power field (HPF), 2–3 pus cells per HPF, and 2–3 epithelial cells per HPF. Abdominal and pelvic ultrasound scan findings included mild hepatomegaly, right nephrolithiasis, bilateral simple renal cysts, and prostatomegaly. Serology tests for leptospira, scrub typhus, malaria, and dengue were negative. A peripheral blood smear revealed eosinophilia, with 10% eosinophils. Histopathological examination revealed full-thickness necrosis of the epidermis with infiltration of inflammatory cells into the dermis. According to the Naranjo and ALDEN algorithm, the causality was assessed as a definite adverse drug reaction. The mortality rate was estimated to be 35% using SCORTEN criteria.

His vital signs were regularly monitored throughout his hospital stay. The use of allopurinol was discontinued. He received intravenous (IV) fluids and was started on IV injection of

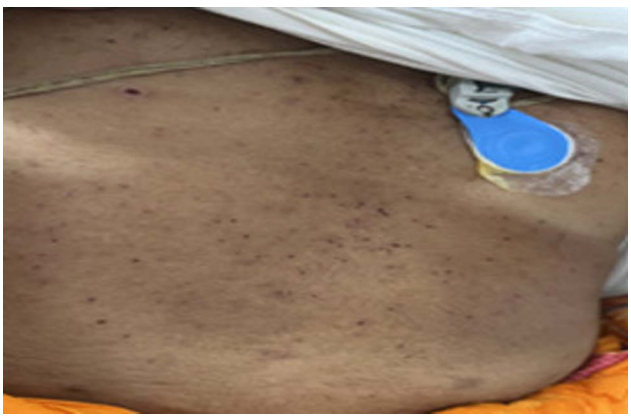

Figure 1. Hyperpigmented macular lesions over the abdomen.

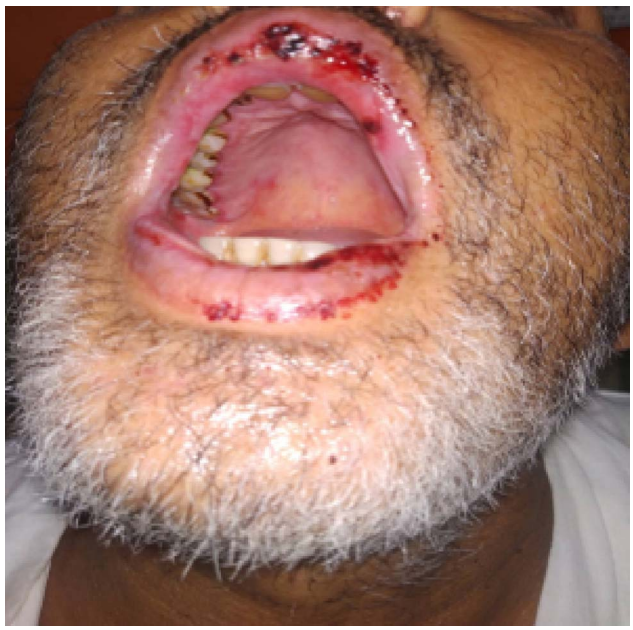

Figure 2. Multiple well-defined ulcerations on the lips and buccal cavity.

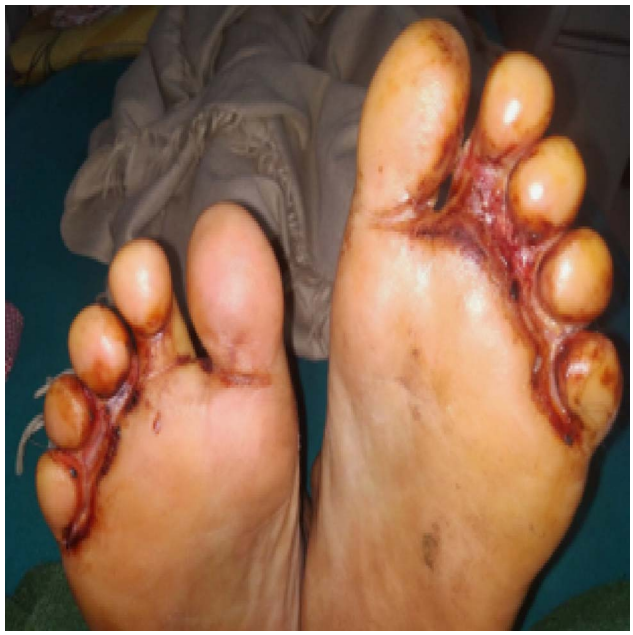

Figure 3. Denudation of skin with bleeding between the toes of both legs.

dexamethasone 6 mg once daily for 3 days. Additionally, he was administered prophylactic antibiotics including IV injection of ceftriaxone (given for 5 days), IV injection of doxycycline (given for 1 day), and IV injection of clindamycin for 4 days. Simple dressing using paraffin gauze with topical fusidic acid and betamethasone was performed to manage skin and mucous membrane wounds. Gradually, he began to exhibit improvement, as indicated by the healing ulcers on his lips and buccal cavity, as well as the gradual disappearance of the rash. Red blood cell and white blood cell levels normalized, reaching 4.5 million/mm^3 and 4900/mm^3, respectively, by the fourth day of admission. Platelet levels showed gradual improvement, registering at 105 000 per mm^3 on the same day. No transfusions of red blood cells, plasma, or platelets were required for these improvements. The patient was discharged on the 5th day after admission with oral steroids, oral antibiotics, topical ointments, and scheduled weekly follow-up appointments. All laboratory investigations, including CBC reports, were normal during his first follow-up appointment, which occurred one week after his discharge. The patient was compliant with the prescribed medications. The steroid was gradually tapered during each subsequent follow-up appointment and stopped after four weeks from discharge.

Discussion

SJS/TEN is a rare and unusual hypersensitivity reaction to certain drugs with an incidence of 1.8 per 106 persons per year[1,3]. The drugs suspected to cause SJS belonged to various classes, including antiepileptics, antiretrovirals, sulphonamides, NSAIDs, antituberculosis (ATT) drugs, fluoroquinolones, and penicillin[7]. Allopurinol was noted to be the most frequently associated drug with SJS/TEN[1,4]. The Human leukocyte antigen (HLA)-B*58:01 allele serves as a genetic marker for allopurinol-induced severe cutaneous adverse reactions in Asian populations[8,9]. Asian patients were found to be at a 2-fold higher risk of developing SJS or Toxic Epidermal Necrolysis (TEN) when compared with Caucasian patients[1]. The genetic risk factors for SJS are more prevalent in the Asian population but due to inadequate healthcare regulations and financial constraints, pharmacogenetic testing for high-risk drugs such as allopurinol and carbamazepine is not feasible in many Asian regions[10].

Cases reported for allopurinol-induced SJS involved middle-aged adults to an elderly population, similar to our case[11,12]. Other commonalities included the indication for allopurinol use, which was gout in all cases, and the duration of drug use ranging from 1 to 2 months[11,12]. The presentation also resembled our case, beginning with a maculopapular rash that affected both the skin and mucosal surfaces[11,12].

Common hematological manifestation of SJS include anemia, leukopenia, and neutropenia but pancytopenia is an exceedingly rare occurrence[5,6]. Pancytopenia was noted with a platelet count of 81 000/mm^3, while the red blood cell (RBC) count was 2.5 million/mm^3 and the white blood cell (WBC) count was 3800/mm^3 in our study. Pancytopenia in patients with SJS or TEN typically begins with severe lymphopenia, which may result from a direct antigen reaction with the cells or antigens affecting bone marrow function[13]. However, the precise mechanism of pancytopenia associated with SJS has not yet been established. Our study hypothesized that the cause of pancytopenia in SJS could be either the direct cytotoxicity of drugs or immune-mediated damage to the bone marrow cells. Additional studies are necessary to establish the precise pathophysiology of the condition. Liver injury is a common association of SJS, characterized by elevated liver enzymes, bilirubin levels, and other functional parameters[14]. In our case, there was a notable increase in serum aminotransferase levels, along with mild hepatomegaly observed on ultrasound.

In some studies, discontinuation of allopurinol and management with steroid and prophylactic antibiotics have been effective[6,12]. Similar to these findings, our case improved after discontinuing allopurinol and initiating IV steroid and prophylactic antibiotics. In previous studies, pancytopenia associated with SJS was managed with red blood cell transfusion and fresh frozen plasma transfusion[6]. Unlike managing pancytopenia with blood cell or plasma or platelet concentrate transfusion, pancytopenia was conservatively managed in our study. Further studies are required to establish precise management strategies for managing SJS associated with pancytopenia.

Patient perspective

The patient expressed contentment with the care received and their progress toward recovery.

Conclusion

SJS is a rare and unusual adverse effect caused by certain drugs like allopurinol. Pancytopenia is an exceedingly rare occurrence in the rare disorder SJS. The exact pathophysiology of SJS associated with pancytopenia has not yet been fully elucidated. Our study hypothesized that the cause of pancytopenia in SJS could be either the direct cytotoxicity of drugs or immune-mediated damage to the bone marrow cells. Additional studies are necessary to establish the precise pathophysiology of the condition. Moreover, our study also indicates that pancytopenia can resolve in SJS without the need for blood cells or plasma or platelet concentrate transfusion. Once more, further studies are required to establish precise management strategies for managing SJS associated with pancytopenia.

Ethical approval

This is a case report. So, it does not require a formal ethical committee approval.

Consent

A written informed consent was obtained from the patient and his legal guardian to publish this case report and any accompanying images.

Source of funding

No funding was used in this study.

Author contribution

P.P.: conceptualization, data curation, formal analysis, writing draft. S.S.: data curation, formal analysis, writing draft. A.S.: data curation, formal analysis, writing draft. S.M.: formal analysis,

reviewing and editing draft. B.A.: reviewing and editing draft, supervision.

Conflicts of interest disclosure

No conflict of interest.

Research registration unique identifying number (UIN)

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Guarantor

Bibek Adhikari.

Data availability statement

The data that support the findings of this study are available from the corresponding author on valid request.

Provenance and peer review

Not commissioned and externally peer-reviewed.

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