



Early-Stage Stevens–Johnson Syndrome with Oral and Cutaneous Manifestations Following Recent Drug Administration: A Case Report

¹ Alfiyah Reviani Rahmayunita

¹ Anwar Medika General Hospital, Sidoarjo, East Java, Indonesia

Corresponding Email : alfiyah.reviani@yahoo.com

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ABSTRACT

Introduction: Stevens–Johnson syndrome (SJS) is a rare, life-threatening, immune-mediated mucocutaneous reaction most frequently triggered by medications (1). Early-stage SJS often presents with fever, oral ulceration, and widespread erythematous macules before blistering or epidermal detachment occurs, making it easily misdiagnosed as a viral exanthem or erythema multiforme major (2). Delayed recognition increases morbidity and mortality (3).

Case Illustration: A 49-year-old female presented with progressive lip swelling, painful oral ulcers, dysphagia, and a rapidly spreading purplish-red maculopapular rash over the entire body, following sequential administration of ketoconazole, prednisone, cetirizine, chloramphenicol eye drops, loratadine, and dexamethasone over 48 hours. On admission, she was febrile (38.2°C), tachycardic (115 bpm), and tachypneic (24 breaths/min). Physical examination revealed multiple erythematous macules on the trunk, extremities, and oropharynx, along with labial crusting

and ulceration. No blistering or positive Nikolsky sign was present. A working diagnosis of early-stage SJS versus erythema multiforme major was made. The patient was hospitalized, all suspected drugs were withdrawn, and she received intravenous dexamethasone, diphenhydramine, ranitidine, topical vaseline, saline mouthwash, and topical desoximetasone. By day two, she developed blood-tinged saliva, throat discomfort, vomiting, and bilateral rales, prompting airway monitoring.

Discussion: The temporal relationship between drug administration and symptom onset strongly supported drug-induced SJS (4). The absence of epidermal detachment at presentation confirmed early-stage disease (5). Management focused on immediate drug withdrawal, aggressive supportive care, and daily monitoring for respiratory compromise (6). The use of systemic corticosteroids in early SJS remains controversial but may be beneficial within 48–72 hours (7).

Conclusion: Early recognition, immediate withdrawal of culprit drugs, hospitalization, and vigilant monitoring for airway involvement are essential in suspected early-stage SJS to prevent progression to full-thickness epidermal necrosis and reduce mortality.

Keywords: Stevens–Johnson syndrome, drug eruption, oral ulceration, maculopapular rash, early diagnosis

INTRODUCTION

Stevens–Johnson syndrome (SJS) is a severe cutaneous adverse reaction (SCAR) characterized by widespread erythematous macules, atypical target lesions, mucosal involvement, and eventual epidermal detachment (1). Along with toxic epidermal necrolysis (TEN), SJS represents a spectrum of life-threatening conditions most commonly induced by medications, although infections and vaccines have also been implicated (2). The estimated annual incidence of SJS/TEN is approximately 2 to 7 cases per million person-years, making it a rare but critically important condition for clinicians to recognize promptly (3). Mortality in SJS is approximately 5–10%, increasing to 30% in TEN, with sepsis and respiratory failure being the leading causes of death (4). Early-stage SJS may present with prodromal symptoms such as fever, malaise, sore throat, cough, and arthralgias, followed by the rapid emergence of painful oral ulcers and cutaneous erythematous macules (5). At this stage, full-thickness epidermal necrosis may not yet be visible, creating a diagnostic challenge. However, it is precisely this early window that offers the best opportunity to halt progression by withdrawing culprit drugs and initiating supportive care (6). Delayed diagnosis, often due to misidentification as erythema multiforme major, a viral exanthem, or even an allergic contact dermatitis, has been associated with increased disease severity and mortality (7).

Research Objective: The primary objective of this case report is to describe in detail the clinical presentation, diagnostic reasoning, and stepwise hospital management of a 49-year-old female patient with suspected early-stage Stevens–Johnson syndrome following sequential exposure to multiple drugs, including ketoconazole, prednisone, cetirizine, chloramphenicol eye drops, loratadine, and dexamethasone.

Benefits of the Study: This case report provides practical, real-world clinical insights for residents and specialists in dermatology, internal medicine, and emergency medicine. It emphasizes the importance of obtaining a meticulous drug history, recognizing early mucocutaneous signs before blistering occurs, and implementing a systematic inpatient management protocol including

fluid resuscitation, topical oral care, systemic corticosteroids, and daily monitoring of airway and pulmonary status. Furthermore, this report highlights the challenges of managing SJS in settings where intensive care resources may be limited.

Hypothesis: We hypothesize that the patient's clinical syndrome—characterized by fever, painful oropharyngeal ulceration, lip crusting, and widespread erythematous macules appearing 48–72 hours after initiation of multiple new medications—represents a drug-induced type IV hypersensitivity reaction consistent with early-stage Stevens–Johnson syndrome. We further hypothesize that immediate withdrawal of all suspected drugs combined with aggressive supportive care and systemic corticosteroids can stabilize the condition and prevent progression to epidermal detachment.

Research Gap: A thorough review of the existing literature reveals that the majority of published case series and clinical studies on SJS focus on the advanced stages of the disease, where frank blistering, positive Nikolsky sign, and extensive epidermal detachment are already present (8). There is a relative paucity of detailed clinical reports focusing specifically on the **early-stage** of SJS, particularly with predominant oropharyngeal involvement before any cutaneous bullae formation (9). Moreover, most reports originate from tertiary care centers with immediate access to burn units and intensive care, leaving a gap in the literature regarding early recognition and management in secondary-level hospitals (10).

Novelty: This case report offers several novel contributions. First, it provides a **day-by-day** clinical documentation of early-stage SJS, including vital signs, physical examination findings, and therapeutic adjustments from day one to day two of hospitalization. Second, it uniquely emphasizes the **oropharyngeal and respiratory monitoring** in a patient who developed new-onset rales and throat discomfort on day two, underscoring the potential for subclinical laryngeal or pharyngeal involvement even without stridor. Third, it describes the use of systemic dexamethasone in early-stage SJS without initial skin detachment, a practice that remains controversial but is detailed here with clinical reasoning. Fourth, it highlights management strategies applicable to **resource-limited settings** where SCORTEN scoring may be incomplete and intensive care may not be immediately available.

CASE REPORT

Patient Identity and Demographics: The patient was a 49-year-old Indonesian female, married, with a body weight of 70 kilograms. She presented to the emergency department of RSU Anwar Medika Sidoarjo with complaints that had evolved over the preceding three days. No significant past medical history was reported, and she had no known drug allergies prior to this episode. Her family history was unremarkable for autoimmune or severe cutaneous disorders.

Chief Complaint on Admission: The patient's primary complaints at presentation were progressive swelling of both lips, severe pain inside the oral cavity, difficulty swallowing (dysphagia), a persistent sensation of dryness in the throat, and the appearance of reddish-purple bumps over her entire body that had started the night before admission.

History of Presenting Illness (Detailed Chronology): Approximately three days prior to hospital admission, the patient had sought treatment at a primary care clinic for complaints of vaginal itching and eye discomfort. The clinic physician prescribed oral ketoconazole, oral prednisone, oral cetirizine, and chloramphenicol eye drops. On the following day (two days before admission), after taking the first doses of these medications, the patient noticed that her lips began to swell progressively. She did not immediately return to the clinic. On the next day (one day before admission), she visited the internal medicine outpatient clinic of a different hospital. The internist prescribed oral loratadine and oral dexamethasone, presumably as treatment for a suspected allergic reaction. However, after taking these new medications, the patient developed a widespread eruption of red bumps over her entire body, starting on the trunk and spreading to the extremities within hours. Additionally, she reported having a fever that had been present for three days, measured up to 38.5°C at home. The combination of worsening lip swelling, oral pain, and new generalized rash prompted her to seek emergency care.

Past Medical, Surgical, and Medication History: The patient had no history of hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, or liver disease. She had no prior history of adverse drug reactions, no history of herpes simplex infection, and no

personal or family history of autoimmune bullous diseases. She was not taking any regular medications prior to this illness. There was no history of smoking, alcohol use, or illicit drug use.

Review of Systems: On admission, a systematic review of systems revealed the following:

1. **General:** fatigue, subjective fever, chills.
2. **Head, Eyes, Ears, Nose, Throat:** bilateral eye discomfort (improved after eye drops), dry throat, painful swallowing, lip swelling, oral pain.
3. **Respiratory:** mild shortness of breath, no cough, no sputum production.
4. **Cardiovascular:** palpitations (associated with fever), no chest pain.
5. **Gastrointestinal:** decreased appetite, no nausea, no vomiting, no abdominal pain.
6. **Genitourinary:** vaginal itching (initial complaint), no dysuria, no hematuria.
7. **Skin:** generalized pruritic reddish-purple bumps, no blistering noted by the patient.
8. **Neurologic:** no headache, no photophobia, no confusion.

Vital Signs on Admission (Day 1): On initial assessment in the emergency department, the patient appeared weak and was noted to have visible shortness of breath at rest. Her Glasgow Coma Scale (GCS) was 4/5 (E4V5M6), indicating full consciousness. Blood pressure was elevated at 136/109 mmHg, which may have reflected pain or distress. Heart rate was 115 beats per minute (tachycardia), respiratory rate was 24 breaths per minute (tachypnea), and tympanic temperature was 38.2°C (fever). Oxygen saturation measured by pulse oximetry was 96% on room air, which was within acceptable limits.

Physical Examination Findings (Day 1): A complete physical examination was performed.

General appearance: The patient was awake, alert, cooperative but appeared uncomfortable due to oral pain.

1. **Head and neck:** Conjunctivae were not injected, sclera were anicteric, no cervical lymphadenopathy was palpated. The neck was supple.
2. **Cardiovascular examination:** Heart sounds S1 and S2 were single and regular, no murmurs, no gallops, no rubs.
3. **Pulmonary examination:** On auscultation, vesicular breath sounds were present bilaterally. No rales (crackles) were heard, and no wheezing was present.

4. **Abdominal examination:** The abdomen was soft, flat, and non-tender. Bowel sounds were normoactive. No organomegaly was palpated.
5. **Extremities:** The extremities were warm to touch. Capillary refill time was less than two seconds, indicating adequate peripheral perfusion. No peripheral edema was noted.

Mucocutaneous Examination (Day 1): This was the most revealing part of the physical examination.

1. **Oral cavity and perioral region:** The labia oris (lips) showed prominent swelling, multiple areas of crusting (crustae), and superficial ulcerations. The oral mucosa, including the buccal surfaces, hard palate, and soft palate, exhibited multiple erythematous macules. The patient experienced severe pain when the oral mucosa was touched with a tongue depressor. The oropharynx, including the tonsillar pillars and posterior pharyngeal wall, also showed scattered erythematous macules.
2. **Skin:** Over the entire body, including the trunk, back, upper extremities, lower extremities, and palms, there were multiple, widespread, discrete and confluent erythematous macules. The lesions were non-blanching, slightly raised in some areas, and ranged in color from bright red to purplish-red. No vesicles, bullae, or frank blisters were present at this time. No target lesions with three concentric zones (typical of erythema multiforme) were identified. The Nikolsky sign (shearing of epidermis with lateral pressure) was not tested because no blistering was present.
3. **Genital area:** The patient reported vaginal itching as an initial symptom, but no active ulcers or lesions were visualized on external examination.



Figure 1. Mucocutaneous Examination

Table 1. Laboratory Findings on Admission

Parameter	Result	Unit	Reference Range
Hemoglobin (HGB)	14.1	g/dL	12 - 16
Hematocrit (HCT)	42.5	%	36 - 46
White Blood Cell (WBC)	19.06 H	thousand cells/ μ L	4.1 - 11

Platelet (PLT)	255	thousand cells/ μ L	140 - 440
Red Blood Cell (RBC)	5.03	million cells/ μ L	4 - 5.2
Mean Corpuscular Volume (MCV)	84.4	fL	80 - 150
Mean Corpuscular Hemoglobin (MCH)	28.0	pg	26 - 34
Mean Corpuscular Hemoglobin Concentration (MCHC)	33.2	g/dL	31 - 36
RDW-SD	42.5	fL	35 - 56
RDW-CV	13.3	%	11 - 16
Procalcitonin (PCT)	0.242	%	0.11 - 0.28
Platelet Distribution Width (PDW)	15.9	%	9 - 17
Mean Platelet Volume (MPV)	9.5	fL	6.8 - 10
P-LCC	61	thousand cells/ μ L	30 - 90
P-LCR	24.0	%	11 - 45
Basophil Percentage (BAS%)	0.1	%	0 - 2
Eosinophil Percentage (EOS%)	0.0	%	0 - 5
Lymphocyte Percentage (LYM%)	8.9 L	%	13 - 40
Monocyte Percentage (MON%)	6.7	%	0 - 10.3
Neutrophil Percentage (NEU%)	84.3 H	%	47 - 80
Basophil Absolute Count (BAS#)	0.02	thousand cells/ μ L	0 - 0.1
Eosinophil Absolute Count (EOS#)	0.00	thousand cells/ μ L	0 - 0.5
Lymphocyte Absolute Count (LYM#)	1.71	thousand cells/ μ L	1 - 4

Monocyte Absolute Count (MON#)	1.27 H	thousand cells/ μ L	0.1 - 1.2
Neutrophil Absolute Count (NEU#)	16.06 H	thousand cells/ μ L	2.5 - 7.5
Random Blood Glucose	119	mg/dL	90 - 200
Urea			
Urea	45.0	mg/dL	10 - 50
Blood Urea Nitrogen (BUN)	20.93	mg/dL	10 - 50
Creatinine	1.07	mg/dL	1.0 - 1.5
Sodium (Na)	126.9	mmol/L	135 - 155
Potassium (K)	3.43	mmol/L	3.5 - 4.9
Chloride (Cl)	113.3	mmol/L	96 - 113

Abbreviations: H = High (above reference range), L = Low (below reference range)

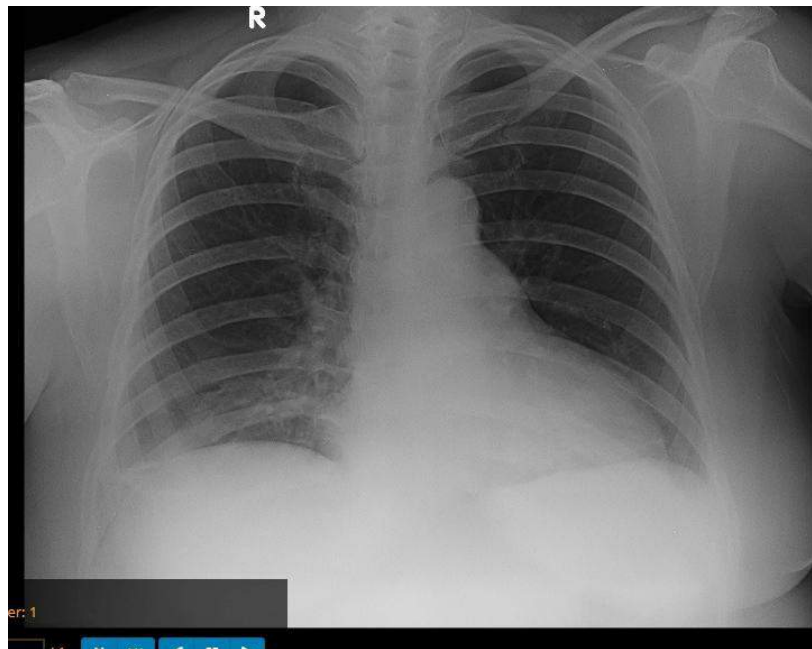


Figure 2. Thorax X-Ray

Working Diagnosis and Differential Diagnosis: Based on the combination of fever, recent multiple drug exposures, painful oral and oropharyngeal ulceration, and widespread erythematous

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macules without blistering, the working diagnosis was **early-stage Stevens–Johnson syndrome**. The primary differential diagnosis was **erythema multiforme major**, which can also present with mucosal involvement and skin lesions but is more commonly associated with herpes simplex virus infection and typically features typical target lesions (7). Other differential diagnoses considered included acute generalized exanthematous pustulosis (AGEP), which was less likely due to the absence of pustules; drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), which was less likely due to the absence of eosinophilia and organ involvement; and a severe viral exanthem, which was considered but less likely given the rapid temporal relationship to drug administration.

Initial Management Plan (Day 1): Upon establishing the working diagnosis of suspected early-stage SJS, the following immediate interventions were implemented. First, **all suspected culprit drugs** were discontinued immediately, including ketoconazole, prednisone, cetirizine, chloramphenicol eye drops, loratadine, and dexamethasone. Second, the patient was **hospitalized** for close monitoring, as outpatient management is inappropriate for suspected SJS. Third, **aggressive supportive care** was initiated: intravenous crystalloid fluids (Ringer's lactate) were started to maintain hydration, given the patient's poor oral intake due to oral pain. Fourth, **pharmacological therapy** was prescribed: (a) intravenous dexamethasone 3×1 ampoule (each ampoule containing 5 mg, total 15 mg/day), (b) intravenous diphenhydramine 3×1 (antihistamine for pruritus and possible mast cell stabilization), (c) intravenous ranitidine 1 ampoule every 12 hours (for gastric protection and possible H₂ blockade). Fifth, **topical therapies** were initiated: (a) thick application of white petrolatum (vaseline) to the lips every 2–4 hours to prevent drying and cracking, (b) NaCl (saline) mouthwash after each meal and as needed for oral hygiene, (c) topical desoximetasone (a potent corticosteroid) applied to skin lesions twice daily to reduce local inflammation. Sixth, **monitoring parameters** were established: daily monitoring of lesion progression, daily oral and oropharyngeal examination, monitoring for any signs of epidermal detachment (blistering, positive Nikolsky sign), urine output measurement, and daily vital signs. Seventh, the need for **airway and eye monitoring** was documented, with a low threshold to consult ophthalmology and ear-nose-throat (ENT) specialists if symptoms progressed.

Day 2 of Hospitalization – Detailed Clinical Course: On the second day of hospitalization, the patient's condition evolved in several important ways. **Subjective complaints:** The patient reported that she had vomited more than five times during the preceding 24 hours. Additionally, she noted that her saliva was mixed with blood (blood-tinged saliva). She complained of a persistent sensation of a lump in her throat (globus sensation) and felt as though there were open sores in her throat. Her appetite remained poor, and she had been unable to eat solid foods. Urine output was measured at 900–1000 mL over the previous 24 hours, which was considered minimally acceptable but borderline given her poor intake. **Vital signs on day 2:** General condition remained weak, and she still appeared short of breath. GCS was unchanged at 456. Blood pressure was 128/70 mmHg (improved from day 1). Heart rate was 118 beats per minute (persistent mild tachycardia). Temperature was 37.8°C (decreased but still low-grade fever). Respiratory rate remained 24 breaths per minute. Oxygen saturation was 96% on room air. **Physical examination on day 2:** The cardiovascular examination was unchanged. The abdominal examination remained normal. However, the **pulmonary examination** revealed a new finding: on auscultation, vesicular breath sounds were present but now **rales (crackles) were heard bilaterally** in both lung fields. No wheezing was present. The **mucocutaneous findings** on day 2 were unchanged from day 1: multiple erythematous macules persisted over the entire body and oropharynx, and labial crusting and ulceration remained present. No new blistering or skin detachment had appeared.

Revised Planning on Day 2 : Based on the new symptoms of blood-tinged saliva, globus sensation, vomiting, and bilateral rales on auscultation, the medical team made several adjustments. First, it was documented that there was a **possibility of erosive oral/oropharyngeal mucosa** extending into the upper airway, and strict observation for bleeding was ordered. Second, regarding the **urine output of 900–1000 mL per day**, the team judged this as still acceptable but noted that intake remained poor; therefore, continued monitoring of intake–output was essential, and maintenance intravenous crystalloids (Ringer's lactate) were continued. Third, **medication adjustments** were made: (a) intravenous dexamethasone was reduced to 2 × 1 ampoule per day based on clinical progress, (b) intravenous diphenhydramine was given once daily at night only (1 ×

1), (c) ranitidine 1 ampoule every 12 hours was continued, (d) vaseline and oral care were continued. Fourth, an important **diagnostic consideration** was raised: the patient's shortness of breath and new bilateral rales required differentiation between (a) increased oropharyngeal secretions that were being aspirated, (b) early laryngeal edema, (c) primary pulmonary involvement, or (d) simple atelectasis. The plan was to monitor the airway closely and, if symptoms worsened or if stridor developed, to consult ENT and Pulmonology specialists immediately. No chest X-ray was performed on day 2 due to limited resources, but it was considered.

Outcome: As of day 2 of hospitalization, the patient had not progressed to blistering or skin detachment. The early intervention of drug withdrawal and systemic corticosteroids appeared to have stabilized her mucocutaneous condition. However, the new respiratory symptoms (rales) and oropharyngeal bleeding required ongoing vigilance.

DISCUSSION

Epidemiology and Etiology: Stevens–Johnson syndrome is a rare but severe adverse drug reaction with an incidence of approximately 2 to 7 cases per million person-years (1). More than 200 medications have been implicated as triggers, but the highest-risk drugs include sulfonamides, aromatic anticonvulsants (phenytoin, carbamazepine, phenobarbital), allopurinol, nevirapine, and nonsteroidal anti-inflammatory drugs (NSAIDs) of the oxicam type (2,3). In this case, the patient received ketoconazole (an antifungal), prednisone (a corticosteroid), cetirizine (a second-generation antihistamine), chloramphenicol eye drops (an antibiotic), loratadine (another antihistamine), and dexamethasone (a potent corticosteroid). Among these, **ketoconazole** has been reported as a rare but documented cause of SJS in the literature (4). **Chloramphenicol**, although less common in systemic form, has also been associated with severe cutaneous reactions when administered topically or systemically (5). Interestingly, the patient received both prednisone and dexamethasone prior to the full development of the rash, which may have partially suppressed the immune response and delayed or attenuated the presentation, possibly explaining why she remained in the early stage without blistering by day two (6).

Pathophysiology: SJS is a type IVc hypersensitivity reaction mediated by cytotoxic T lymphocytes (7). The inciting drug or its metabolite acts as a hapten, binding to self-proteins and creating a neoantigen that is presented by major histocompatibility complex (MHC) class I molecules on keratinocytes or dendritic cells (8). This activates drug-specific CD8⁺ cytotoxic T lymphocytes, which then migrate to the skin and mucosa. Upon re-encountering the drug antigen, these CD8⁺ T cells release cytotoxic granules containing perforin, granzyme B, and granulysin (9). Granulysin has been identified as a key mediator of keratinocyte apoptosis in SJS/TEN, and its levels correlate with disease severity (10). Additionally, the Fas-Fas ligand interaction pathway contributes to widespread keratinocyte death (11). The result is massive apoptosis of basal keratinocytes, leading to the characteristic clinical findings of erythematous macules, blister formation, and full-thickness epidermal necrosis. The mucosal surfaces (oral, ocular, genital, and respiratory epithelium) are particularly vulnerable because of their high expression of drug-metabolizing enzymes and immune cell density (12). In our patient, the prominence of oropharyngeal and labial involvement followed by widespread cutaneous macules without blistering is consistent with the earliest phase of this pathophysiological process, before macroscopic detachment occurs.

Temporal Relationship and Drug Culprit Identification: One of the most critical steps in managing suspected SJS is identifying the most likely culprit drug(s) so that it can be withdrawn immediately. The typical latency period between drug initiation and symptom onset in SJS ranges from 4 days to 4 weeks, but in cases of re-exposure, symptoms can appear within 48 hours (13). In our patient, the first symptoms (lip swelling) appeared approximately 48 hours after starting the first set of drugs (ketoconazole, prednisone, cetirizine, chloramphenicol). The more extensive rash appeared after the second set (loratadine, dexamethasone). This temporal pattern suggests that any of these drugs could be the trigger, but ketoconazole and chloramphenicol are the less commonly used agents with known SJS associations (4,5). The use of the ALDEN (Algorithm of Drug Causality for Epidermal Necrolysis) score is recommended in such cases to quantify the likelihood of drug causality, but it requires detailed information on previous exposures, which was not fully

available (14). Nevertheless, given that the patient had no prior history of drug reactions, all drugs were discontinued as a precaution.

Differential Diagnosis: Early SJS vs. Erythema Multiforme Major: The most important differential diagnosis in this case was erythema multiforme (EM) major. Both conditions present with mucosal ulcers and skin lesions, but there are key distinguishing features (15). EM major is typically triggered by infections, especially herpes simplex virus (HSV), rather than medications. The skin lesions in EM major are **typical target lesions** with three concentric zones (a dusky central zone, an edematous pale ring, and an erythematous outer ring). In contrast, SJS presents with **atypical target lesions** (only two zones) or flat, erythematous macules without central clearing (16). Furthermore, EM major tends to have a more acral distribution (hands, feet, extremities), while SJS is more widespread and often involves the trunk (17). In our patient, the skin lesions were described as “multiple erythematous macules” without typical target morphology, and they were distributed over the entire body including the trunk, which favors SJS over EM major. Additionally, there was no history of HSV infection, and the rapid temporal relationship to multiple new drugs further supported drug-induced SJS. Other differentials included **acute generalized exanthematous pustulosis (AGEP)**, which presents with hundreds of small non-follicular pustules on an erythematous base, usually starting in the intertriginous areas; our patient had no pustules (18). **DRESS syndrome** typically presents with fever, rash, facial edema, lymphadenopathy, eosinophilia, and internal organ involvement (liver, kidney), none of which were present in our patient at the time of admission (19).

SCORTEN Score and Prognosis: The SCORTEN (Severity of Illness Score for Toxic Epidermal Necrolysis) is a validated prognostic scoring system originally developed for TEN but often applied to SJS as well (20). It assigns one point for each of seven independent risk factors present within the first 24 hours of admission: age >40 years, presence of malignancy, heart rate >120/min, initial body surface area (BSA) of detachment >10%, serum urea >28 mg/dL, serum glucose >252 mg/dL, and serum bicarbonate <20 mmol/L (21). Each additional point increases the predicted mortality. In our patient, age was 49 (>40 → +1 point). Heart rate was initially 115 and later 118 (not >120 → 0 points). BSA detachment was 0% (→ 0 points). Malignancy was absent (→

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0 points). Unfortunately, serum urea, glucose, and bicarbonate were not measured at admission due to limited laboratory resources, so the SCORTEN could not be fully calculated. However, even with only one point, the estimated mortality is approximately 3–5% (22). The absence of blistering by day two is a favorable prognostic sign, as most patients who progress to severe SJS or TEN develop blistering within 24–48 hours of rash onset (23).

Management of Early-Stage SJS: A Step-by-Step Analysis

Withdrawal of Culprit Drugs: The single most important intervention in SJS is immediate withdrawal of all suspected drugs (24). The half-life of the culprit drug correlates with prognosis; drugs with a long half-life (e.g., ketoconazole has a terminal half-life of 2–8 hours, but its active metabolites may persist longer) can continue to drive the immune reaction even after discontinuation (25). In our patient, all six drugs were stopped immediately upon admission.

Supportive Care: Supportive care is the cornerstone of SJS management and includes intravenous fluid resuscitation, nutritional support, pain management, wound care, oral hygiene, and prevention of infections (26). Our patient received maintenance Ringer's lactate, which is appropriate for euvolemic patients. However, given her poor oral intake and vomiting on day two, closer monitoring of electrolytes and urine output was necessary. The urine output of 900–1000 mL/day is acceptable (approximately 0.6–0.7 mL/kg/hour for a 70 kg patient), which is above the threshold for acute kidney injury (27). Nevertheless, the development of vomiting and blood-tinged saliva raised concerns for possible oropharyngeal erosions extending into the esophagus, which is a known complication of SJS (28).

Oral and Oropharyngeal Care: Oral involvement in SJS is almost universal and can be extremely painful, leading to dehydration and malnutrition (29). Our patient's management included thick vaseline application to the lips, NaCl mouthwash, and topical desoximetasone on skin lesions. However, topical corticosteroids in the oral cavity are often insufficient to control inflammation in SJS; systemic corticosteroids were used instead (30). The use of NaCl mouthwash (saline) is non-irritating and helps maintain oral hygiene, but for severe oral ulcers, some guidelines recommend antiseptic mouthwashes such as chlorhexidine (31). No such antiseptic was used in our patient.

Systemic Corticosteroids: The use of systemic corticosteroids in SJS/TEN remains one of the most debated topics in dermatology (32). Some retrospective studies and small prospective trials suggest that high-dose corticosteroids (e.g., intravenous dexamethasone 1.5 mg/kg/day or methylprednisolone 1 g/day for 3 days) initiated within 48–72 hours of rash onset may halt disease progression and reduce mortality (33). However, other studies have shown no benefit or even increased risk of sepsis due to immunosuppression (34). A meta-analysis published in 2022 concluded that corticosteroids may be beneficial in early SJS (before significant skin detachment) but are harmful in TEN (35). Our patient received intravenous dexamethasone (approximately 15 mg/day, which is equivalent to 0.2 mg/kg/day – a relatively modest dose). The dose was reduced on day two to 10 mg/day (2×1 ampoule). This dose is lower than that used in some published protocols, but in resource-limited settings, such dosing may still provide benefit without excessive immunosuppression (36). The fact that our patient did not progress to blistering by day two could be attributed to the corticosteroids, to the withdrawal of culprit drugs, or to the natural history of her disease (which may have been mild SJS from the outset).

Antihistamines and H2 Blockers: Diphenhydramine (a first-generation H1 antihistamine) was given for symptomatic relief of pruritus, but it does not alter the underlying immune-mediated keratinocyte apoptosis (37). Ranitidine (an H2 blocker) was given for gastric protection, which is reasonable given the stress of hospitalization and the use of corticosteroids (38). However, ranitidine has no known role in directly treating SJS.

Topical Corticosteroids on Skin: Desoximetasone, a potent topical corticosteroid (group III/IV), was applied to skin lesions. There is no strong evidence that topical corticosteroids alter the course of SJS, but they may reduce local inflammation and provide symptomatic relief (39). In widespread disease, however, extensive application of potent topical steroids may increase systemic absorption and add to the immunosuppressive burden.

New-Onset Rales and Respiratory Concerns on Day 2: One of the most significant developments on day two was the auscultation of bilateral rales in a patient who previously had clear lung fields. Several explanations must be considered. First, **oropharyngeal erosions** can lead to difficulty swallowing, pooling of secretions, and microaspiration, causing bibasilar crackles (40).

The patient's complaint of a "lump in the throat" and blood-tinged saliva supports the possibility of extensive pharyngeal and laryngeal erosions. Second, **early laryngeal edema** or supraglottic involvement in SJS can lead to stridor and respiratory distress; although our patient did not have stridor, the new rales could be an early warning sign (41). Third, **primary pulmonary involvement** in SJS is rare but has been described, manifesting as pneumonitis or acute respiratory distress syndrome (ARDS) (42). Fourth, **simple atelectasis** due to shallow breathing from pain and weakness could also produce crackles. The management plan appropriately called for close monitoring and consideration of ENT and Pulmonology consultation. In an ideal setting, flexible laryngoscopy would be performed to visualize the upper airway directly, and a chest X-ray would be obtained to rule out pneumonia or aspiration (43).

Comparison with Published Case Reports: Our case shares similarities with a 2019 case report by Lee et al., who described a 52-year-old woman with early SJS presenting with oral ulcers and erythematous macules after taking ketoconazole for vulvovaginal candidiasis (44). In that case, the patient also received systemic corticosteroids and did not progress to blistering. A 2021 series by Garcia-Doval et al. emphasized that early-stage SJS is often missed because physicians wait for blistering to appear, leading to a median diagnostic delay of 2–3 days (45). Our patient was diagnosed and treated on day one, which may explain her favorable early outcome. Another study by Hiraiwa et al. (2020) reported that the presence of oral mucosal lesions is the strongest predictor of SJS progression, and patients with oral lesions alone (without skin blisters) still require hospitalization and aggressive management (46).

Clinical Pearls and Lessons Learned: Despite these limitations, several important clinical lessons emerge. First, **never wait for blisters** to diagnose SJS; the presence of fever, oral ulcers, and widespread macules in the setting of recent drug exposure is sufficient to suspect early SJS and admit the patient. Second, **stop all non-essential drugs immediately** – do not try to identify the single culprit at the bedside. Third, **systemic corticosteroids** can be considered in early SJS but should be used with caution, and the patient must be monitored closely for infection. Fourth, **respiratory symptoms** (shortness of breath, throat discomfort, new rales) should prompt immediate consideration of upper airway involvement; even without stridor, ENT evaluation is

warranted. Fifth, **eye examination** should be performed daily by a trained physician or ophthalmologist, as ocular complications can be silent initially.

CONCLUSION AND RECOMMENDATIONS

Conclusion: Early-stage Stevens–Johnson syndrome is a medical emergency that can be easily misdiagnosed as a benign viral exanthem or erythema multiforme major. This case of a 49-year-old female with fever, painful oral ulceration, labial crusting, and widespread erythematous macules following sequential administration of ketoconazole, prednisone, cetirizine, chloramphenicol, loratadine, and dexamethasone illustrates the critical importance of early recognition. The patient was hospitalized, all suspected drugs were withdrawn, and she received intravenous dexamethasone, diphenhydramine, ranitidine, and topical supportive care. By day two, she had not progressed to blistering, suggesting that early intervention was beneficial. However, new respiratory symptoms (bilateral rales) and blood-tinged saliva on day two underscored the need for vigilant airway monitoring. This case confirms that a high index of suspicion, immediate drug withdrawal, aggressive supportive care, and daily reassessment of mucocutaneous and respiratory status are essential to prevent progression to full-thickness epidermal necrosis and reduce mortality.

Recommendations for Clinical Practice: Based on this case and a review of the literature, we offer the following recommendations for clinicians managing suspected early-stage SJS:

1. **Maintain a high index of suspicion:** Any patient presenting with fever, painful oral ulcers, and a widespread maculopapular rash within 4 days to 4 weeks of starting a new medication should be presumed to have early SJS until proven otherwise.
2. **Admit all suspected patients:** Outpatient management is unacceptable; early SJS can progress to TEN within hours.
3. **Immediately withdraw all non-essential drugs:** Do not attempt to identify the single culprit at the bedside; stop all drugs started in the preceding 4 weeks unless absolutely life-saving.

4. **Perform a baseline SCORTEN:** Measure serum urea, glucose, bicarbonate, and calculate initial BSA of detachment (even if 0%) to establish prognosis.
5. **Initiate aggressive supportive care:** Intravenous fluids, oral hygiene (saline mouthwash, vaseline), pain control, and nutritional support.
6. **Consider systemic corticosteroids:** In early SJS (no blistering), a short course of moderate-to-high dose corticosteroids (e.g., IV dexamethasone 0.5–1.5 mg/kg/day) may be considered, but stop if blistering appears.
7. **Perform daily complete physical examination:** Pay special attention to the oral cavity, eyes (conjunctiva, cornea), genitalia, and lung auscultation. New rales or throat discomfort should prompt immediate ENT consultation.
8. **Consult ophthalmology early:** All SJS patients should have an ophthalmologic examination within 24–48 hours to prevent blindness.
9. **Obtain a skin biopsy** for histopathology and direct immunofluorescence to confirm diagnosis and rule out other blistering disorders.
10. **Arrange long-term follow-up:** Even patients with early SJS can develop late sequelae including nail dystrophy, ocular sicca, and chronic oral ulcers.

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