Steven Johnson Syndrome with Severe Oral Implications and Management

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ABSTRACT

Background: Steven Johnson Syndrome (SJS) is an acute mucocutaneous syndrome that predominantly involve the skin and mucous membranes. SJS is an immune-mediated disease that have been associated with erythema multiforme (EM). The most common triggers are viruses, food allergies, autoimmune reactions and medicine. The medicines that most commonly cause SJS are non-steroidal anti-inflammatory drugs, antibiotics, antifungals, and anticonvulsants. Case: A 32-year-old man was consulted from the Dermatology Department with a diagnosis of drug induce SJS and was given cetirizine and dexamethasone. The patient presented to the Oral Medicine Department complaining of mouth pain, dysphagia, ulcers, oedema and haemorrhagic of the lips, difficult eating, drinking and speaking. Extra-oral examination found that the surface of the lips was covered with a white layer, bloody and crusted, and erythematous rash on his neck, arm, abdomen, palms and feet, with a diameter of 2-6 mm. Intra-oral examination found multiple ulcers and erosive lesions that spread on the tongue, palate, buccal and labial mucosa. This condition established as an oral lesion related to SJS. Case Management: The management of the oral lesion was given corticosteroid mouthwash, 0.12% chlorhexidine digluconate, lip compress with 0.9% NaCl and 1% hydrocortisone ointment. Conclusion: Steroid mouthwash to suppress inflammation as well as a combination of 0.12% chlorhexidine digluconate antiseptic drug suppresses the infection process and complications that continue in the oral cavity and 0.9% NaCl solution as a moist wound healing. This therapy plays an important role in the healing process of oral lesions in patients with SJS.

Keywords: Drugs induced, Oral lesion, Treatment, SJS

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INTRODUCTION

Steven Johnson Syndrome (SJS) is an acute hypersensitivity reaction characterized by cutaneous necrosis. This disease is rare but life-threatening diseases. SJS was first recognized in 1922 by two clinicians, Dr. Stevens and Dr. Johnson, whose cause was still unknown. Immune complex-mediated hypersensitivity reactions are an ongoing condition of erythema multiforme. SJS is a disorder that occurs with features of erythema, vesicles, bullae, purpura on the skin of the body as well as the mucosa of the eyelids and oral mucosa. The exact cause of SJS is currently unknown, however there are predisposing factors such as viruses, food allergies, autoimmune reactions and drug reactions.

The mechanism of the syndrome in SJS is a hypersensitivity reaction, usually not long after the drug is injected or taken and this event is not dose related. Clinically seen, it is widespread, especially in the body, peeling of the epidermis occurs approximately 10-30% of the body surface area and usually involves the mucous membranes of two or more organs. A more in-depth history is needed regarding previous medical history. Predilection generally occurs in children and young adults, especially men. The oral signs of SJS are the same as those of erythema multiforme, the difference being that it involves more skin and mucous membranes, with more severe general symptoms, including fever, malaise, headache, cough, chest pain, diarrhea, vomiting and arthralgia.

Incidence and epidemiology were seen from observational studies on the epidemiology of SJS using validated clinical data in various European countries. In 1995-2013 the incidence rate was 5.76 at 1,000,000 cases per year, occurring in patients aged 1-10 years to 80 years. Mortality rates in childhood were found to be lower than in old age. Indonesia does not have definitive data on the morbidity of SJS. Based on data from Dermatology and Venereology 5th edition of the Faculty of Medicine, University of Indonesia in 2007.

Drugs that often cause SJS in Indonesia are analgesic/antipyretic drugs (45%), carbamazepine (20%), herbal medicine (13.3%) and the rest are other drug classes such as amoxicillin, cotrimoxazole, dilantin, chloroquine and ceftriaxone.

This case report aims to describe the appropriate management for oral lesions of SJS, the patient gets a nutritional balance and help the healing process of the lesion.

CASE

A 32-year-old man was consulted from the Department of Dermatology and Venereology with a diagnosis of drugs induce Steven Johnson Syndrome. The patient presented to the Oral Medicine Department complaining of pain in the mouth, dysphagia, ulcers, oedema of the lips, haemorrhagic crusts of the lips, difficult to eat, drink and speak. Extraoral examination found that the surface of the lips was covered with a white layer, bloody and crusted, and erythematous rash on his neck, arm, abdomen, palms and feet, with a diameter of 2-6 mm. Intra-oral examination revealed multiple ulcers and erosive lesions on the tongue, palate, buccal mucosa and labial mucosa.

Figures 1. a and b. dry lips, edema, erythema and serosanguinolent crusting; c. White plaque on the tongue;
d,e and f. Erosive, erythematous, irregular lesions on the palate, right and left buccal mucosa; g, h, i and j. Blackish red vesicles on the palms, feet as well as the abdomen and neck.

Intra-oral examination of the lips showed clinical signs of dry, exfoliative lips, oedema of the upper and lower lips accompanied by erythema and serosanguinolent crusts, easy bleeding and pain (Figures 1. a and b). Upper and lower lips have multiple superficial erosive lesions, erythematous base of irregular shape, and very painful. White plaques were seen on the dorsum of the tongue, and on the right and left lateral sides of the tongue (Figures 1. c), on the palate and right and left buccal mucosa, shallow, and multiple erosive lesions were found with an erythematous base and irregular edges (Figures 1. d, e and f). The palm and feet as well as the abdomen and neck have blackish red papules and vesicles (Figures 1. g, h, i and j).

CASE MANAGEMENT

Based on the history and clinical examination, the patient’s history was taking ciprofloxaxin due to cough and fever. Medicines are given by the health clinic where the patient is treated. The drug is taken 2 days later then symptoms appear in the body. the diagnosis was made as an oral lesion associated with Steven Johnson Syndrome. The management in Dermatology department are the administration of cetirizine and dexamethasone as well as the results of laboratory tests including anti-HSV 1 and HSV 2 with non-reactive IgG IgM results, TPHA TITER@ and VDRL with non-reactive results, PCT@ with High ratio (0, 36%), SGOT (AST) with a low value ratio (8 U/L), AP Thoracic examination with no visible bronchopneumonia and cardiomegaly and a negative PCR test for COVID.

The management treatment are prednisone 5 mg mixed with 10 ml of distilled water to be gargled 1-3 minutes and then discarded, 3 times a day, and after 1 hour gargling with prednisone 5 mg followed by, chlorhexidine digluconate 0.12% mouthwash 3 times a day, compress the lips using 0.9% NaCl dripped on sterile gauze 3-5 times a day with a long compress for 30 minutes and 1% hydrocortisone ointment is applied to the lips 3 times a day. The dentist is educated the patients and their families about the use of drugs accordance with the rules of drug administration and to always maintain dental and oral hygiene.

The patient’s symptoms began to improve on day 5, marked by improving conditions on the lips. The patient is able to speak, eat, drink well and rinse his mouth and brush his teeth slowly. Intra-oral examination showed erythematous and hyperkeratotic areas in almost the entire oral cavity, right and left buccal mucosa, upper and lower labial, and palatal areas. The dermatology department continuing the management of the skin of the patients.

After 3 weeks, the symptoms in the oral cavity showed a very significant improvement. Intraoral examination showed erythema and hyperkeratotic conditions with healing occurs in almost the entire oral cavity. Patients are allowed to consume soft foods orally. Therapy from dermatology department was continued and the oral disease section was chlorhexidine digluconate 0.12% mouthwash and the patient was still asked to maintain his oral health.

Figure 2. a, b, c, d, e, f and g Clinical features of healing at visit 3
DISCUSSION

The case of Stevens Johnson Syndrome in this patient was found with features of oedema of the lips, crust and easy bleeding, so an examination of HSV 1 HSV 2 IgG IgM was carried out with non-reactive results, then the suspicion of SJS related to the role of the virus could be denied with the results of a non-reactive HSV titer. The definitive diagnosis in this patient was an oral lesion associated with Steven Johnson syndrome caused by a drug reaction.

Drug reactions are described through 4 pathophysiological processes, which are drug-specific CD8+ cytotoxic lymphocytes, apoptotic processes, Fas-Fas ligand (FasL), granule-mediated exocytosis and tumor-alfa necrosis factor (TNF-alpha).\(^\text{14}\) SJS can involve the interaction and binding of certain drug-associated antigens or metabolites with type 1 major histocompatibility complexes (MHCs) or cellular peptides to form immunogenic compounds.\(^\text{15}\)

Reactions that occur usually start from day 2 to day 30 after taking certain drugs. In this patient, vesicles appeared on the body on the 2nd day after taking ciprofloxaxin and mefenamic asthma, previously the patient had no history of excessive drug allergic reactions. Hypersensitivity reactions are thought to be caused by drug reactions after being consumed by the patient. Several theories can explain the condition of patients with drug-related hypersensitivity reactions, including apoptotic process found in cytotoxic granules, is the main cause of keratinocyte apoptosis, the second process is Fas-fas ligand (FasL) expressed on activated cytotoxic T cells can also destroy keratinocytes through the production of intracellular caspasas, the third process is Cytotoxic lymphocytes secrete perforin and Granzyme B which create channels in the target cell membrane activating Caspasas. The fourth process by which TNF-alpha can cause apoptosis and induce Nitrous oxide (NO) which is also induced by TNF-alpha and interferon (IFN)-alpha that stimulated Caspasases enzymes.\(^\text{13}\)

Ciprofloxaxin normally in the body works with the help of CYP1A2 and CYP3A4 enzyme metabolism, but in SJS patients the process is inhibited.\(^\text{16,17}\) Some literature describes the SJS process associated with ciprofloxaxin being activated by CD8+ cells and cytotoxicity to keratinocytes occurs through activation of the enzymes Granzyme B and granulysin in the Fas-Fas ligand (Fasl) pathway. Epidermal cell apoptosis, which can be mediated through keratinocyte Fas-Fasl interactions or through the release of cytotoxic T cells from perforin and Granzyme B, is also associated with tissue damage to skin and mucosal tissues.\(^\text{14-20}\) It can be seen that the apoptotic process, Fas-fas ligand (FasL), Cytotoxic lymphocytes, TNF-alpha, that damage or inflammation of tissue in the skin and oral cavity is closely related to drug-related hypersensitivity reactions.

Mucosal conditions mostly involving the oral mucosa can cause erythema, edema, peeling, ulceration, crusting and necrosis. Seen in the oral mucosa, abnormalities can be in the form of ulcers on the lips, tongue, palate and buccal mucosa.\(^\text{15,16}\) Based on U.K guidelines for the management of Stevens–Johnson syndrome/toxic epidermal necrolysis in adults 2016 in the treatment of SJS, especially in the oral cavity, requires topical analgesics, topical antiseptics, corticosteroid ointments and corticosteroid mouthwashes. in this case we use prednisone 5 mg as anti-inflammatory drugs is considered only to reduce the severity of ulcers in the oral cavity.\(^\text{17}\) prednisone gargling can relieve complaints and reduce symptoms in the oral cavity because there is an inflammatory reaction by suppressing the inflammatory process, hydrocortisone ointment 1% is used to treat redness, swelling and itching. Hydrocortisone belongs to a class of drugs called corticosteroids that act as anti-inflammatory and suppress the inflammatory process. Considered very effective for complaints in the oral cavity function generally suppresses cytokine and chemokine responses.
related to inflammation and inflammation in the oral cavity. [18]

Topical hydrocortisone is used to treat redness, swelling and itching. Hydrocortisone belongs to a class of drugs called corticosteroids that act as anti-inflammatory and suppress the inflammatory process.

Treatment of ulcers in the oral cavity can use hydrocortisone ointment 1% and prednisone 5 mg mixed with 10 ml of saline water or 10 ml of distilled water, prescribed for 7-10 days with 2-4 times daily use. [17] The topical therapy used in this case involves several methods of transporting topical drugs across the oral mucosa, namely passive diffusion (passing and entering mucosal cells, and passing between mucosal cells), carrier mediated transport (paths mediated by membrane proteins) and endocytosis (macromolecular pathways and drug material into mucosal cells and mucoadhesion occurs). [19]

The mechanism of 0.9% NaCl solution in the treatment of lesions on the lips of SJS patients as a moist wound healing that has a moisturizing principle. [20] The goal is to maintain moisture in the lesion to facilitate cell movement in the wound, and accelerate the granulation process which reaches 40% compared to the dry state, keep the surface of the lesion moist so that the development and migration of epithelial tissue increases. [21][22] This condition will optimize the activity of neutrophils, macrophages, and fibroblasts. The basic theory in the process of healing lesions with the moist principle includes accelerating fibrinolysis, accelerating angiogenesis, reducing the risk of infection, accelerating the process of formation of growth factors, and accelerating the formation of active cells. [22][23]

CONCLUSION

Steroid mouthwash to suppress inflammation as well as a combination of 0.12% chlorhexidine digluconate antiseptic drug suppresses the infection process and complications that continue in the oral cavity and 0.9% NaCl solution as a moist wound healing. This therapy plays an important role in the healing process of oral lesions in patients with SJS.

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