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Stevens Johnson Syndrome Toxic Epidermal Necrolysis Overlap Triggered by Paracetamol and Exacerbated by Cephalosporin and Fluorokuinolon: A Case Report

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Keywords
steven johnson syndrome, toxic epidermal necrolysis, paracetamol, ceftraixone, levofloxacin

Abstract
Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) as rare but life-threatening type IV hypersensitivity reactions, characterized by epidermal necrolysis, bullae, skin desquamation, and mucosal involvement. Most cases are triggered by medications and carry a high mortality rate, especially in *TEN*. Management requires early discontinuation of the trigger medication, a multidisciplinary approach, and intensive supportive therapy. The report describes a 40-year-old Russian man who presented with widespread skin peeling, pain, and burning sensation, accompanied by ocular and oral mucosal involvement. Symptoms began after paracetamol consumption and worsened following administration of ceftriaxone and levofloxacin. Physical examination revealed extensive skin and mucosal involvement with a positive Nikolsky sign and body surface area (*BSA*) involvement of 32%. Laboratory tests showed leukocytosis and elevated C-reactive protein (*CRP*). The diagnosis of *SJS/TEN* overlap was established, with the aforementioned drugs as suspected triggers. The patient received supportive therapy, including discontinuation of antibiotics, rehydration, corticosteroids, antihistamines, mucosal protection, and wound care, along with consultations from ophthalmology and otolaryngology services. Effective management of *SJS/TEN* requires prompt discontinuation of trigger drugs, intensive supportive therapy, and multidisciplinary coordination to minimize complications and mortality.

INTRODUCTION

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are rare but potentially life-threatening type IV hypersensitivity reactions characterized by extensive epidermal necrolysis, bules, skin desquamas, and mucosal involvement (Zimmerman & Dang, 2019). Both are differentiated based on the surface area of the body involved: SJS <10%, TEN >30%, and SJS/TEN overlap 10–30% (Chuenwipasakul et al., 2023; Panpruk et al., 2021; Tan et al., 2021).

SJS-TEN is a rare disease, in general the incidence of SJS is 1-6 cases/million population/year, and the incidence of TEN is 0.4-1.2 cases/million population/year (Dhamasari et al., 2021; Sari & Pemayun, 2020). The incidence of SJS is estimated at 2-3% per million population per year in the United States and in European countries, while in Indonesia cases of SJS occur around 12 cases per year (Abdulah et al., 2017; Lee et al., 2023; Mulianto & Lidjaja, 2025; Sutedja et al., 2025). According to Banjarnahor et al., in 2019-2021, the incidence of SJS

at Soetomo Hospital was 28 cases of Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN) successfully analyzed, consisting of 15 men (53.6%) and 13 women (46.4%), with the largest age group being 19–44 years old (35.7%). The TEN mortality rate is 25-35%, while the SJS mortality rate is 5-12% (Chiu & Chiu, 2025; Hsu et al., 2016).

Most cases of SJS/TEN are triggered by the use of medications, especially antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory drugs (OAINS) (Abulatan et al., 2023; Castellana et al., 2025; Diana et al., 2020; Frey et al., 2019). These reactions generally appear within the first 8 weeks of treatment, and most triggering medications begin to cause reactions after being used for 4-28 days continuously. Early manifestations usually include fever, malaise, and maculopapular erythematous lesions that quickly develop into bules and erosion of the skin and mucosa. At a further level it is accompanied by systemic symptoms such as fever, and body aches (Ames et al., 2017; Weng et al., 2021). SJS has a fairly high morbidity and mortality rate even though the incidence of this condition is quite rare, so prompt and appropriate medical treatment is essential to prevent serious complications.

The management of SJS/TEN requires a multidisciplinary approach accompanied by the earliest possible termination of drugs suspected as triggers. Supportive therapy is very important in the management of acute phase SJS/TEN. Until now, the choice of definite and optimal systemic therapy is still debated.[6] In this case report, we discuss a 40-year-old man who developed SJS/TEN after the use of certain medications, with an emphasis on clinical diagnosis, supportive management, and consideration of additional pharmacological therapies.

This study aims to describe in depth the cases of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) triggered by paracetamol and exacerbated by the administration of cephalosporin and fluoroquinolone antibiotics, with a focus on clinical diagnosis, supportive management, and additional pharmacological therapy. This study also aims to explore the importance of stopping suspicious drugs as soon as possible as well as a multidisciplinary approach in the management of SJS/TEN to reduce complications and improve patient clinical outcomes.

This research provides practical benefits for medical personnel in understanding the management of SJS/TEN, by providing insights into the importance of early detection, discontinuation of causative drugs, and multidisciplinary patient management. In addition, this study also enriched clinical knowledge related to supportive and pharmacological therapies needed in the treatment of SJS/TEN patients, as well as providing information about the risks of certain medications that can trigger these reactions. Theoretically, this research contributes to the development of guidelines for the management of SJS/TEN, which is expected to increase awareness and handling of this condition in the future.

RESEARCH METHOD

This study used a descriptive case study method to describe the clinical problems faced by patients with SJS/TEN. Patient data is collected through medical interviews, physical examinations, and analysis of medical records. Supporting examinations such as thoracic CT-scans, ECGs, and thoracic X-rays are performed to establish the diagnosis. Treatment was carried out with a multidisciplinary approach, including discontinuation of causative drugs, rehydration, corticosteroid therapy, and wound and mucosal treatment. The results of the study

were analyzed descriptively to describe the care patients received and the progression of clinical conditions during treatment, with a focus on complication reduction and clinical improvement.

RESULTH AND DISCUSSION

A 40-year-old Russian male came in with complaints of peeling skin almost all over the body accompanied by pain and burning sensation. Initially, the patient feels itching, heat, and redness appears in the back area and then spreads to the face, eyes, arms, and legs. Patients have difficulty opening their eyes due to thick secretions, pain when swallowing, and dry, chapped and bleeding lips. Fever begins to be felt on the third day. This complaint has been going on for approximately 15 days, starting after the patient took paracetamol and worsening after receiving ceftriaxone and levofloxacin therapy.

At the vital signs examination, blood pressure was 110/80 mmHg, pulse was 88 times/minute, breathing rate was 18 times/minute, temperature was 36.8°C, and oxygen saturation was 98% in room air. Physical examination showed extensive involvement of the skin and mucosa. There is a bilateral erosion of the palpebra, hyperemic conjunctiva with white secretions (fig. 1). The lips are eroded with hemorrhagic crusta. The face and back show macular erythema, epidermolysis, and erosion. (Figure 2) The irisiformis erythema macula appears on the palms of the hands, as well as epidermolysis and necrotic tissue on some toes. (Figure 3). Bular lesions and macular erythema are also found in the penile gland and scrotum. (Fig. 4). Nikolsky (+) with a 32% body surface area (BSA) involvement

Laboratory examination of leukocytes 13,290/mm^3, C-Reactive Protein (CRP) 12 mg/dL, and Blood Urea Nitrogen (BUN) 28 mg/dL, creatinine and electrolyte values within normal limits. Procalcitonin <0.10 ng/mL. Albumin is 3.99 g/dL, and blood sugar is 115 mg/dL.

Based on clinical history, physical examination, and laboratory findings, the patient was diagnosed with Stevens-Johnson Syndrome (SJS), most likely as a result of an allergic reaction to paracetamol, ceftriaxone and levofloxascin.

Patients received supportive therapy in the form of discontinuation of all antibiotics and rehydration with crystalloid fluid, dexamethasone injection 3x10mg given with a dose reduction for 20 days, ranitidine injection 2x50mg, Zithromax 1x1000mg for 7 days, Interhistine 3x1tab, and sucralfate 4x15ml. The skin lesions were cleaned with NaCl, given Sufratul, and covered with sterile gauze. Lip lesions are applied with Kenalog, while the irritated skin area is given salicylate powder. Patients are also consulted to an ophthalmologist to get Cendo Xitrol Ointment 3x1 a day, Lyteers ED 8xgtt1 ODS and ENT specialists get Oral Gargling Mynosep/Betadin berries every 4 hours. On day 28, the patient was consulted with an internal medicine specialist regarding a decrease in albumin (3.46g/dL) and was given 3x1 Onoiwa therapy.

After 35 days of treatment, the patient showed improvement in the condition with skin and mucosal improvement, and then the patient was returned to the country of origin for further treatment. With multidisciplinary and supportive treatment, it is hoped that patients can go through the acute phase and avoid serious complications such as secondary infections or systemic organ failure which are generally the cause of mortality in cases of SJS.

Figure 1

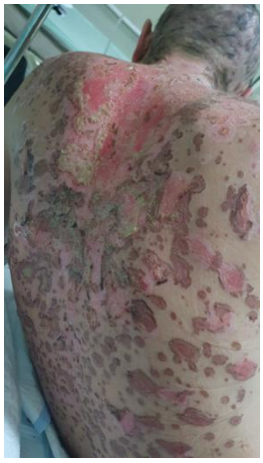

Figure 2

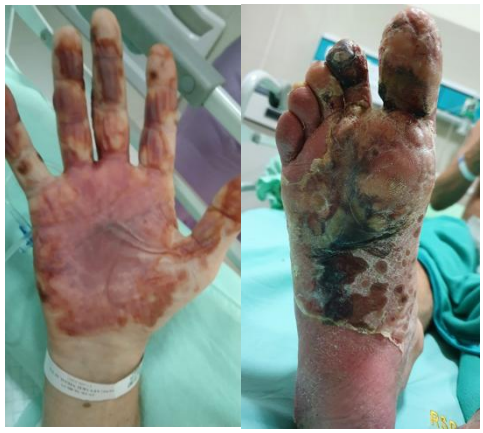

Figure 3

Figure 4

Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are progressive but potentially life-threatening dermatological emergencies characterized by extensive epidermal necrolysis and thorough exfoliation. This widespread skin loss can lead to serious complications such as sepsis, multiple organ failure, and death.[1,2]

This disease can occur at any age, but the risk increases with age over 40 years. In most cases, TEN occurs as a result of an idiosyncratic immune reaction to certain medications. There are some medications that are most often triggered, for example antibiotics (especially sulfonamides), anticonvulsants, NSAIDs, and allopurinol. Nonsteroidal anti-inflammatory drugs (OAINS) are suspected to be related to the incidence of CJS, there are differences in the level of risk between these drug groups. Oxicam derivatives showed the highest level of risk, acetic acid derivatives such as diclofenac had a moderate risk, while propionate acid derivatives such as ibuprofen did not show an increased risk. According to research, there are risks in types of antibiotics such as cephalosporins, quinolone, tetracycline and aminipenicillin. Most reactions begin to arise after the drug is used for 4-28 days continuously and the greatest risk arises within the first 8 weeks. This is in accordance with what happens in patients, symptoms appear after taking paracetamol for 5 days, then complaints arise and are aggravated by the administration of antibiotics ceftriaxone and levofloxacin.[4.5]

This reaction arises because it is mediated by the activation of cytotoxic T lymphocytes, especially CD8+ cells, which recognize drug antigens presented by keratinocytes through *human leukocyte antigen* (HLA) molecules. This activation triggers the release of cytotoxic molecules such as granzyme B, perforin, Fas ligand (FasL), and granulysin, which causes massive apoptosis of keratinocytes, resulting in extensive damage to the epidermis. Infiltration of inflammatory cells also exacerbates the process of tissue damage and causes clinical symptoms in the form of bubbles, skin erosion, and extensive desquamation. In addition to the skin, this process also involves mucosal tissues such as the conjunctiva, oral mucosa, and genital mucosa, as seen in the case of this patient.[5]

The clinical picture of SJS or TEN, which is a severe hypersensitivity reaction that is usually triggered by medication, in this case it is possible paracetamol. The prodromal stage in the form of fever and malaise as well as the initial symptoms of redness and itching on the skin mark the beginning of systemic inflammatory processes. Subsequently, the skin involvement develops into an erythematous lesion that expands and turns into a bular with a positive Nikolsky sign, indicating separation of the epidermal layer due to skin cell necrosis. In addition, mucosal involvement is evident with severe oral mucositis causing pain when swallowing, ulceration of bleeding lips, and ocular mucosal involvement causing eyes to be difficult to open and feel dirty. Bullic lesions in the genitalia confirm that more than one mucosal surface is involved, according to the classic picture of SJS/TEN. The surface area of the affected skin in patients is 32%.[1.4]

The Disease Severity Score on Toxic Epidermal Necrolysis (SCORTEN) is based on seven clinical and laboratory variables, and can be used to predict the risk of death in a patient. Based on available clinical data and laboratory results, the patient's SCORTEN score was three points, with an affected surface area of 32%, indicating a mortality risk of 35.3%.[5] SJS-TEN requires optimal management, namely early detection and discontinuation of drugs suspected as the cause. Supportive care includes, maintaining fluid balance, electrolytes, nutrients, aseptic skin care, eye and oral mucosal care.[4]

The airways should be monitored regularly and additional oxygen can be provided if needed. In the event of respiratory distress, endotracheal intubation should be performed by an expert. Resuscitation of fluids using crystalloids. The target of resuscitation is to maintain adequate tissue perfusion by achieving a mean arterial blood pressure (MAP) of >65 mmH and urine production of 0.5–1 ml/kg/hour. Aseptic wound care is very important to prevent secondary infection until re-epithelialization occurs. Initial consultation with an ophthalmologist is very important to prevent long-term eye complications in the form of simblepharon, chronic keratoconjunctivitis, and blindness. Therefore, multidisciplinary collaboration between dermatologists, ophthalmologists, ENT doctors and other treatment teams is indispensable in the comprehensive management of SJS patients.[6.7]

High-dose corticosteroid therapy (prednisolone 1-2mg/kgBB or dexamethasone 8-16mg/day intravenously) may be given in the first 72 hours after onset to prevent wider spread, followed by 7-10 days, followed by a gradual dose reduction (*tapering off*). The function of corticosteroids is to suppress the function of monocytes and lymphocytes (helper T cells 1 and 2) and suppress the immune reaction by inhibiting cytokines. According to Dina *et al, the* administration of high-dose corticosteroids during the acute phase can reduce mortality rates without increasing the risk of sepsis and reepithalization.[7,8,12]

Other therapy options that can be given are Intravenous Immunoglobulin (IVIg), cyclosporine, and plasmapheresis. IVIg contains immune antibodies inhibiting apoptosis pathways mediated by FasL and its receptors. Some studies have shown that IVIg can decrease antigen-specific T-CD4+ cell responses, suppressing the activation of T-CD8+, perforin and CD107 cells. Cyclosporine is a class of immunosuppressive and immunomodulatory drugs, inhibiting CD8+ activation and providing antiapoptosis effects through Fas-L inhibition. The dose of cyclosporine given generally starts at 3 mg/kgBB/day for 10 days. Plasmapheresis is the separation of plasma from the blood to remove causative factors such as drugs, drug metabolites, inflammatory mediators, and antibodies and then replace them with replacement fluids, such as albumin. Tepapi plasmapheresis may be considered as an alternative therapy in patients with severe TEN, especially if it is unresponsive to initial therapy, including corticosteroids and cyclosporin.[7,8,9]

The patient was given intravenous corticosteroids, namely with dexamethasone with an initial dose of 3x10mg for 3 days and tapering *off* for up to 20 days of treatment, this is in line with the case report conducted by Shrestha AB *et al* and Mkhoyan A *et al*. The patient also received the antibiotic Zithromax 1x1000mg for 7 days because a blood test found lexocytosis.[10,11] Ophthalmologist therapy is given Cendo Xitrol 3x1 which functions to treat infections and inflammation in the eyes. The ENT doctor is given Mynosep gargle every 4 hours. After 35 days of treatment, the patient's clinical complaints and skin lesions improved.

CONCLUSION

A 40-year-old Russian man developed Stevens-Johnson Syndrome (SJS)/ Toxic Epidermal Necrolysis (TEN) overlap, a rare life-threatening type IV hypersensitivity reaction triggered by paracetamol and exacerbated by ceftriaxone and levofloxacin, presenting with widespread skin peeling, pain, burning sensation, fever, ocular and oral mucosal erosions, positive Nikolsky sign, and 32% body surface area involvement, alongside leukocytosis and elevated C-reactive protein. Diagnosis was confirmed clinically, with management emphasizing immediate discontinuation of culprit drugs, multidisciplinary supportive care including rehydration, high-dose dexamethasone (tapering over 20 days), ranitidine, azithromycin, antihistamines, sucralfate, aseptic wound care, topical treatments, and consultations with ophthalmology and otolaryngology, leading to clinical improvement after 35 days without major complications. This case underscores the value of early intervention in reducing mortality (estimated at 35.3% via SCORTEN score) in medication-induced SJS/TEN. Future research should investigate prospective pharmacovigilance studies on paracetamol and antibiotic combinations in diverse populations, including genetic HLA associations in non-Western cohorts, to refine risk stratification and preventive guidelines.

REFERENCES

Abdulah, R., Suwandiman, T. F., Handayani, N., Destiani, D. P., Suwantika, A. A., Barliana, M. I., & Lestari, K. (2017). Incidence, causative drugs, and economic consequences of drug-induced Stevens–Johnson syndrome, toxic epidermal necrolysis, and SJS–TEN overlap and potential drug–drug interactions during treatment: A retrospective analysis at an Indonesian referral hospital. *Therapeutics and Clinical Risk Management*, 13, 919–925.

Abulatan, I. T., Ben-David, S. G., Morales-Colon, L. A., Beason, E., Fakoya, A. O., & Abulatan, I. (2023). A compilation of drug etiologies of Stevens–Johnson syndrome and toxic epidermal necrolysis. *Cureus, 15*(11). https://doi.org/10.7759/cureus.49401

Ames, N. J., Powers, J. H., Ranucci, A., Gartrell, K., Yang, L., VanRaden, M., Leidy, N. K., & Wallen, G. R. (2017). A systematic approach for studying the signs and symptoms of fever in adult patients: The Fever Assessment Tool (FAST). *Health and Quality of Life Outcomes, 15*(1), 84. https://doi.org/10.1186/s12955-017-0663-8

Banjarnahor, L. E., Suharto, S., & Wulandari, D. (2023). Profile of Stevens–Johnson syndrome and toxic epidermal necrolysis patients at inpatient hospital. *World Journal of Advanced Research and Reviews, 18*(2), 1–8. https://doi.org/10.30574/wjarr.2023.18.2.0357

Castellana, E., Budau, P. M., & Chiappetta, M. R. (2025). Pharmacovigilance and Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN): 55 years of retrospective analysis of the FDA Adverse Event Reporting System (FAERS) database. *Hospital Pharmacy*. https://doi.org/10.1177/00185787251337610

Chiu, H.-Y., & Chiu, Y.-M. (2025). Risk of cardiovascular morbidity and mortality in Stevens–Johnson syndrome/toxic epidermal necrolysis survivors. *JAMA Dermatology, 161*(4), 391–398. https://doi.org/10.1001/jamadermatol.2024.5173

Chuenwipasakul, D., Washrawirul, C., Panpruk, R., Wititsuwannakul, J., Charoenchaipiyakul, K., Buranapraditkun, S., Puangsricharern, V., Klaewsongkram, J., & Rerknimitr, P. (2023). Correlations between histopathologic findings, serum biomarker levels, and clinical outcomes in Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). *Scientific Reports, 13*(1), 13620. https://doi.org/10.1038/s41598-023-40764-7

Dhamasari, P. M. A., Salsabilla, R., & Ramadhan, A.-T. (2021). Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). *KESANS: International Journal of Health and Science, 1*(3), 304–315.

Diana, R., Rahayu, T., Wirawan, E. P., Dhamayanti, M. E., Yuliarto, D., & Irawanto, M. E. (2020). Pathophysiology and management therapy of Stevens–Johnson syndrome and toxic epidermal necrolysis. *Journal of General Procedural Dermatology & Venereology Indonesia, 5*(1), 28–35.

Frey, N., Bodmer, M., Bircher, A., Jick, S. S., Meier, C. R., & Spoendlin, J. (2019). Stevens–Johnson syndrome and toxic epidermal necrolysis in association with commonly prescribed drugs in outpatient care other than antiepileptic drugs and antibiotics: A population-based case–control study. *Drug Safety, 42*(1), 55–66. https://doi.org/10.1007/s40264-018-0736-5

Hsu, D. Y., Brieva, J., Silverberg, N. B., & Silverberg, J. I. (2016). Morbidity and mortality of Stevens–Johnson syndrome and toxic epidermal necrolysis in United States adults. *Journal of Investigative Dermatology, 136*(7), 1387–1397. https://doi.org/10.1016/j.jid.2016.03.023

Lee, E. Y., Knox, C., & Phillips, E. J. (2023). Worldwide prevalence of antibiotic-associated Stevens–Johnson syndrome and toxic epidermal necrolysis: A systematic review and meta-analysis. *JAMA Dermatology, 159*(4), 384–392. https://doi.org/10.1001/jamadermatol.2022.6289

Mkhoyan, A., Hashmi, M. F., Khan, F., Gyulazyan, N., Asoyan, V., & Nersisyan, V. (2023). Stevens–Johnson syndrome: A case report of possible cephalosporin-induced cutaneous adverse reaction. *Journal of Infection in Developing Countries, 17*(10), 1493–1496. https://doi.org/10.3855/jidc.18301

Mulianto, N., & Lidjaja, L. N. (2025). Drug-induced Stevens–Johnson syndrome and toxic epidermal necrolysis: A retrospective study on causative agents and patient profiles in

an Indonesian hospital setting. *Bioscientia Medicina: Journal of Biomedicine and Translational Research, 9*(7), 7967–7980.

Panpruk, R., Puangsricharern, V., Klaewsongkram, J., Rerknimitr, P., Kittipibul, T., Chongpison, Y., & Buranapraditkun, S. (2021). Clinical parameters and biological markers associated with acute severe ocular complications in Stevens–Johnson syndrome and toxic epidermal necrolysis. *Scientific Reports, 11*(1), 20275. https://doi.org/10.1038/s41598-021-99693-3

Sari, L. G. M. P., & Pemayun, T. D. (2020). Stevens–Johnson syndrome–toxic epidermal necrolysis overlap in a 61-year-old woman: A case report. *Intisari Sains Medis, 11*(2), 606–609.

Shrestha, A. B., Shrestha, S., Yadav, P. K., Adhikari, L., & Yadav, A. (2022). Cefixime-induced Stevens–Johnson syndrome: A case report from Bangladesh. *Annals of Medicine and Surgery, 79*, 104089. https://doi.org/10.1016/j.amsu.2022.104089

Sutedja, E., Suwarsa, O., Pangastuti, M., Firdaus, C. P., Dwiyana, R. F., Rizqandaru, T., Mustaram, A. A., Muslima, P., & Sabila, A. A. (2025). Understanding the gap between acute complications and long-term sequelae in patients with Stevens–Johnson syndrome and toxic epidermal necrolysis in Bandung, West Java, Indonesia: Experience from two institutions. *Clinical, Cosmetic and Investigational Dermatology*, 18, 979–988.

Tan, M. L. L., Kwong, H. L., Ang, C. C., Tey, H. L., Lee, J. S. S., & Becker, D. L. (2021). Changes in connexin 43 in inflammatory skin disorders: Eczema, psoriasis, and Stevens–Johnson syndrome/toxic epidermal necrolysis. *Health Science Reports, 4*(1), e247. https://doi.org/10.1002/hsr2.247

Weng, L.-M., Su, X., & Wang, X.-Q. (2021). Pain symptoms in patients with coronavirus disease (COVID-19): A literature review. *Journal of Pain Research*, 14, 147–159. https://doi.org/10.2147/JPR.S269206

Zimmerman, D., & Dang, N. H. (2019). Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). In *Oncologic critical care* (pp. 1–15). Springer. https://doi.org/10.1007/978-3-030-20161-6_6