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RESEARCH ARTICLE

Intracerebral Hemorrhage in the Setting of Lamotrigine-Induced Stevens-Johnson Syndrome: A Case Report

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ABSTRACT

Stevens-Johnson syndrome is a rare but life-threatening severe cutaneous adverse reaction that may involve multiple organ systems and is commonly associated with medication exposure. Although clinicians are familiar with complications such as sepsis, shock, and multiorgan dysfunction, rare neurological complications may be overlooked. We report the case of a 41-year-old Saudi male with epilepsy who developed Stevens-Johnson syndrome following recent initiation and dose escalation of lamotrigine. The patient presented with fever, generalized malaise, and a rapidly progressive diffuse erythematous maculopapular rash associated with painful oral erosions and systemic symptoms. Examination demonstrated widespread skin involvement with mucosal lesions consistent with Stevens-Johnson syndrome. The patient was admitted for close monitoring due to the severity of the reaction and risk of rapid deterioration. During hospitalization, he developed sudden severe headache, repeated vomiting, fluctuating level of consciousness, and objective unilateral weakness. These findings prompted urgent neurological evaluation, and non-contrast computed tomography of the brain revealed an acute intracerebral hemorrhage with intraventricular extension. The patient was subsequently managed in an intensive care setting with multidisciplinary involvement from dermatology, neurology, neurosurgery, and critical care teams. Supportive management of Stevens-Johnson syndrome was continued alongside neurological monitoring and management of the intracranial hemorrhage. The patient's neurological status gradually improved, with concurrent clinical improvement of the cutaneous manifestations following discontinuation of the suspected medication. This case highlights an uncommon but important complication of Stevens-Johnson syndrome and emphasizes that neurological deterioration should not automatically be attributed to sepsis or systemic inflammation. New focal neurological deficits, severe headache, vomiting, or unexplained decline in consciousness should prompt urgent investigation for intracranial pathology. Maintaining diagnostic vigilance and recognizing atypical disease progression may facilitate early diagnosis and improve outcomes in patients with severe drug-induced reactions.

KEYWORDS

Stevens-Johnson Syndrome, Rash, Oral Mucosa, Fever, Brain Hemorrhage, Sepsis.

ARTICLE INFORMATION

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Introduction

Stevens-Johnson syndrome (SJS) is a rare, severe mucocutaneous hypersensitivity reaction characterized by extensive epidermal necrosis, detachment of the skin, and involvement of one or more mucosal surfaces. Together with toxic epidermal necrolysis

(TEN), it represents a spectrum of the same disease process, with classification based primarily on the extent of epidermal detachment. SJS is defined by involvement of less than 10% of the body surface area, TEN involves more than 30%, and cases with 10% to 30% epidermal detachment are classified as SJS/TEN overlap. Although uncommon, these conditions are associated with substantial morbidity and mortality and remain among the most serious dermatologic emergencies encountered in clinical practice. Early recognition, prompt withdrawal of the offending agent, and aggressive supportive management are essential to improve outcomes. [1,4,8]

The estimated annual incidence of SJS and TEN ranges from one to six cases per million population, with variations reported across different geographic regions and patient populations. Despite their rarity, these disorders account for a disproportionate number of dermatologic intensive care admissions because of their rapid progression and the potential for life threatening systemic complications. Mortality is estimated to range from approximately 5% to 10% in SJS and may exceed 30% in patients with TEN, particularly in elderly individuals and those with significant comorbidities. Several factors influence prognosis, including age, extent of skin detachment, renal impairment, malignancy, and metabolic abnormalities. The SCORTEN severity score remains the most widely used prognostic tool and has been validated for predicting mortality in patients with SJS and TEN. [4,8,10]

The pathogenesis of SJS is complex and involves a delayed type IV hypersensitivity reaction mediated predominantly by cytotoxic T lymphocytes and natural killer cells. Following exposure to an offending trigger, activated immune cells release several cytotoxic mediators, including granulysin, perforin, granzyme B, and Fas ligand, which induce widespread keratinocyte apoptosis. Among these mediators, granulysin has been identified as a key contributor to epidermal destruction and is strongly associated with disease severity. Genetic susceptibility also plays an important role in disease development, with several human leukocyte antigen alleles demonstrating strong associations with drug induced SJS in specific ethnic populations. These findings have contributed to the implementation of pharmacogenetic screening before initiating certain high risk medications in selected populations. [4,13,14]

Medications remain the leading cause of SJS and TEN worldwide. High risk drugs include aromatic anticonvulsants such as carbamazepine, phenytoin, lamotrigine, and phenobarbital, as well as sulfonamide antibiotics, allopurinol, nonsteroidal anti inflammatory drugs of the oxicam group, nevirapine, and several newer targeted therapies. The highest risk generally occurs within the first eight weeks after initiation of the offending medication, although the timing may vary depending on prior exposure and individual susceptibility. Infectious agents, particularly *Mycoplasma pneumoniae*, herpes simplex virus, and other viral infections, are recognized causes, especially among children and young adults. In a small proportion of patients, no identifiable trigger can be established despite extensive evaluation. [4,9,13]

Patients typically present with a prodromal illness characterized by fever, malaise, sore throat, cough, conjunctival irritation, and generalized fatigue several days before the appearance of cutaneous lesions. This is followed by the rapid development of painful erythematous or purpuric macules that gradually coalesce and progress to blistering and epidermal detachment. Mucosal involvement is present in most patients and frequently affects the oral cavity, eyes, and genital tract, resulting in painful erosions that interfere with oral intake, vision, and urinary function. The Nikolsky sign is commonly positive, reflecting the loss of epidermal integrity. Because the early manifestations may resemble more common viral exanthems or drug eruptions, diagnosis during the initial stages can be challenging, potentially delaying appropriate management. [1,4,10]

The diagnosis of SJS is primarily clinical and is supported by characteristic skin findings, recent exposure to a high risk medication or infection, and histopathological examination when necessary. Skin biopsy typically demonstrates full thickness epidermal necrosis with subepidermal separation and sparse lymphocytic inflammation. Although histopathology is useful in confirming the diagnosis and excluding alternative blistering disorders, treatment should not be delayed while awaiting biopsy results if clinical suspicion is high. Early discontinuation of the suspected causative agent remains the single most important intervention and has consistently been associated with improved survival. [4,10,13]

Management requires a multidisciplinary approach involving dermatologists, intensivists, ophthalmologists, burn specialists, and other disciplines according to the pattern of organ involvement. Supportive care remains the cornerstone of treatment and includes meticulous wound care, fluid and electrolyte replacement, nutritional support, pain control, temperature regulation, and prevention of secondary infection. Patients with extensive skin detachment are frequently managed in specialized burn or intensive care units because their physiologic disturbances closely resemble those observed in major burn injuries. The use of systemic therapies including corticosteroids, intravenous immunoglobulin, cyclosporine, tumor necrosis factor inhibitors, and other immunomodulatory agents continues to be debated. Although several studies and recent systematic reviews suggest potential benefits with selected therapies, evidence remains heterogeneous, and treatment decisions are often individualized according to disease severity, institutional experience, and patient characteristics. [4,5,6,10]

Complications are common and frequently determine patient outcomes. Loss of the skin barrier predisposes patients to dehydration, electrolyte disturbances, bacterial infection, and sepsis, which remains one of the leading causes of death in affected individuals. Respiratory complications including pneumonia, airway epithelial sloughing, and acute respiratory distress syndrome may further contribute to morbidity. Ocular involvement occurs in the majority of patients and ranges from mild conjunctivitis to severe corneal ulceration, symblepharon formation, chronic dry eye disease, and permanent visual impairment. Long term sequelae involving the skin, nails, oral cavity, and genitourinary tract may significantly affect quality of life long after recovery from the acute illness. Consequently, clinical attention is often directed toward preventing infection, maintaining hemodynamic stability, and preserving organ function during the critical phase of the disease. [4,6,10,15]

In contrast, neurological complications of SJS have received relatively little attention in the literature and remain poorly understood. Reported manifestations include seizures, encephalopathy, aseptic meningitis, peripheral neuropathy, cranial nerve involvement, and various immune mediated neurological disorders, although these events are exceedingly uncommon. Whether these complications result from direct immune mediated injury, severe systemic inflammation, metabolic disturbances, treatment related effects, or secondary complications of critical illness remains uncertain. Their rarity has limited the ability to establish clear pathogenic mechanisms or evidence based management strategies, and most available data originate from isolated case reports or small case series. As a result, neurological deterioration in patients with SJS may initially be attributed to more common causes such as sepsis, electrolyte imbalance, hypoxia, or medication effects rather than primary intracranial pathology. [11,13,14]

Among these uncommon neurological manifestations, intracranial hemorrhage represents an exceptionally rare and potentially catastrophic complication. Only isolated reports have described spontaneous intracerebral or intracranial bleeding occurring during the course of SJS or TEN, and the true incidence remains unknown. Several mechanisms have been proposed, including severe systemic inflammation, endothelial injury, disseminated intravascular coagulation, thrombocytopenia, coagulopathy, and profound multiorgan dysfunction, although a direct causal relationship has not been established. Because critically ill patients with SJS frequently develop altered mental status related to sepsis, shock, metabolic abnormalities, or sedative medications, neurological decline may not immediately prompt neuroimaging. Consequently, intracranial hemorrhage may remain unrecognized until significant neurological injury has occurred, contributing to delayed diagnosis and poor outcomes. Increased awareness of this rare complication is therefore important, particularly in patients who develop unexplained neurological deficits or persistent deterioration despite otherwise appropriate supportive management.

The present case describes a patient with Stevens-Johnson syndrome who developed intracranial hemorrhage during the acute phase of illness, an exceptionally uncommon complication that remains sparsely reported in the literature. While current management of SJS appropriately prioritizes early withdrawal of the offending agent, aggressive supportive care, and recognition of complications such as sepsis and shock, clinicians should remain aware that serious neurological events may also occur. By presenting this case, we aim to highlight an underrecognized manifestation of SJS, emphasize the importance of maintaining a broad differential diagnosis when neurological deterioration develops, and contribute to the limited literature regarding intracranial hemorrhage in this rare but life threatening condition.

Case Presentation

A 41-year-old Saudi male with a known history of epilepsy presented to the hospital with fever, generalized malaise, and a rapidly progressive skin eruption. The patient had recently been started on lamotrigine for seizure control, with a subsequent dose escalation during the weeks preceding presentation. Shortly after the dose increase, he developed a diffuse erythematous maculopapular rash that progressively worsened and was associated with mucosal involvement, particularly painful oral erosions. The skin eruption was accompanied by fever, fatigue, and generalized systemic symptoms, raising suspicion for a severe cutaneous adverse reaction.

On examination, the patient appeared ill but was initially hemodynamically stable. Dermatological examination revealed a widespread erythematous maculopapular eruption involving the trunk, upper and lower extremities, with areas of skin tenderness and early epidermal detachment. Oral examination demonstrated multiple painful erosions involving the buccal mucosa and lips with difficulty in oral intake (Figure 1). The clinical features, recent exposure to lamotrigine, and presence of mucosal involvement were consistent with Stevens-Johnson syndrome.

The patient was admitted to a high dependency care setting for close monitoring due to the severity of the reaction and the risk of rapid clinical deterioration. During the course of hospitalization, he developed new neurological symptoms characterized by a sudden severe headache, repeated episodes of vomiting, and progressive neurological deterioration. Neurological assessment revealed objective unilateral weakness, with fluctuating level of consciousness reflected by changes in the Glasgow Coma Scale score during serial examinations.

Given the acute neurological decline, urgent neuroimaging was performed. Computed tomography of the brain demonstrated an acute intracerebral hemorrhage with extension into the ventricular system (Figure 2). This finding represented a rare neurological complication occurring during the acute phase of Stevens-Johnson syndrome.

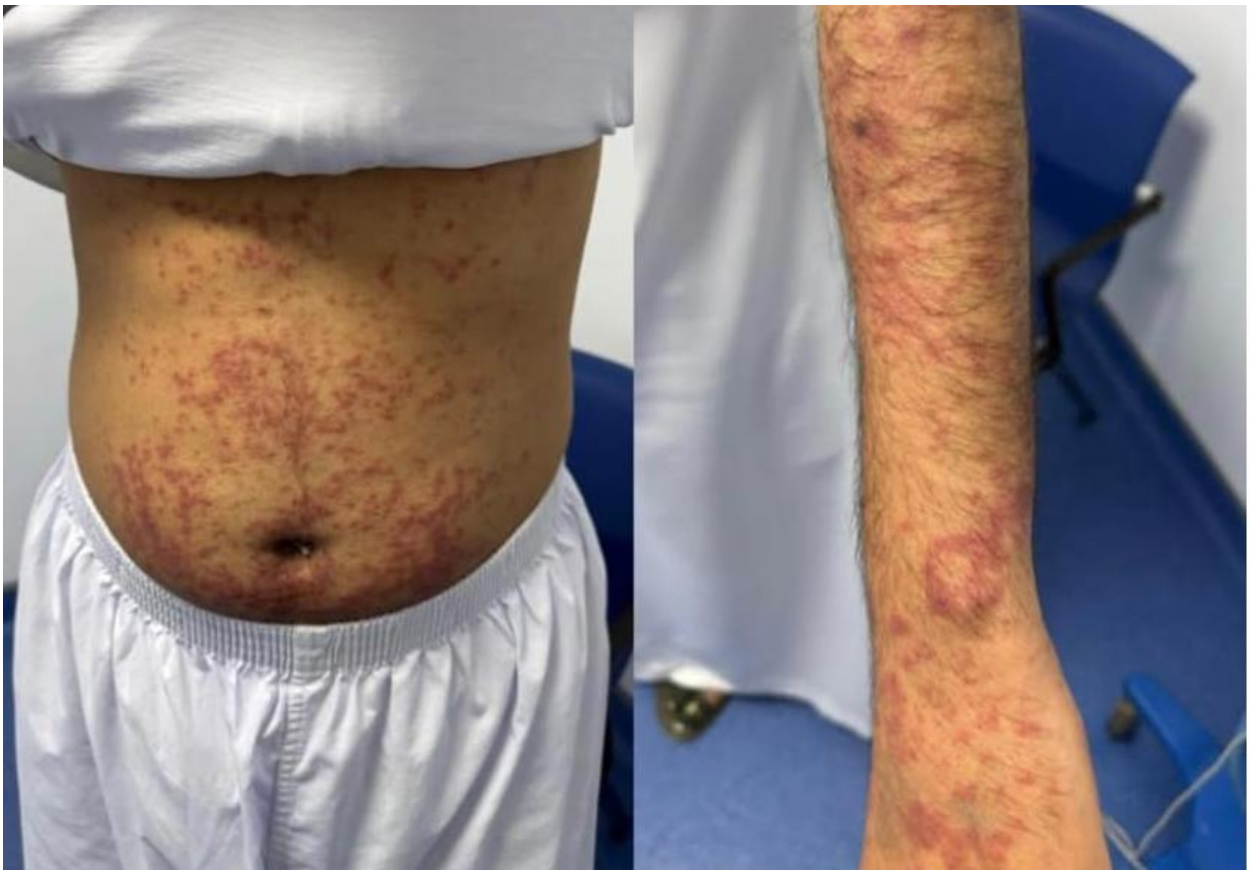

Figure 1. Diffuse erythematous maculopapular eruption involving the trunk and extremities with mucosal involvement characterized by painful oral erosions, consistent with Stevens-Johnson syndrome.

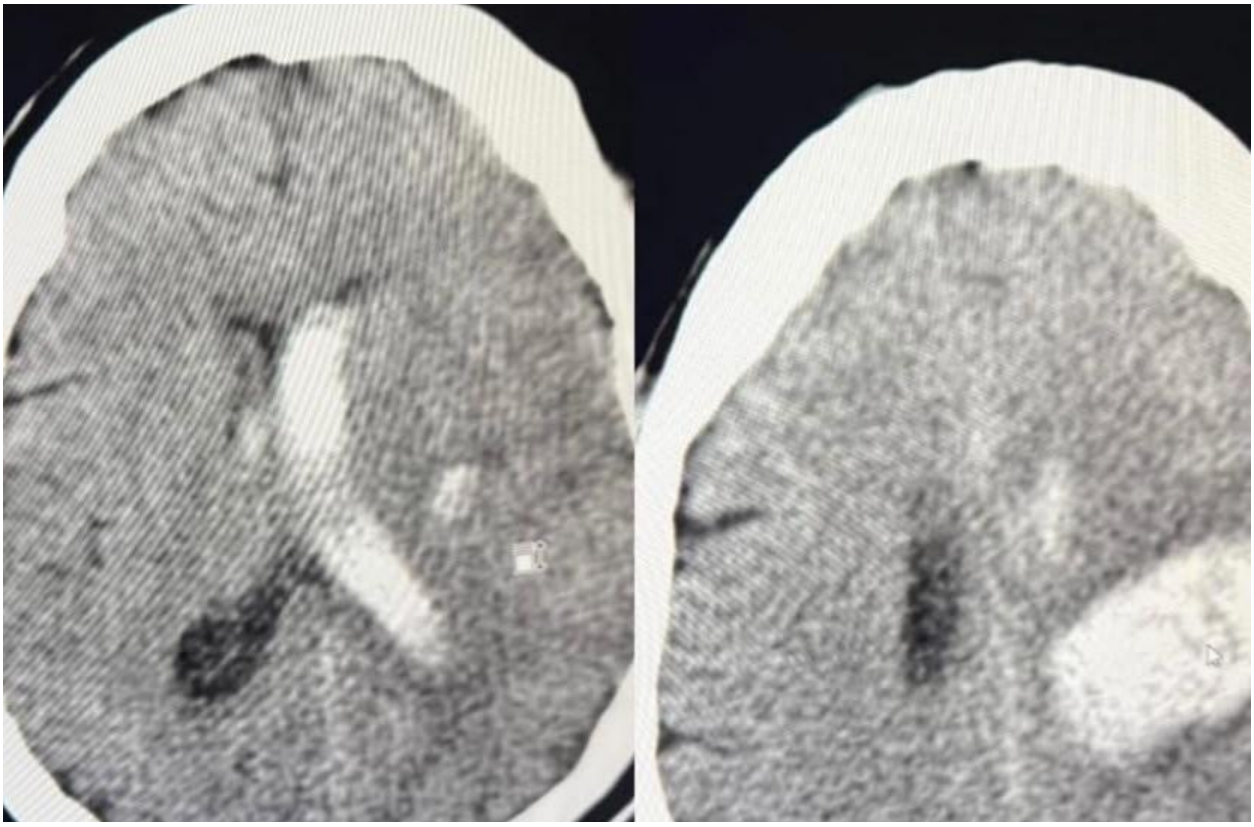

Figure 2. Non-contrast computed tomography of the brain demonstrating acute intracerebral hemorrhage with intraventricular extension.

Management course

Management began upon the patient's arrival to the emergency department, where the initial assessment focused on the severity of the suspected Stevens-Johnson syndrome and the risk of systemic complications. Given the extensive skin involvement, mucosal lesions, fever, and systemic symptoms following recent lamotrigine exposure, the patient was placed in a monitored setting with continuous vital sign assessment. Two peripheral intravenous lines were secured, and blood samples were obtained for urgent investigations including complete blood count, inflammatory markers, coagulation profile, renal function, liver function tests, electrolytes, blood glucose, and blood cultures to assess for possible systemic involvement and infectious complications.

The suspected offending medication was immediately discontinued after careful review of the patient's medication history. The patient was managed in a high dependency care area due to the potential for rapid deterioration associated with severe cutaneous adverse reactions. Initial supportive care focused on maintaining adequate hydration, monitoring fluid balance, controlling fever and pain, and assessing for early signs of complications. Regular skin examinations were performed to evaluate progression of epidermal involvement, while mucosal involvement was monitored because of the risk of impaired oral intake and secondary complications.

During the early course of hospitalization, the patient's condition was closely monitored with repeated clinical assessments. Despite stabilization of his dermatological symptoms, he developed new neurological manifestations characterized by severe headache, recurrent vomiting, and a decline in neurological status. Serial neurological examinations demonstrated fluctuating consciousness with changes in the Glasgow Coma Scale score and the development of objective unilateral weakness. These findings raised concern for an acute intracranial process rather than the more commonly encountered complications of severe infection, metabolic abnormalities, or medication related sedation.

In view of the acute neurological deterioration, urgent neuroimaging was arranged. A non-contrast computed tomography scan of the brain demonstrated an acute intracerebral hemorrhage with extension into the ventricular system. Following confirmation of the hemorrhage, the patient's management priorities shifted toward neurological stabilization and prevention of further deterioration. The neurology, neurosurgery, and intensive care teams were involved for multidisciplinary assessment and ongoing management planning.

The patient was transferred to an intensive care setting for closer neurological and physiological monitoring. Serial assessments of consciousness level, pupillary responses, and neurological deficits were performed to identify any evidence of progression. Continuous monitoring was maintained because of the risk of worsening hemorrhage, increased intracranial pressure, and further neurological decline. Repeat laboratory investigations were performed to evaluate for potential contributing factors, including platelet abnormalities, coagulation disturbances, and other systemic complications that may increase bleeding risk.

Management of the intracerebral hemorrhage was guided by the patient's neurological status, radiological findings, and overall clinical condition. Blood pressure was monitored closely and controlled within appropriate targets to reduce the risk of hematoma expansion while maintaining adequate cerebral perfusion. Measures were taken to minimize factors that could worsen intracranial pressure, including careful fluid management, head positioning, and avoidance of unnecessary fluctuations in physiological parameters.

The patient's coagulation profile and platelet count were reviewed repeatedly during the clinical course. Any abnormalities identified were addressed promptly according to the patient's condition and specialist recommendations. Given the coexistence of severe cutaneous disease and intracranial bleeding, treatment decisions required careful consideration to balance the risks of thrombosis, bleeding, and complications related to prolonged critical illness.

The underlying Stevens-Johnson syndrome continued to require comprehensive supportive management. The patient received ongoing wound care, nutritional support, and monitoring for secondary infection. Regular assessment of mucosal involvement was performed, particularly regarding oral intake and the risk of dehydration. Screening for infectious complications was continued because sepsis remains one of the most significant causes of morbidity and mortality in patients with severe SJS.

Throughout the admission, repeated multidisciplinary discussions were conducted involving dermatology, intensive care, neurology, and neurosurgery teams. The unusual combination of severe cutaneous drug reaction and intracerebral hemorrhage required individualized decision making, as neurological deterioration in patients with SJS may initially be attributed to more common causes such as sepsis, shock, or metabolic disturbances. The identification of intracranial hemorrhage allowed appropriate escalation of neurological monitoring and targeted management.

Follow-up brain imaging was performed to evaluate the stability of the hemorrhage and assess for progression or ventricular complications. Serial neurological examinations were continued to monitor recovery and identify persistent deficits. The patient's level of consciousness gradually improved with stabilization of the intracranial event, while the cutaneous manifestations of SJS showed gradual clinical improvement with supportive care and continued avoidance of the suspected trigger.

During the later phase of hospitalization, attention was directed toward recovery from both the dermatological and neurological complications. Rehabilitation needs were assessed according to the patient's neurological status, particularly because of the initial unilateral weakness. The patient continued to receive follow-up care from the involved specialties to monitor for delayed complications of SJS and the long-term consequences of intracerebral hemorrhage.

Before discharge, the patient and family were counseled regarding the diagnosis of Stevens-Johnson syndrome, the importance of permanent avoidance of lamotrigine and related high-risk medications, and the need for future medication review before starting new therapies. Follow-up appointments were arranged with relevant specialties for monitoring of neurological recovery, seizure management, and potential long-term complications of the severe cutaneous reaction.

Discussion

Stevens-Johnson syndrome (SJS) is one of the most severe forms of drug-induced hypersensitivity reactions and remains associated with substantial morbidity and mortality despite advances in diagnosis and supportive care. The present case highlights an uncommon but clinically important complication of SJS: intracerebral hemorrhage with intraventricular extension. While clinicians managing SJS are generally familiar with complications such as sepsis, shock, respiratory failure, acute kidney injury, and extensive mucosal damage, neurological deterioration is often attributed to these more common systemic complications. This case emphasizes that sudden neurological changes in patients with SJS should not always be assumed to represent infection-related encephalopathy or metabolic disturbance, and that rare but life-threatening intracranial pathology should remain part of the differential diagnosis. [1,4,10,11]

Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) represent a spectrum of severe mucocutaneous reactions characterized by widespread keratinocyte apoptosis, epidermal detachment, and mucosal involvement. The distinction between SJS and TEN is based mainly on the extent of epidermal detachment, with SJS involving less than 10% of body surface area and TEN involving greater than 30%. Although uncommon, these conditions represent dermatological emergencies because of their rapid progression and the potential for systemic involvement. Mortality is primarily related to complications rather than the skin disease itself, with infections, respiratory complications, multiorgan dysfunction, and severe inflammatory responses contributing significantly to poor outcomes. [1,2,4]

Drug exposure remains the most important trigger of SJS, with several medications carrying a particularly high risk. Antiepileptic drugs, especially aromatic anticonvulsants and lamotrigine, are among the most frequently implicated medication classes. The risk is highest during the early period following treatment initiation or rapid dose escalation, which is consistent with the clinical course observed in the present case. The association between lamotrigine and SJS has led to strict recommendations regarding gradual dose escalation and careful monitoring during the first weeks of therapy. Despite these precautions, severe reactions may still occur, particularly in susceptible individuals. [9,13,14]

The pathophysiology of SJS involves a complex immune-mediated process resulting in extensive apoptosis of keratinocytes. Drug metabolites or drug-related antigens trigger activation of cytotoxic T lymphocytes and natural killer cells, which release inflammatory mediators including granulysin, perforin, and granzyme B. Granulysin has been identified as a major mediator of keratinocyte destruction and correlates with disease severity. In addition to direct skin injury, this widespread immune activation may contribute to systemic inflammation, endothelial dysfunction, and abnormalities affecting multiple organ systems. These mechanisms provide a possible link between severe cutaneous reactions and rare extracutaneous complications, although the exact pathways leading to neurological injury remain incompletely understood. [13,14,19]

The initial clinical priorities in SJS appropriately focus on early recognition, immediate discontinuation of the causative medication, and prevention of the common complications responsible for mortality. Current guidelines emphasize supportive care as the foundation of treatment, including fluid and electrolyte management, wound care, nutritional support, pain control, temperature regulation, and surveillance for infection. Patients with extensive disease often require management in intensive care units or specialized burn facilities because the physiological consequences resemble those seen in major burns. [10,11]

Infectious complications remain one of the most significant concerns in severe SJS. Loss of the protective skin barrier, immune dysregulation, invasive procedures, and prolonged hospitalization increase the risk of bacterial infection and sepsis. Recent systematic reviews have highlighted infection as a major contributor to adverse outcomes in SJS and TEN, explaining why clinicians often prioritize surveillance for septic complications when patients deteriorate. However, this clinical focus may create a diagnostic challenge when deterioration occurs through less common mechanisms. In patients with new neurological symptoms, assuming sepsis as the sole explanation may delay recognition of intracranial events. [6]

Neurological involvement in SJS is uncommon but has been increasingly recognized. Reported manifestations include encephalopathy, seizures, aseptic meningitis, peripheral neuropathy, and other inflammatory neurological syndromes. The mechanisms remain uncertain but may include immune-mediated injury, systemic inflammatory activation, medication effects, metabolic disturbances, or complications related to critical illness. Because these manifestations are rare and nonspecific, neurological symptoms in patients with SJS are often initially attributed to more frequent causes such as infection, hypoxia, electrolyte abnormalities, or sedative medications. [11,13,19]

The present case provides an important clinical lesson regarding the evaluation of neurological deterioration in severe SJS. The development of sudden severe headache, vomiting, unilateral weakness, and fluctuating consciousness represents a pattern that should prompt consideration of an acute intracranial process rather than generalized encephalopathy alone. These findings are particularly important because they represent focal neurological abnormalities, which are less typical of uncomplicated sepsis-associated encephalopathy. Recognition of focal signs is therefore a valuable clinical cue that should trigger urgent neurological assessment and brain imaging.

Intracerebral hemorrhage is an exceptionally rare complication in patients with SJS, and its true frequency remains unknown. Unlike more commonly reported complications such as infection or organ failure, hemorrhagic neurological events have received limited attention in the literature. Several mechanisms may theoretically contribute, including systemic inflammation, endothelial injury, coagulation abnormalities, thrombocytopenia, disseminated intravascular coagulation, or severe physiological stress during critical illness. However, because available evidence is limited mainly to isolated reports, a direct causal relationship between SJS and intracranial hemorrhage cannot be established. [11,19]

One of the major challenges in recognizing intracranial hemorrhage in SJS is the presence of multiple competing explanations for neurological decline. Patients with severe SJS may develop altered mental status due to sepsis, hypotension, medication effects, renal dysfunction, or metabolic abnormalities. As a result, clinicians may initially pursue investigations focused on systemic causes while overlooking structural neurological disease. The presence of sudden headache, recurrent vomiting, new focal neurological deficits, or an unexplained decline in consciousness should therefore be considered warning signs that require evaluation beyond routine sepsis assessment.

The clinical approach to neurological deterioration in SJS should be guided by the nature of the symptoms rather than the underlying diagnosis alone. Diffuse confusion without focal findings may be consistent with systemic illness, whereas asymmetric weakness, cranial nerve abnormalities, seizures, or abrupt changes in consciousness should raise suspicion for intracranial pathology. In this context, bedside neurological examination remains a critical diagnostic tool. Frequent reassessment is particularly important because patients with SJS may deteriorate rapidly and because early neurological findings may be subtle before significant progression occurs.

The occurrence of intracerebral hemorrhage in the setting of SJS raises several important clinical questions regarding possible mechanisms and contributing factors. Although a direct association has not been firmly established, severe systemic inflammation may play a role through widespread endothelial activation and vascular dysfunction. The inflammatory state

observed in SJS involves extensive immune activation, cytokine release, and tissue injury, which may theoretically affect vascular integrity. In addition, critically ill patients with severe cutaneous reactions may develop abnormalities in coagulation pathways, including thrombocytopenia, consumption of clotting factors, or disseminated intravascular coagulation. Therefore, when neurological deterioration occurs, evaluation of platelet count, coagulation parameters, and evidence of systemic coagulation abnormalities is essential. [10,11,13]

Another important consideration is that patients with SJS are often exposed to multiple medications during hospitalization, including analgesics, antimicrobial agents, anticonvulsants, and other supportive therapies. Some medications may influence neurological status or bleeding risk, making clinical interpretation more challenging. In patients with a history of epilepsy, as in the present case, changes in mental status may initially raise concern for seizure activity or postictal states. However, the presence of severe headache, vomiting, and focal neurological deficits should prompt clinicians to consider alternative diagnoses, including intracranial hemorrhage. This distinction is clinically important because treatment pathways differ significantly depending on whether the neurological deterioration is caused by seizure activity, systemic illness, or structural brain pathology.

Brain imaging plays a central role in evaluating acute neurological deterioration in patients with SJS. Non-contrast computed tomography of the brain remains the first-line imaging modality in suspected intracerebral hemorrhage because it is rapidly available, highly sensitive for acute bleeding, and capable of identifying important features such as hematoma location, size, mass effect, and ventricular extension. In the present case, CT imaging provided the critical diagnostic information by demonstrating intracerebral hemorrhage with intraventricular extension, explaining the patient's acute neurological decline. This highlights the importance of maintaining a low threshold for neuroimaging when patients with severe systemic disease develop new focal neurological findings.

The presence of intraventricular extension carries additional prognostic significance because it is associated with a higher risk of increased intracranial pressure, hydrocephalus, and neurological deterioration. Although the management of intracerebral hemorrhage depends on multiple factors including hematoma size, location, neurological status, and underlying cause, early recognition remains one of the most important determinants of outcome. In patients with SJS, where attention is often directed toward skin failure and systemic complications, recognition of intracranial extension may be delayed unless neurological changes are actively investigated.

A key clinical challenge in this case is distinguishing expected complications of severe SJS from signs indicating a separate neurological emergency. Fever, altered mental status, and systemic deterioration are common in severe SJS and may appropriately raise concern for infection or sepsis. However, certain findings should prompt immediate reconsideration of the diagnosis. Sudden onset severe headache is not a typical manifestation of uncomplicated SJS. Similarly, vomiting associated with declining consciousness may suggest increased intracranial pressure rather than generalized systemic illness. The appearance of unilateral weakness is particularly significant because focal neurological deficits indicate localized brain dysfunction and should trigger urgent evaluation.

This case also highlights the importance of avoiding diagnostic anchoring in critically ill patients. Once a diagnosis of SJS has been established, clinicians may unintentionally attribute all subsequent clinical changes to the known disease process. This is particularly relevant in conditions with multisystem involvement, where deterioration can result from several overlapping mechanisms. While sepsis and shock remain common and important considerations, they should not prevent investigation of other potentially reversible causes when new clinical features emerge. Experienced clinicians often rely on identifying changes that are inconsistent with the expected disease course, and this principle is particularly valuable in rare complications.

The management of SJS itself has evolved considerably over recent years, although supportive care remains the foundation of treatment. Multiple systemic therapies have been studied, including corticosteroids, intravenous immunoglobulin, cyclosporine, and biologic therapies targeting inflammatory pathways. However, evidence remains variable because of the rarity of the condition and the difficulty of conducting large randomized trials. Recent reviews suggest that cyclosporine and other immunomodulatory strategies may provide benefit in selected patients, but treatment decisions should be individualized according to disease severity, contraindications, and local expertise. [5,19,20]

The role of immunomodulatory therapy becomes particularly complex when severe complications such as intracerebral hemorrhage occur. Clinicians must balance control of the underlying inflammatory disease against the potential risks associated with immunosuppression in a patient with active bleeding or possible infection. This emphasizes the importance of multidisciplinary decision making involving dermatology, intensive care, neurology, neurosurgery, and other relevant specialties. The rarity of intracranial hemorrhage in SJS means that standardized management pathways are lacking, and clinical judgment remains essential.

Another important lesson from this case is the need for careful neurological monitoring in high-risk SJS patients. While frequent assessment of skin involvement, fluid status, renal function, and infection markers is standard practice, neurological examination should also be incorporated into routine reassessment. Monitoring consciousness level, pupillary responses, and the presence of new focal deficits can provide early warning signs of neurological complications. This is particularly important in patients with risk factors such as older age, severe systemic inflammation, coagulation abnormalities, or pre-existing neurological disease.

Lamotrigine-associated SJS deserves particular attention because of the established relationship between rapid dose escalation and severe cutaneous reactions. Current recommendations emphasize slow titration and immediate discontinuation if concerning symptoms develop. However, even with appropriate prescribing practices, clinicians should remain aware that severe reactions can occur. The present case reinforces the importance of medication history as a central component of evaluating patients with new mucocutaneous symptoms, especially when neurological deterioration develops later during hospitalization. [9,13]

From an educational perspective, several practical clinical cues emerge from this case. First, not all deterioration in SJS represents sepsis or shock. Second, focal neurological deficits should never be attributed solely to systemic inflammation without appropriate evaluation. Third, severe headache and vomiting in a critically ill patient are neurological warning signs that warrant urgent assessment. Finally, the presence of a rare complication should not discourage clinicians from considering it when the clinical pattern is concerning. Rare events are often missed not because they cannot be diagnosed, but because they are not considered.

The present case expands the clinical spectrum of Stevens-Johnson syndrome by highlighting intracerebral hemorrhage as a rare but potentially devastating complication. Although current guidelines appropriately emphasize prevention and management of common complications, clinicians should remain vigilant for neurological emergencies that may occur during the course of the disease. Early recognition of atypical deterioration, prompt neuroimaging, and multidisciplinary collaboration are essential to improving outcomes in patients with severe SJS.

In conclusion, Stevens-Johnson syndrome remains a complex systemic disease in which mortality is driven largely by complications rather than the cutaneous manifestations alone. While infection, shock, and organ failure remain the most recognized threats, this case demonstrates that intracranial hemorrhage should be considered when neurological deterioration is abrupt, focal, or disproportionate to the patient's overall condition. Awareness of these clinical warning signs may allow earlier diagnosis, prevent delays in treatment, and improve outcomes in patients experiencing this rare but serious complication.

Conclusion

This case highlights an important diagnostic pitfall in the management of Stevens-Johnson syndrome: the assumption that all deterioration in these patients is caused by common complications such as sepsis, shock, or multiorgan failure. Although these remain the major contributors to mortality, this case demonstrates that rare neurological complications can occur and may be overlooked unless clinicians maintain a high level of suspicion. Several important lessons emerge. First, neurological deterioration in SJS should not automatically be attributed to systemic illness. The development of sudden severe headache, vomiting, focal neurological deficits, or fluctuating consciousness represents a different clinical pattern that should prompt urgent evaluation for intracranial pathology. Second, establishing a diagnosis of SJS should not lead to diagnostic closure. A confirmed diagnosis explains the initial presentation but does not exclude the possibility of additional life-threatening complications. Careful reassessment is essential whenever new findings appear that do not fit the expected disease course. This case also emphasizes the importance of routine neurological assessment in critically ill patients with severe drug reactions. While attention is often focused on skin involvement, infection surveillance, and organ function, subtle neurological changes may provide the earliest indication of a serious complication. Although intracerebral hemorrhage is exceptionally rare in SJS, clinicians should recognize that uncommon diagnoses can become the correct diagnosis when the clinical pattern is concerning. The most valuable clinical skill is not only recognizing common complications but also identifying when a patient's course deviates from what is expected. Ultimately, this case expands the understanding of SJS as a multisystem disease and highlights the need for vigilance, curiosity, and timely investigation when neurological abnormalities develop. Early recognition of atypical deterioration may prevent delayed diagnosis and improve outcomes in patients with severe SJS.

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