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THE IMPORTANT ROLE OF ORAL MEDICINE SPECIALIST IN MANAGEMENT OF STEVENS-JOHNSON SYNDROME PATIENT

Nuri Fitriasari,[1,2*] Eko Rotary Nurtito,[1,3] Nanan Nur'aeny,[4] Indah Suasani Wahyuni.[4]
[1]Resident of Oral Medicine Specialist Study Program, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia.
[2]Medical Staff Group of Dental and Oral Health Department, Dr. Hasan Sadikin Central Hospital, Bandung, Indonesia
[3]Medical Staff Group of Dental and Oral Health Department, Dental Specialty Hospital, Bandung, Indonesia
[4]Lecturer of Oral Medicine Department, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia.

ABSTRACT
Introduction: Stevens-Johnson Syndrome (SJS) is an acute hypersensitivity reaction that manifests on the skin, oral mucosa, ocular, gastrointestinal, genital and anal area. It is also potentially life-threatening in concern of dehydration and infection. Oral mucosal lesions due to SJS resulted in a significant decrease of patient's quality of life. When the oral mucosa involved, the intake of nutrients and fluids is disrupted contributing to electrolyte imbalance that aggravates dehydration. Moreover, oral mucosal lesions have become an entry point for infection. **Purpose:** This case report describes the important role of oral medicine specialists in the management of oral mucosal lesions in SJS patient. **Review:** A 26-year-old female patient was referred from the Department of Dermatology and Venereology with a diagnosis of SJS et causa suspected paracetamol and/or amoxycillin. The complaints comprised of pain on the lips and oral cavity, difficulty in mouth opening, and pain when swallowing. The management for oral lesions included: history taking, external and intra oral examinations, dexamethasone mouthwash, nystatin oral suspension, and sodium chloride (NaCl) 0.9% solution. The patient showed improvement in oral mucosal lesions within 3 weeks of treatment that was provided by oral medicine specialist and medical team collaboration. **Conclusion:** Based on this case report, the role of oral medicine specialist is very important as part of the management team for SJS patient. Oral medicine specialist can reduce morbidity that results from oral mucosal involvement. Collaboration with oral medicine specialist since the beginning of treatment is the key to success in SJS management.

Keywords: *Oral medicine specialist, Oral mucosal lesion, Stevens-Johnson Syndrome.*

Correspondence author: Nuri Fitriasari. Oral Medicine Specialist Study Program, Faculty of Dentistry, Universitas Padjadjaran, Jl. Sekeloa Selatan Nomor 1, Bandung, Jawa Barat, Indonesia. nuri.fitriasari@gmail.com

INTRODUCTION

Stevens-Johnson Syndrome (SJS) was first proposed by Albert Mason Stevens and Frank Chambliss Johnson in 1922 as an acute hypersensitivity reaction, manifested on the skin and mucous membranes that cause immune complex activity and creatinocyte apoptosis. This condition is generally caused by drugs, bacterial or viral infections.[1–3]

Although SJS was a rare condition with an incidence of 0.05 to 2 people per one million population per year, it became a concern due to the high morbidity and mortality rates.[1] A research conducted by Adhi et. al. reported that the incidence of SJS cases in Indonesia was around 12 cases per year. In Indonesia, the most common cause of SJS was drug use that included analgesic/ antipyretic (45%), followed by carbamazepine

(20%), and herbal medicine (13.3%). The mortality rate in SJS reached 5-15% in the total number of cases.[4]

Prodromal symptoms of SJS appeared within one to three weeks after the exposure to the suspected drug. Non-specific fever, malaise, headache, cough, flu symptom-like, conjunctivitis, ulceration of the mucous membranes, were reported in up to 90% of SJS patients.[5,6] The most common involvement of mucous membrane can be observed in oral mucosa (100%) and followed by genital area (58%). The nasal membrane and anal area are rarely involved with the symptoms (8% and 4%).[4,7] The mucous membrane lesions developed and expanded into skin lesions within three days after the prodromal symptoms. Skins lesions present as erythematous macules with black purpura at the central that is also referred as atypical target lesions. Oral mucosal lesions displays hemorrhagic crusts on the lips and multiple ulcers or erosions.[1–3,5,8,9]

The involvement of oral mucosal lesions causes disruption in speech, mastication, and swallowing function. This will lead to the disturbance in nutrients and fluids intake causing electrolyte imbalances that aggravate dehydration. Oral mucosal lesions in SSJ can became an entry point for infection, which is a major cause of morbidity and mortality.[2,5,10]

One of the main symptoms in SJS is severe oral mucosal lesions, appearing for 7-10 days or more. Therefore, adequate management from oral medicine specialist is required for such lesions.[5,11] The management of oral manifestations in SJS encompasses the competencies of oral medicine specialist, but it has not been clearly stated in scientific articles. This case report describes the management of oral mucosal lesions in SJS patient by oral medicine specialist as part of the collaborative team.

LITERATURE REVIEW

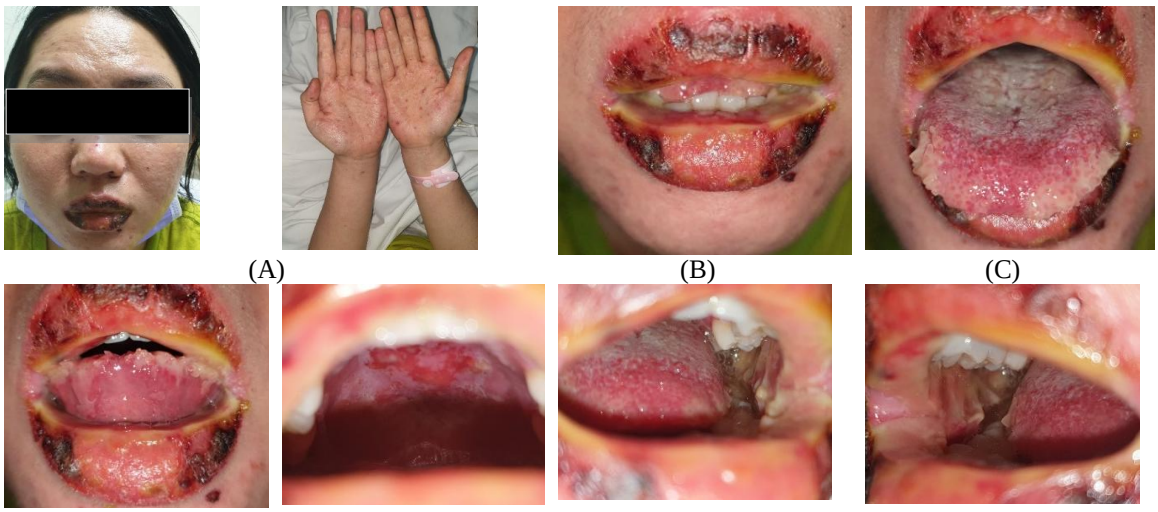
A 26-year-old female was referred from the Department of Dermatology and Venereology to Dental and Oral Health Department of Dr. Hasan Sadikin General Hospital. The chief complaint prevailed four days before the initial visit, which was redness in both eyes accompanied by fever and headache. Two days later, prior the visit to the hospital, patient noticed that her lips were blistered and covered with reddish black scab that easily bleed, along with aches and painful sensation when opening her mouth, and pain when swallowing. This condition caused difficulty in eating. On the following day, the appearance of blisters on the lips emerged. Reddish spots and blisters were observed on the palms and spread to the other parts of the body, accompanied with nausea and vomiting. History of drug use demonstrated the consumption of paracetamol and amoxycillin to cure a toothache.

The extra oral examinations (Figure 1 (A)) uncovered non anaemic conjunctiva, reddish sclera, symmetrical face, with erosions and red-black crusted around the nose. The lip lesions were haemorrhagic and tend to bleed (Figure 1 (B)). Dermatologic lesions comprised generalized distributed multiple erythematous macules, erosions, and crusts in nearly all parts of the body, with a body surface area (BSA) value of 4%.

Intra oral examination revealed multiple ulcers and erosions covered with yellowish-white pseudomembrane on the buccal mucosa, palate, ventral tongue, and lateral tongue (Figure 1 (C,D,E,F)). There were also white plaques that could be scrapped off without leaving erythematous area on the dorsal surface of the tongue (Figure 1 (C)). Gums, floor of the mouth, and teeth were unable to evaluate because of the limitation in mouth opening. Laboratory tests carried out covered haematological examination of 8 parameters including erythrocyte index. Increased haemoglobin level was remarked while other parameters were within normal limit (Table 1).

Based on the history taking, extra and intra oral examination, and laboratory tests finding, the patient was diagnosed with SJS et causa suspected paracetamol and/or amoxicillin. Department of Dermatology and Venereology managed the condition by administering 0.9% NaCl infusion therapy (1500 ml/24 hours), dexamethasone injection 27.5 mg/day, and intravenous injection of omeprazole 1x40 mg/day. Treatments for skin lesions included the compression using 0.9% NaCl solution and the application of 0.2% dexamethasone cream 2 times daily. Meanwhile, the management for oral mucosal lesions prescribed by the Oral Medicine Specialist comprised of lip compression using 0.9% NaCl solution, followed by the compression using 5 mg dexamethasone solution dissolved in 500 ml of distilled water for 5 minutes three times a day. The dexamethasone solution is also used to rinse or applied as a mouthwash for 1 minute before spitting out the liquid. The procedure was carried out 3 times daily using 10 ml of solution.

After three days of treatments, there were improvements in lips and lateral tongue condition. Lip crust was less visible (Figure 2 (A)) and erosion on the lateral of the tongue diminished (Figure 2 (B)), yet the patient still experienced pain from mouth opening. The treatment of lip compression using 0.9% NaCl and dexamethasone solution (5 mg / 500 ml) were continued, as well as the instruction for gargling.



(A) (B) (C)

(D) (E) (F)

Figure 1. (A) Skin lesions (face and palm). (B) Haemorrhagic crust on the lip. (C) Erosions on lateral border of the tongue and pseudomembranous plaques on the dorsum of the tongue. (D) Erosions on the ventral of the tongue (E) Erythematous erosions on palatal area. (F) Ulcerations on left and right buccal mucosa.

Table 1. Haematological examination results.

Examination	Value	Unit	Normal range
8 parameters of haematology			
Haemoglobin	15.9	g/dl	12.3-15.3
Haematrocrite	45.0	%	36.0-45.0
Leukocyte	7.42	10^3/ul	4.50-11.0
Erithrocyte	5.23	10^6/ul	4.2-5.5
Thrombocyte	211	10^3/ul	150-450
Erithrocyte index			
MCV	86.0	Fl	80-96
MCH	30.4	Pg	27.5-33.2
MCHC	35.3	%	33.4-35.5

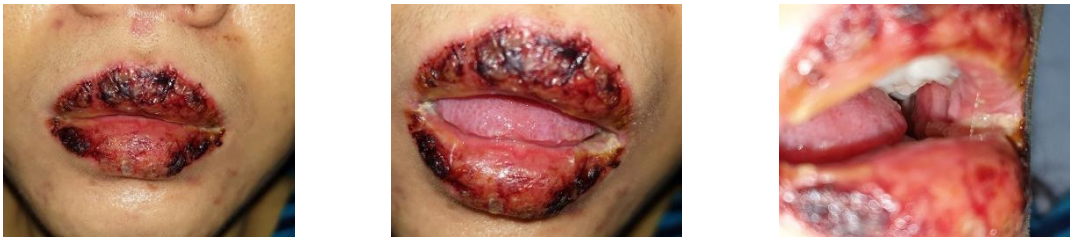
On the fifth day of treatment, crust on the lips was worsened as the patient peeled the crust until they bled and merely performed the lip compression twice daily, less than what was previously instructed (Figure 3 (A)). Improvements were notably observed in tongue and buccal mucosa (Figure 3 (B) and (C)). The patient began to consume porridge and other soft foods, and the treatment was resumed with the same prescriptions and instructions as before. This visit emphasized more on communication, information, and education (CIE) to restrain the patient from peeling the lip crusts.

On the seventh day of treatment, crusting of the lips had diminished (Figure 4 (A)), correspondingly with the reduction of lesions on lateral and ventral tongue, palate, and buccal mucosa (Figure (C),(D),(E)). The yellowish white plaque still persisted on the 2/3 dorsal posterior of the tongue which could be scrapped and leaving an erythematous area (Figure 4 (B)). Difficulty in eating and drinking were also reduced as the patient gradually able to open her mouth wider. The oral lesions management continued as before. Plaque on the dorsal tongue lead to the diagnosis of Oral Candidiasis, so that Nystatin oral suspension as antifungal was added 4x2 ml/day.

On the eleventh day of treatment, the patient was allowed to go home and received outpatient care. The patient controlled her condition nine days after her discharge to Oral medicine specialist in Dental and Oral Health Department. There were no complaints remained and oral function had returned to normal. Extra oral examination showed no hemorrhagic crust (Figure 5 (A)) and intra oral examination no longer presented Oral Candidiasis yet leaving a manifestation of coated tongue (Figure 5 (B)). Erosions and ulcerations were not discerned at the time of this visit (Figures 5 (C) and (D)). Upcoming treatment was aimed to maintain oral health over teeth and tongue brushing, nutritional intake maintenance and adequate daily hydration. The patient was also requested to avoid medications that were suspected as the cause of SJS.

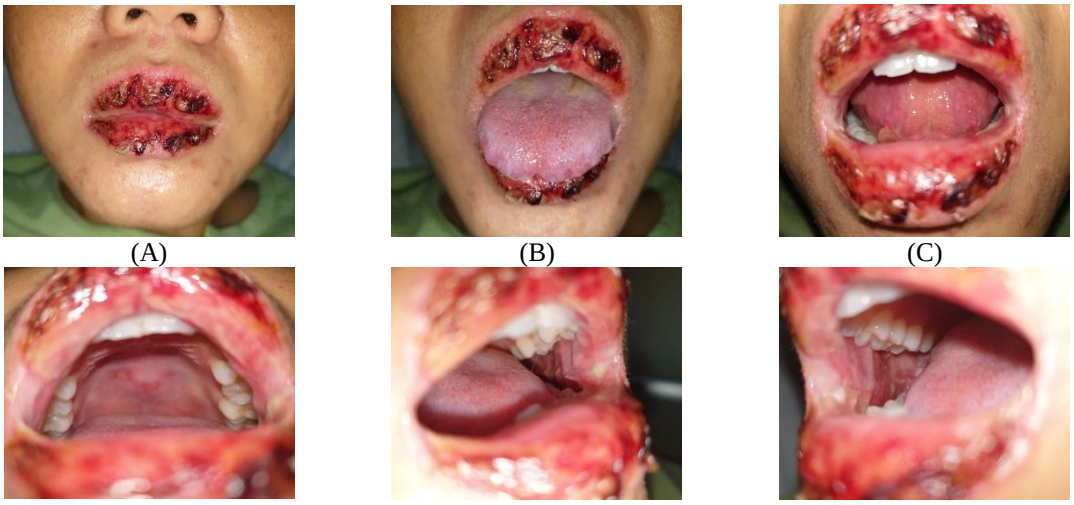
(A) (B)

Figure 2. (A) Hemorragic crusts of the lip diminished. (B) Erosions on lateral of the tongue diminished



(A) (B) (C)

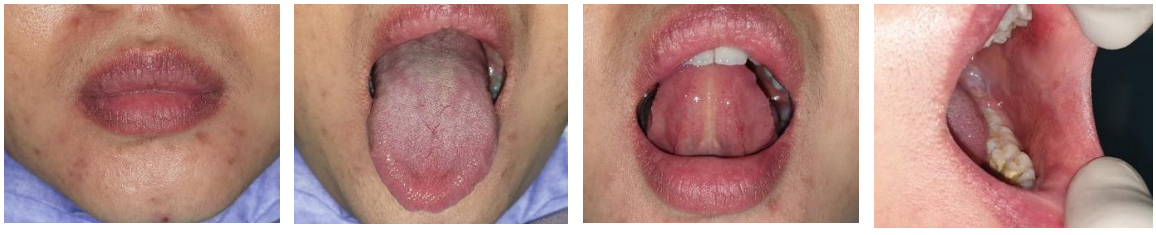
Figure 3. (A) Hemorragic crusts of the lip worsened. (B) Erosions on lateral of the tongue diminished. (C) Ulcerations on buccal mucosa diminished.



(A) (B) (C)

(D) (E)

Figure 4. (A) Hemorragic crusts of the lip diminished. (B) Erosions on the lateral of the tongue diminished and pseudomembranous plaque on the dorsum of the tongue was observed. (C) No erosions presented on the ventral of the tongue. (D) Erythematous erosions on palatum diminished. (E) Ulcerations on left and right buccal mucosa diminished.



(A) (B) (C) (D)

Figure 5. (A) No crusts presented on the lip. (B) Coated tongue. (C) No erosions presented on the ventral of the tongue. (D) No ulcerations observed on buccal mucosa.

RESULTS AND DISCUSSION

Around 75% of SJS cases were caused by drugs use. Groups of medications that frequently induced SJS were antiepileptic drugs (phenytoin, phenobarbital, carbamazepine), antibacterial drugs (sulfonamides), and nonsteroidal anti-inflammatory drugs (oxicam derivatives, allopurinol). In this case report, patients had a history of consuming paracetamol and amoxycillin. Non-iatrogenic agents, such as infections, vaccinations, radiation, sun exposure, pregnancy, and malignancy, can also generate SJS.[1,6,9]

Patient experienced clinical prodromal signs and symptoms which were important parameters in SJS, namely malaise, rash, fever, cough, arthralgia, myalgia, flu-like symptom, headache, anorexia, nausea, vomiting, and/or without diarrhea. Conjunctivitis usually occur 1-3 days before skin lesions appear in the form of intense erythema that is rapidly progressing to epidermolysis, blisters, erosion of the mucous membranes, hemorrhagic crust on the lips, extreme pain, and dehydration which can cause shock and hypovolemic death.[12]

In 1956 Alan Lyell, a dermatologist, revealed a condition of skin and mucous membranes that resembled SJS. This condition is known as toxic epidermal necrolysis (TEN) or Lyell's syndrome. Both SJS and TEN develop severe cutaneous adverse reactions (SCAR) characterized by erythematous skin lesions and extensive release of erosions or ulcerations of the mucous membrane.[8,9]

The parameter that differentiates SJS and TEN is the level of body involvement affected with the lesion known as body surface area (BSA). If the BSA value is less than 10%, the condition is categorized as SJS with a mortality rate of 1-5%. BSA value between 10%-30% is considered within the overlap category of SJS and TEN, whereas the BSA value of more than 30% is evaluated as TEN with a mortality rate between 25% and 35%. The diagnosis in this case report was SJS with a BSA value of 4%. In addition, there is also a severity assessment score for SJS or TEN called SCORTEN that is inclined to mortality variables.[8,9,12]

The pathogenesis of SJS cannot yet be fully understood, but several theories express an immunological process as the cause that provoke such condition in which a hypersensitivity reaction take place. Hypersensitivity reactions are mediated by cytotoxic T lymphocytes and natural killer cells resulting in apoptosis of keratinocytes. CD8+ T cells can recognize antigens and bind to the major histocompatibility complex molecule I, then activate two types of cytotoxic signals. The first signal releases perforin, granzyme B, and granulysin which enter the cytosol from the target cell and finally trigger apoptosis. The second signal is the expression of the FAS ligand which binds the FAS molecule on the surface of the target cell and results in apoptosis. Keratinocyte apotosis causes separation of the epidermis from the dermis, producing blistered skin lesions that are typical in SJS. This triggers the release of cytokines (TNF-alpha) which results in more inflammation and eventually leads to necrosis.[2,8,13]

Erythema and oral ulceration are the initial complaints of the patient but may not be remarkably concerned. In the literature, early diagnosis of SJS can solely be made based on the presence of lesions in the oral cavity.[1] Oral mucous membrane involvement in the acute phase is one that was described by Stevens and Johnson in 1922 in around 71-100% of the patients.[14]

The assessment of dental and oral condition, especially attention to the involvement of the oral mucosa, in the acute and chronic stage must be done from the beginning. The United Kingdom guideline (U.K Guideline) for the management of SJS averred that routine examination of oral mucosal conditions is important in the acute phase. Daily routine cleaning of the oral mucosa with mouthwash containing saline solution or corticosteroids or non-steroid anti-inflammatory drugs can be given in the spray formula.[15] The management of oral mucosal lesions performed on patient in this case report was in accordance with these guidelines. Routine follow-up that has been assigned could assess the state of dental and oral health, as well as monitored the improvement in the therapy. Lip compression using 0.9% NaCl solution was served as a moisturizer and encouraged wound healing. This solution can reduce inflammation due to the ability to attract intralesional fluid via osmotic process. Therefore, this solution exhibits an anti-inflammatory effect that operates to reduce pain and erythema, and also maintains the moisture of the lesion to promote tissue elasticity.[16,17]

Complications of SJS in the chronic phase of oral mucosa were first described in the 1980s through several case reports, showing permanent loss of tongue papillae, abnormal root development, and dental hypoplasia. Until the 2000s, chronic mouth complications were

relatively found more often. Several studies have suggested signs and symptoms of oral disorders in patients with a history of SJS, such as an increase in the prevalence of decayed teeth, severe tooth eruption abnormalities, and perturbation in salivary production. These will lead to the promotion in the growth of destructive bacteria and an increase in the prevalence of Oral Candidiasis.[14]

SJS is a life-threatening condition that shows the utmost resemblance with a burn, hence supportive care and rehydration become important parts of therapy since patients may suffer from severe dehydration. Symptomatic management of oral mucosal lesions is required to allow patients to ingest food and water past the oral cavity, maintain nutritional balance and prevent dehydration.

Haematology tests performed on this patient exhibited a mild increase in hemoglobin levels. This occurs as a result of body compensatory mechanism due to bleeding. SGOT and SGPT values were also spotted to increase from normal values, SGOT value of 316 U/L (normal range 15-37 U/L) and SGPT value of 343 U/L (normal range 14-59 U/L). Those values specified a disturbance in liver function, because most drugs are metabolized in the liver. Liver and skin are the most common organs involved in drug allergic reactions.[18,19]

The results of other haematology tests showed a decrease in creatinine and albumin level below the normal. Creatinine value of 0.40 mg/dl (normal range 0.6-1.0 mg/dl) and albumin of 2.68 g/dl (normal range 3.4 -5 g/dl) indicated a decline in kidney function in this patient. Kidney disorders are also the common complicating conditions which may be observed in patients with SJS.[20]

The morbidity and mortality rates in people with hypersensitivity, in this case SJS, are high, so that the alignment of collaborative team consisting of multidisciplinary dental and medical experts is needed. Based on this case report, the role of oral medicine specialist is very important as part of the management team for SJS patient. Oral medicine specialist can alleviate the morbidity due to the involvement of oral mucosa. Collaboration of various multidiscipline since the beginning of treatment is the key to success in the management of SJS.[21,22]

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