



Stevens–Johnson Syndrome/Toxic Epidermal Necrolysis in a Pediatric Patient With Dengue Hemorrhagic Fever: A Case Report

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ABSTRACT

Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute, life-threatening mucocutaneous reactions characterised by widespread epidermal necrosis. These conditions are characterised by skin blisters and involvement of the oral, nasal, ocular, and genital mucosa. SJS/TEN are immune-mediated hypersensitivity reactions, most often due to drugs. Infections, including viruses, have also been associated with SJS/TEN. Reactivation of latent viruses can lead to drug eruptions.

Case Illustration: A 4-year-old boy presented with a 4-day history of fever, abdominal and leg pain, followed by diffuse erythematous maculopapular rashes on the face, upper and lower limbs. Laboratory tests showed leukocytosis, thrombocytopenia, and

positive dengue IgM and IgG antibody test, leading to an initial diagnosis of Dengue Hemorrhagic Fever with viral exanthema. He was treated with ceftriaxone and metronidazole. Several days later, oral ulcers, conjunctival injection, dark erythematous rashes, and skin desquamation developed. The clinical course prompted a revised diagnosis of SJS.

Discussion: *SJS/TEN are acute damage skin conditions and mucosal epithelium as a result of immune-mediated responses. The exact pathogenesis of SJS remains unclear; however, drug exposure is recognized as the primary trigger. In certain cases, SJS may also be induced by viral infections. This case report aims to review current knowledge regarding various aspects of SJS and the potential role of viral infections in drug-induced hypersensitivity reactions.*

Conclusion : *Based on existing case reports and journals, it cannot be denied that viral infections play a role in the development of SJS/TEN.*

Keywords : *SJS, TEN, Viral exanthema, Dengue Hemorrhagic Fever*

INTRODUCTION

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe adverse drug reactions characterized by widespread epidermal necrolysis. These conditions are manifested by cutaneous blistering and involvement of the mucous membranes of the oral cavity, nose, eyes, and genitalia. Stevens–Johnson syndrome (SJS) involves less than 10% of the body surface area and is characterized by significant detachment of the skin and mucosal epithelium, particularly affecting the oropharyngeal, ocular, urogenital, and anal mucosae. In contrast, TEN involves more than 30% of the body surface area, whereas cases involving 10–30% are classified as SJS/TEN overlap. The mortality rates of SJS and TEN are approximately 1–5% and 25–30%, respectively, and survivors may experience long-term multi-organ sequelae following the acute phase.¹

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) is an immune-mediated hypersensitivity reaction, with more than 200 drugs implicated in its development. Common triggers include nonsteroidal anti-inflammatory drugs (NSAIDs), sulfonamide derivatives, β -lactam antibiotics, anticonvulsants, antiretroviral agents, contrast media, and allopurinol.¹ Epidemiological studies have demonstrated that drug hypersensitivity reactions account for approximately 70–80% of reported cases, particularly those associated with NSAIDs, antibiotics, and anticonvulsants. Clinical manifestations may occur within the first few days after initiation of a new medication and may develop up to eight weeks following exposure.²

In the pediatric population, the clinical manifestations of SJS may resemble viral exanthematous illnesses, such as measles, rubella, or other viral infections characterized by fever and generalized rash.³ This similarity in presentation frequently results in delayed diagnosis and appropriate management.⁴ Although less common, other triggering mechanisms of SJS have been associated with vaccination or infection, particularly viral infections. The most frequently implicated viruses include human immunodeficiency virus (HIV), influenza virus, herpes simplex virus, and Epstein–Barr virus (EBV). Viral, bacterial, and other infectious agents may precipitate this condition, and vaccines against meningococcal B disease, yellow fever, and influenza have also

been associated with reported cases.⁴ However, the association with less common pathogens, such as cytomegalovirus or dengue virus, is exceedingly rare, with only a limited number of cases reported to date.

Several mechanisms have been proposed to explain the association between viral infections and SJS/TEN. Following viral infection, the host immune response may induce a state of heightened immune activation, thereby increasing susceptibility to exaggerated reactions to subsequently administered medications. In addition, virus-induced production of proinflammatory cytokines and chemokines, particularly interferon- γ (IFN- γ), may disrupt immune homeostasis by upregulating the expression of major histocompatibility complex class II (MHC II) molecules on antigen-presenting cells, thereby enhancing drug-hapten presentation and T-cell activation. Another proposed mechanism involves the reactivation of latent viruses, which may contribute to delayed hypersensitivity reactions through the generation of immunogenic antigens and subsequent immune dysregulation.⁴

The role of viral infections in the pathogenesis of SJS/TEN remains incompletely understood. Current evidence suggests two possible pathways. First, certain viral infections may directly induce SJS/TEN in the absence of drug exposure. Second, viruses may act as catalysts or triggers by modifying immune responses or altering drug metabolism.⁴ We report a case of SJS potentially associated with dengue virus infection, a relationship that has rarely been described in the literature and presents significant challenges in identifying the underlying etiological agent.⁵ This case highlights the potential role of dengue infection in the development of SJS and provides valuable insights for clinicians in recognizing and managing similar cases.

CASE ILLUSTRATION

A 4-year-old boy presented on August 28, 2025, with a 4-day history of fever. The fever was accompanied by abdominal pain, productive cough, myalgia involving the upper and lower extremities, and the appearance of erythematous rashes on the affected areas (Figures 1A–C). The patient had decreased appetite but maintained adequate oral fluid intake. There was no history of

epistaxis or gingival bleeding. He had not passed stool for the preceding 4 days, whereas urinary output remained normal. The patient had no significant past medical history. However, several children in his neighborhood had recently been diagnosed with dengue fever. His immunization history was incomplete.



Figure 1. (A–C) Clinical photographs obtained on hospital day 1 demonstrating multiple diffuse erythematous maculopapular eruptions of miliary to lenticular size.

On physical examination, the patient was alert and oriented, and his vital signs were within normal limits. Laboratory investigations performed on August 28, 2025, revealed leukocytosis (white blood cell count, 15,600/ μ L) and thrombocytopenia (platelet count, 96,000/ μ L). Serological testing for dengue demonstrated positive dengue IgM and IgG antibodies, and a diagnosis of dengue hemorrhagic fever (DHF) was established.

During hospitalization, the patient received intravenous fluid resuscitation with Ringer's lactate (1,200 mL/day), intravenous omeprazole (10 mg twice daily), intravenous ondansetron (2 mg three times daily), paracetamol (150 mg as needed for fever), intravenous dexamethasone (5 mg three times daily), intravenous ceftriaxone (1,000 mg once daily), and intravenous metronidazole (75 mg three times daily). He also received nebulized salbutamol (1 respule) and 3 mL of 0.9% sodium chloride every 8 hours.

On the third day of hospitalization, the platelet count decreased to 32,000/ μ L. From hospital days 4 to 6, the platelet count gradually recovered, reaching 256,000/ μ L on September 2, 2025, and

discharge planning was initiated. However, on day 6, the patient developed generalized erythematous eruptions accompanied by epiphora and recurrent fever. The patient was clinically diagnosed with measles in the absence of confirmatory measles serologic testing. On day 7, the patient remained febrile and developed conjunctival injection with excessive tearing and multiple painful oral ulcers that significantly impaired oral intake. Nystatin oral drops (1 mL four times daily) and curcuma supplementation were prescribed. On day 10, a dermatology consultation was requested, and the patient was diagnosed with viral exanthem.

On hospital day 11, the erythematous lesions became dusky and hyperpigmented (Figures 2A and 2B), accompanied by skin dryness, desquamation, and the development of fluid-filled blisters. Physical examination revealed a positive Nikolsky sign (Figure 2C). Stevens–Johnson syndrome was subsequently suspected, and discontinuation of unnecessary medications was recommended. The antibiotic regimen was changed, and treatment with intravenous methylprednisolone (24 mg/day), cetirizine (5 mg/day), and white petrolatum applied twice daily was initiated.



Figure 2. (A, B) Clinical photographs obtained on hospital day 11 demonstrating multiple, diffuse erythematous plaques with overlying scales. **(C)** Multiple bullae, some of which had ruptured, with a positive Nikolsky sign.

On the same day, ceftriaxone and metronidazole were discontinued and replaced with oral clindamycin (60 mg four times daily). The vesicular lesions progressively evolved into bullae, and by day 14, many of the bullae had ruptured, resulting in widespread epidermal detachment and generalized desquamation (Figures 3A–C). A diagnosis of SJS that developed into TEN was established, and the patient was treated with cetirizine (5 mg/day), white petrolatum twice daily, topical mupirocin cream applied twice daily to eroded areas, intravenous methylprednisolone (31.25 mg/day), and oral clindamycin (60 mg four times daily).

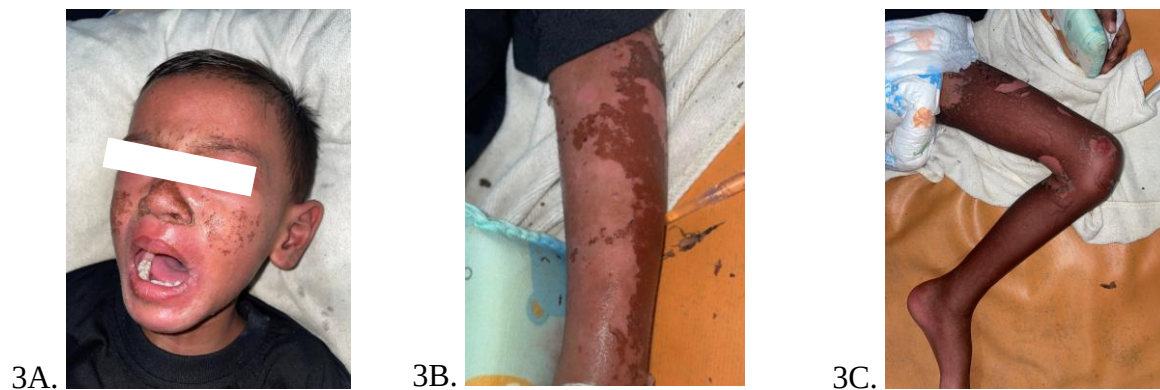


Figure 3. (A–C) Clinical photographs on hospital day 14 showing multiple, diffuse erythematous plaques with overlying scales and widespread desquamation.

From hospital days 16 to 18, the methylprednisolone dose was tapered to 16 mg/day, followed by a further reduction to 8 mg/day from hospital days 19 to 21. By hospital day 19, the patient's condition had markedly improved, with no new erythematous lesions or blister formation observed (Figures 4A–C), and he was subsequently discharged for outpatient follow-up.

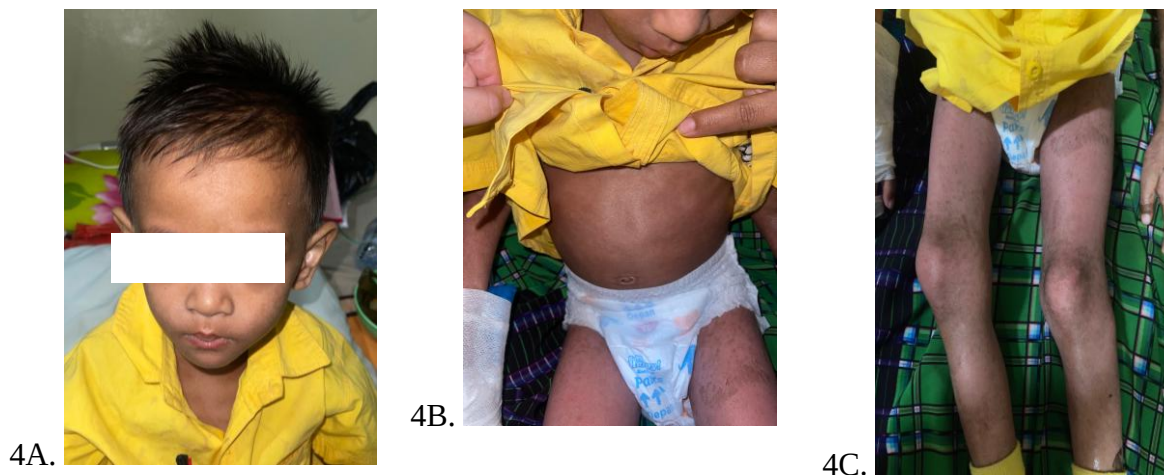


Figure 4. (A–C) Clinical photographs on hospital day 19 showing multiple, diffuse hyperpigmented plaques with residual scaling, consistent with post-inflammatory hyperpigmentation during the recovery phase.

DISCUSSION

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), also known as Lyell’s disease, are rare, life-threatening mucocutaneous disorders characterized by extensive epidermal and mucosal epithelial necrosis resulting from an immune-mediated process. Although the precise pathogenesis remains incompletely understood, medications represent the principal etiologic factor.⁶ *Steven Johnson Syndrome* is defined by epidermal detachment involving less than 10% of the body surface area (BSA), whereas involvement of 10–30% of the BSA is classified as SJS/TEN overlap and involvement of more than 30% of the BSA is defined as TEN. The disease is typically preceded by a prodromal phase consisting of fever, malaise, sore throat, cough, rhinorrhea, and headache that occurs 1–3 days before the onset of mucocutaneous lesions. Subsequently, erythematous macules coalesce and progress to vesiculobullous lesions and epidermal detachment, frequently accompanied by mucosal and systemic involvement.⁶

Epidemiological studies have shown that approximately 70–80% of SJS/TEN cases are attributable to drug hypersensitivity reactions, most commonly associated with nonsteroidal anti-inflammatory drugs, antibiotics, and anticonvulsants. Nevertheless, infections and vaccinations have also been implicated as potential triggers. The viruses most frequently associated with SJS/TEN include human immunodeficiency virus (HIV), influenza virus, herpes simplex virus, and Epstein–Barr virus (EBV). In contrast, the association between SJS/TEN and less common pathogens, such as cytomegalovirus and dengue virus, remains exceedingly rare, with only a limited number of cases reported in the literature.⁵

In the present case, the patient initially presented with fever and thrombocytopenia, followed by the development of generalized erythematous maculopapular eruptions. The subsequent appearance of cough and conjunctivitis led to an initial diagnosis of viral exanthem. This presentation is consistent with the typical manifestations of viral exanthems, which generally begin with fever and prodromal symptoms, including malaise, headache, and upper respiratory tract symptoms.⁷ On hospital day 7, the patient developed painful oral ulcerations and conjunctival involvement, followed by the appearance of widespread vesiculobullous lesions. Physical examination revealed multiple bullae on an erythematous base, some of which had ruptured to form erosions, accompanied by a positive Nikolsky sign. These findings fulfilled the clinical criteria for SJS, a severe mucocutaneous disorder characterized by extensive epidermal necrosis and detachment.⁶ As the extent of epidermal detachment progressed to involve more than 30% of the total body surface area, the diagnosis was subsequently reclassified as TEN.⁶ The development of SJS in this patient was initially suspected to be drug-induced, particularly in association with ceftriaxone or metronidazole, both of which had been administered during hospitalization. The patient had also received paracetamol, which has been implicated in several reports of SJS/TEN occurring in the setting of concurrent viral infections.^{8,9} However, despite the predominance of drug-induced cases, the possibility of virus-associated SJS/TEN should not be overlooked. In our patient, the initial presentation closely resembled viral exanthem, resulting in a delay in diagnosis and highlighting the diagnostic challenge posed by the overlapping clinical manifestations of viral exanthems and early-stage SJS/TEN.

A small proportion of SJS/TEN cases have been associated with infectious agents. Common manifestations of drug hypersensitivity reactions, including maculopapular exanthems and urticaria, often resemble virus-induced eruptions. Furthermore, acute viral infections, such as measles and rubella, may be clinically indistinguishable from drug-induced exanthems. Dengue infection can also mimic other dermatologic conditions, including SJS/TEN, because capillary dilatation and increased vascular permeability may result in generalized macular or maculopapular eruptions, occasionally accompanied by petechiae.³

Viral infections may also act as cofactors that augment immune stimulation and predispose patients to severe cutaneous adverse reactions. Numerous clinical observations have demonstrated that viral infections can trigger or exacerbate drug-induced eruptions. Epstein–Barr virus infection is a well-recognized example, with a markedly increased incidence of cutaneous eruptions among patients receiving β -lactam antibiotics during acute infection. Similarly, herpesviruses have been implicated in the pathogenesis of severe drug reactions, particularly drug reaction with eosinophilia and systemic symptoms (DRESS).¹⁰

Chung et al. reported six cases of SJS associated with Coxsackievirus infection. These patients exhibited characteristic blistering lesions of SJS accompanied by mild erosions of the external lips but lacked the severe hemorrhagic crusting and extensive oral mucosal involvement that are typically observed in classic SJS. Such findings may provide important clinical clues suggesting virus-associated SJS/TEN. Furthermore, Shen et al. demonstrated that viral infections, particularly herpes simplex virus and human herpesvirus 7, may contribute to the development of SJS/TEN by inducing a sensitized immune response. This association was supported by polymerase chain reaction and lymphocyte transformation testing.⁴

Human immunodeficiency virus represents another important viral factor associated with SJS/TEN. The increased susceptibility observed in patients with HIV has been attributed to immune dysregulation secondary to CD4⁺ T-cell depletion and alterations in cytokine profiles. Elevated serum IgE levels and a shift from a T helper type 1 (Th1)-dominant to a T helper type 2 (Th2)-dominant immune response have been proposed to contribute to the increased risk of severe cutaneous adverse reactions in this population.⁴

This case has several limitations. First, it was difficult to determine whether SJS was primarily triggered by dengue virus infection or by medications administered during the course of the illness, particularly given the concomitant use of multiple drugs. Second, the limited number of published cases and studies on virus-associated SJS/TEN restricts our understanding of the pathogenic mechanisms and causal relationship between viral infections and the development of SJS/TEN.

CONCLUSION

In the present case and based on the available literature, several potential mechanisms may explain the development of SJS/TEN in patients with dengue hemorrhagic fever. SJS/TEN may occur as a direct consequence of drug exposure, whereas viral infections may either induce SJS/TEN independently or act as cofactors by modulating immune responses and altering drug metabolism, thereby increasing susceptibility to drug hypersensitivity reactions. Establishing a diagnosis of virus-associated SJS/TEN requires appropriate virological investigations, including serologic testing for suspected pathogens. In our patient, both dengue IgM and IgG antibodies were positive, supporting a recent dengue virus infection.

Nevertheless, the interaction between viral infections and the development of SJS/TEN remains incompletely understood, and the underlying pathogenic mechanisms require further investigation. Furthermore, despite the temporal association with dengue infection, a drug-induced etiology cannot be definitively excluded in this case, particularly given the concomitant exposure to multiple medications.

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