Journal of Pakistan Association of Dermatologists. 2023;**33(3)**:1124-1129.

Case Report

Early Stevens-Johnson Syndrome mimicking secondary syphilis: A case report

Caroline Astrid, Marsha Bianti*, Hillary Fungestu Yoedyanto, Nabilla Wahyu Stradivary, Annisa Eka Putri

Medical Doctor Kramat 128 Hospital Jakarta.
* Department of Dermatology and Venereology Kramat 128 Hospital Jakarta.

Abstract Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is an uncommon life-threatening vesicobullous condition caused by immunologic reactions to several stimuli, usually a reaction to certain medications. A 21-year-old Indonesian male adult came to the emergency department with chief complaints of painful erythematous rashes on his hands and feet, watery eyes, and sore throat. He is also been diagnosed with bipolar disorder and currently still on medication. His rash worsened during initial hospitalization and was given appropriate treatment. Stevens-Johnson syndrome is known to be presented as a systemic mucocutaneous lesions with organ involvement. Syphilis is a sexually transmitted infection. Syphilis is referred to as "the great imitator" since it frequently mimic many other conditions, making a prompt diagnosis challenging. The skin is involved in 70% of syphilis cases presented with maculopapular, vesiculobullous, and ulcerative morphologies. Given that Stevens-Johnson syndrome is an uncommon but dangerous disorder, this instance highlights the significance of pattern recognition in this condition.

Key words
Stevens-Johnson syndrome; Toxic epidermal necrolysis; Syphilis; Vesicobullous lesion.

Introduction

Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is a condition marked by generalized exanthema coupled with a high temperature, catarrhal symptoms, and the involvement of two or more mucosal tissues with their related signs and symptoms (itching, photophobia, conjunctival injection, odynophagia, dysuria, etc.). Stevens-Johnson syndrome may develop into a major, possibly deadly, consequence of secondary syphilis if the condition advances quickly and results in considerable skin necrosis.[1,2]

Syphilis, a disease caused by *Treponema pallidum* transmission through sexual contact, is known as "the great imitator" because it frequently manifests as cutaneous rashes that resemble those of numerous dermatological conditions.[2] Spirochete transmission occurs through direct contact during sexual contact with active lesions or passed during pregnancy from the mother to the fetus through the placenta. The first site of primary syphilis infection is usually marked with a painless ulcer on the genitalia area. If ignored, the secondary stage of syphilis, which is characterized by mucocutaneous rashes that frequently mimics guttate psoriasis, maculopapular drug eruptions, pityriasis rosea Gibert, and other chronic skin disease, accompanied by lymphadenopathy and vague flu-like symptoms. After the latent phase, tertiary syphilis can develop to certain complications, which can cause neurosyphilis, heart and vascular damage, and gummata. Gummata, a sign of severe syphilis, manifests as solitary or many coalescing plaques or nodules with an ulcer on the center and scarring in the

Address for correspondence
Dr. Caroline Astrid
Medical Doctor Kramat 128 Hospital Jakarta.
Ph: 087878291999
Email: carolineastrid@outlook.com

Figure 1 Patient's dermatology status when first arrived at the hospital.

Figure 2 Painful and spreading skin lesions distribution on the second day of hospitalization.

skin, bone, and internal organs. Syphilis is a severe illness with a high fatality rate.[3,4]

Case report

A 21-year-old Indonesian male presented to the emergency department of Kramat 128 Hospital with chief complaints of painless rashes in his hands, feet, arms, and legs. He also experienced fever and sore throat. His symptoms started 4 days ago. His eyes were red, itchy, watery, and have scales with yellowish exudate. This patient also reported to have a painless genital ulcer that healed on its own. He also experienced weight loss, approximately 10 kilograms, in the last three months. He is a bisexual with multiple active sexual partners. He has piercing and multiple tattoos, however he denied having history of intravenous or other illicit drug use.

The patient had been diagnosed with bipolar disorder since 4 years ago and currently on treatment with divalproex sodium 500 mg once daily, lamotrigine 100 mg once daily, quetiapine 300 mg once daily, lorazepam 0.5 mg once daily (as needed), and trihexyphenidyl 2 mg once daily (as needed). The recent addition of his bipolar medication by his psychiatrist was lamotrigine which had been given for the last two months. The physical examination revealed a non-pruritic erythematous-violaceous rash covering his face, torso, and extremities, including his palms and soles, upon his admission to the hospital. The trunk and extremities have a lot of targetoid lesions. Mucosal erosion with honey-colored crust was found mostly on the patient's lower lips. The patient's upper eyelids were also swollen and he was not able to open his eyes properly.

Figure 3 Progressive multiple papules, bullae, swollen eyelids, crusted lips with mucositis on the second day of hospitalization.

The complete blood count showed leucocytosis, anti-HIV test was found non-reactive, and SARS-CoV-2 PCR swab was found negative. This patient was first referred to an internist and diagnosed with pneumonia, bipolar disorder, bacterial conjunctivitis, and suspected secondary syphilis. The initial therapy was oral antibiotics to treat the pneumonia. Additional drugs given were antipiretic as a symptomatic treatment and oral antifungal for his oral thrush. To confirm the suspected secondary syphilis, this patient was consulted to the dermatovenereologist with the differential diagnosis of maculopapular drug eruption. VDRL/TPHA tests were conducted and required some time for the results to come in. Based on the clinical consideration, benzathine penicillin G 2.4 million units via intramuscular in single dose and systemic corticosteroid was given while waiting for the VDRL/TPHA test results. VDRL and TPHA tests were found negative the day after.

On the second day of hospitalization, the irregular purpuric papules-plaques scattered over his back, back, legs, and a few on the arms appeared. The palms and soles were covered in erythematous macules that were almost all confluent. There were numerous huge, deep, complete bullae on the back and a few on the right arm. The oral mucosa and eyelids became more swollen. Within hours, those skin lesions became more extensive and progressively spread to all over the body. The patient then received additional therapy with NaCl 0.9% compress and topical antibiotic for ruptured bullaes.

On the third day, most of the lesions became vesicle-bullaes and were found with a positive direct Nikolsky's sign. The dermato-venereologist suspected SJS/TEN and increased the dose of the systemic corticosteroid. Supportive therapy was also given including fluid administration, topical corticosteroid, warm compresses and systemic antibiotic therapy. He was transferred to another hospital to take a biopsy test. This case demonstrates the significance of identifying patterns in Steven Johnson's syndrome, an uncommon but deadly disorder that must be identified early and treated appropriately.

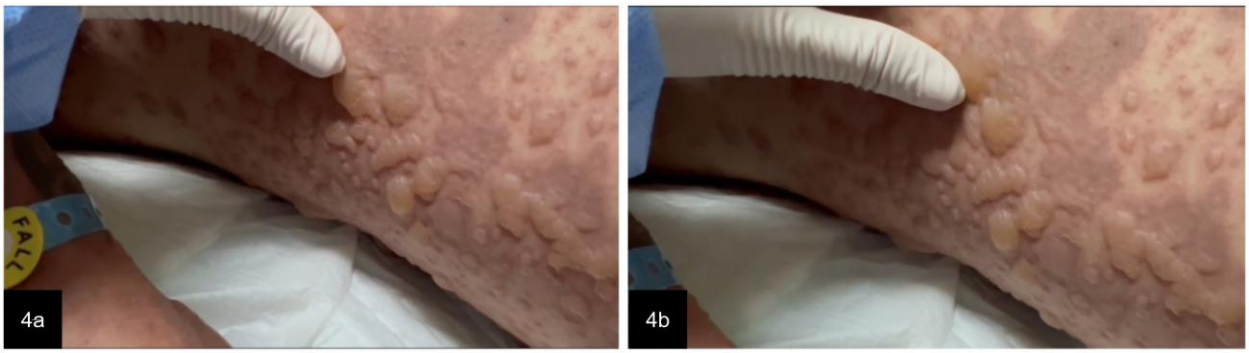

Figure 4 A positive direct Nikolsky's sign.

Figure 5 Painful skin and mucosal lesions on the third day of hospitalization before the patient was being referred to another hospital for further treatment.

Discussion

Syphilis is a treatable sexually transmitted disease. However, according to the Centers for Disease Control and Prevention (CDC), syphilis can lead to serious complications if left untreated, e.g. irreversible neurological (neurosyphilis) and cardiovascular complications. Syphilis infection develops in four stages: primary, secondary, latent, and tertiary. Each stage shows different signs and symptoms.[3,5,6] Resulting manifestation due to the body's inflammatory response to syphilis infection often mimics other diseases, hence the term of syphilis as a great imitator arises.[7]

We described a case that was initially suspected as secondary syphilis, but after being tested, the results were negative. Secondary syphilis has an extensive variety of clinical cutaneous manifestations that usually appear within three months of exposure, some of which include cutaneous lesions accompanied by constitutional signs and symptoms. Due to this patient's unique appearance, it is possible to see the cutaneous signs of the disease at various points in its progression. Giving consideration to the rarity of cases and the variety of cutaneous presentations of secondary syphilis, Stevens-Johnson syndrome is not typically the first differential diagnosis among professionals, as demonstrated in the case of this patient. This case demonstrates the importance of considering SJS/TEN as a differential diagnosis to avoid fatal complications. We must rule out the presence of SJS/TEN when evaluating patients with suspected drug allergies or viral infections.

Stevens–Johnson syndrome is a rare medical emergency caused by immunologic reactions, mostly triggered by certain medications. This life-threatening condition presents as a spectrum of primarily widespread mucocutaneous lesions and also with other organ involvement. This

condition triggers immune-mediated apoptosis. Upon skin biopsy is characterized by full-thickness necrosis of the keratinocytes. Early suspicion and quick withdrawal of the culprit medication are the necessary to stop this fatal reaction.[8] Individual skin lesions' pattern, distribution, and the maximum extent of the epidermal detachment are three clinical criteria to evaluate SJS/TEN. Dermolysis of <10% of the body surface area (BSA) is defined as SJS, 10-30% as SJS/TEN-overlap and >30% as TEN.[9]

We looked at this patient's medication history to look for the suspected drug. This patient took divalproex sodium 500 mg once daily, lamotrigine 100 mg once daily, quetiapine 300 mg once daily, lorazepam 0.5 mg once daily (as needed), and trihexyphenidyl 2 mg once daily (as needed) as his bipolar disorder treatment from his psychiatrist. The recent addition to his bipolar medication was lamotrigine and he took it for the last two months before being hospitalized for his skin condition. In various literature studies, it is known that one of the most common causes of SJS includes allopurinol, sulfonamides, nonsteroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, and lamotrigine.[11] Lamotrigine is a mood stabilizer and anticonvulsant that is often used in the treatment of bipolar disorder.[10]

Generally, drug-induced SJS/TEN will occur within the first few weeks of starting the medication, but in some cases, there can be a delayed presentation. It was found that there was a case of delayed Stevens-Johnson syndrome caused by lamotrigine in 2017 where a male patient in India developed SJS/TEN after 6 months of consuming lamotrigine.[11] This further shows the challenges that can be found in diagnosing SJS/TEN. Skin biopsy is necessary to achieve a better diagnosis in patients with suspected SJS/TEN. Due to the limitation of our hospital facilities, we refer the patient to another hospital for a biopsy and further treatment.

Conclusion

A 21-year-old Indonesian man with discomfort and redness in his eyes, pain in his hands and feet, a rash, and a sore throat was our patient. He was examined by a dermatovenereologist and SJS/TEN was identified. This case demonstrates how syphilis, which is known as the "great imitator", can present with rashes that resemble numerous dermatological conditions, including SJS/TEN, and the significance of identifying the initial lesion and receiving the right treatment because it is a rare but fatal condition.

References

1. Wirya A, Suga H, Kurniadi I, Miyagaki T, Miyazaki M, Sato S. A case of secondary syphilis manifesting erythema multiforme-like skin lesions. *Dermatologica Sin*. 2019;**37(3)**:172–3.
2. Dutt J, Sapra A, Sheth-Dutt P, Bhandari P, Gupta S. Stevens-Johnson Syndrome: a perplexing diagnosis. *Cureus*. 2020;**12(3)**: e7374.
3. Cook OM, Knafo J, Bhaskar R, Salhab M, Nguyen H. Secondary syphilis presenting as erythema multiforme in the setting of AIDS and psoriasis. *Cureus*. 2022;**14(9)**: e29110.
4. H Kawi N, Sihotang EP, Nisa T, Hui B, Causer LM, Januraga PP, *et al.*. Incidence and risk factors for syphilis infection among men who have sex with men: a cohort study from an urban sexual health clinic in Jakarta, Indonesia. *Int J STD AIDS*. 2022; **33(12)**:1065–72.
5. Cherneskie T, Bachmann L, Blank S, Bolan G, Daskalakis DC, Lee E, *et al.*. The diagnosis , management and prevention of syphilis: an update and review. In: Millstone M, Selkowe E, Stevens LM, editors. New York: The New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections and The New York City STD Prevention Training Center. 2019;5–6.

6. Çakmak SK, Tamer E, Karadağ AS, Waugh M. Syphilis: a great imitator. *Clin Dermatol*. 2019;**37(3)**:182–91.
7. Zimmerman D, Dang NH. Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). In: Nates JL, Price KJ, editors. Oncologic Critical Care. Springer Nature Switzerland AG. 2020;267–80.
8. Chang WC, Abe R, Anderson P, Anderson W, Ardern-Jones MR, Beachkofsky TM, *et al.*. SJS/TEN 2019: from science to translation. *J Dermatol Sci*. 2020;**98(1)**:2–12.
9. Besag FMC, Vasey MJ, Sharma AN, Lam ICH. Efficacy and safety of lamotrigine in the treatment of bipolar disorder across the lifespan: a systematic review. *Ther Adv Psychopharmacol*. 2021;**11**:1-37.
10. Tsukagoshi E, Tanaka Y, Saito Y. Implementation of Pharmacogenomic Information on Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. *Front Med*. 2021;**8**:644154.
11. Jha KK, Chaudhary DP, Rijal T, Dahal S. Delayed Stevens-Johnson syndrome secondary to the use of lamotrigine in bipolar mood disorder. *Indian J Psychol Med*. 2017;**39(2)**:209–12.