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Case Report

Management of risk factors and pharmacological therapy in oral pemphigus vulgaris: A Case Report

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Abstract

Introduction: The incidence of pemphigus vulgaris is rare. It often occurs in middle age and the elderly or in the 4th to 5th decades. Women experience it more often than men. Pemphigus vulgaris predominates in patients of Ashkenazi Jewish, Asian or Mediterranean descent. The etiology of pemphigus vulgaris remains unclear, but it can be triggered by several risk factors, such as drugs, radiation, surgery, and some foods. This case report aims to describe a case of oral pemphigus vulgaris caused by stress and food and its management. **Case:** a 45-year-old woman who was hospitalized at Dr. Hasan Sadikin hospital referred from Dermatology and Venerology department to Oral Medicine department with diagnosis pemphigus vulgaris. The risk factors were emotional stress and food preservated. Pharmacology therapy including steroids, anti-fungal, and vitamins. **Discussion:** The management of this patient was carried out by a multidisciplinary team, dermatologist collaborate with oral medicine specialist to support comprehensive therapy. Identification and controlling emotional stress and cessation of food which was suspected as the cause, were the important aspect as an addition to the given pharmacological therapy led to significant improvement of oral pemphigus vulgaris. **Conclusion:** Oral pemphigus vulgaris as a chronic autoimmune disease can be cured if the risk factors can be controlled and close monitoring of pharmacological therapy can be carried out by a team.

Keywords: pharmacology, risk factor, oral pemphigus vulgaris

INTRODUCTION

Pemphigus vulgaris is a chronic autoimmune disease that affects the mucocutaneous. Oral lesions often precede the appearance of skin lesions. The incidence of pemphigus vulgaris is still rare, with a predilection for women being affected more often than men, especially in the 4th and 5th decades of life.[1] The etiology is still unclear, but it is strongly suspected that there is a genetic factor due to the presence of related human leukocyte antigen (HLA), namely DRB1*0402, 1401 and DQB1*0302, 0503.[1-4] Several trigger factors that often cause pemphigus vulgaris including drugs (captopril and penicillamine, which contain sulfhydryl groups, and rifampicin and diclofenac), radiation, surgery, some foods such as garlic, and emotional stress, [1,3] apart from that further more infection and neoplasms can also trigger pemphigus vulgaris.[4]

This paper will discuss the management of pemphigus vulgaris oral lesions in a 45-year-old woman who was hospitalized at Dr. Hasan Sadikin hospital for the third time after being referred from the Department of Dermatology and Venereology as the leader. Special management for disorders in the mouth had been given according to the development of the course of the disease and had a significant improvement, but the most important approach was to motivate the patient to recognize her disease, including efforts to avoid trigger factors as well as increasing the patient awareness to immediately seek for help if the oral lesions reappear

CASE REPORT

Patient Bio

Name : Mrs. IJ

Age : 45 years

Gender: Female

Status : Married

Occupation: Housewife

History Taking:

The patient realized that complaints in the mouth appeared 2 days after eating anchovy. The first complaint that appear was itching, then a few days later canker sores appeared on the lips and in the mouth. She said that having a lot of problems due to her renovated house collapsed suddenly.

Extra Oral Examination:

Lips: dry (+), crusted (+), bleeding (+)

Intra Oral Examination:

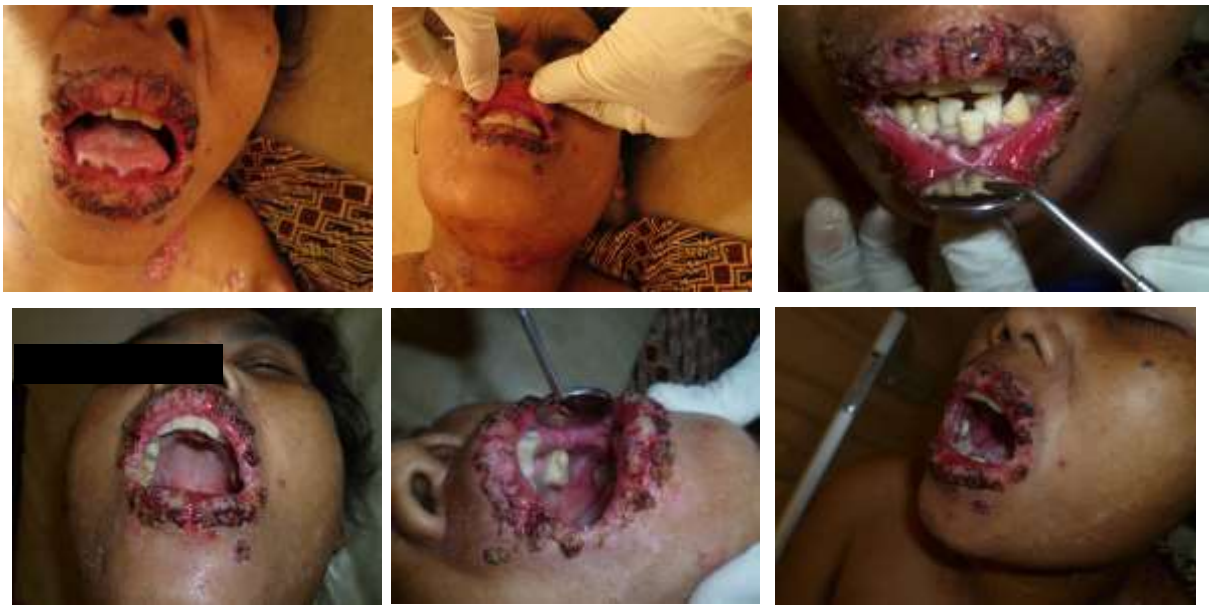
Labial mucosa: upper labial there were no lesions, lower labial there was a dental impressions white plaque.

Buccal mucosa: on the right buccal there there was a dental impressions white plaque, and on the left side there was an erosive area (+), sloughing (+)

Tongue: at the dorsum and ventral of tongue there were erosive (+), sloughing (+), and at the lateral side there was a dental impression white plaque-like lesion

Palatum mole: red spot

Upper and lower gingiva: oedem (+), diffuse erythema



Hematology Test:

Hemoglobin 12g/dL

Hematocrit 37%

Leukocytes 7300/mm^3

Erythrocytes 4,22 million/uL

Platelets 331.000/mm^3

Erythrocyte index:

MCV 86,5 fL

MCH 28,4 pg

MCHC 32,9 %

Clinical Chemistry:

AST (SGOT) 10 U/L 37^0C

ALT (SGPT) 3 U/L 37^0C

Ureum 16 mg/dL

Creatinine 0,69 mg/dL

Dermatology Test:

1. Nikolsky sign (+)
2. Asboe Hansen sign (+)
3. Tzanck examination of the base of the vesicle lesion on the back: acantholytic cells (+)
4. Gram stain examination of pus in erosional lesions on the stomach: PMN 1-3/lpb,

No Gram (+) or Gram (-) bacteria were found.

Working Diagnosis: Pemphigus Vulgaris

Therapy from Oral Medicine Department:

1. Oral hygiene instructions (OHI); Brushing/cleaning the teeth as much as possible at least 2 times a day
2. Gargling Prednisone compounded mouthwash three times a day (3 tablets of 5 mg prednisone which were grinded and dissolved in 2 tablespoons of water)
3. Compounded ointment for the lips 3-4 times a day
4. Candistatin oral suspension 4 times 1 ml every day
5. Multivitaplex 1 time per day

Therapy from the Department of Dermatology and Venereology:

Topical Therapy

1. Compress NaCl 0.9% 2x/day
2. Gentamicin cream 0.1% 2x/day after compress
3. Occlusive compresses with vaseline album for lips 2x/day

Systemic Therapy:

1. Infusion of 0.9% NaCl 1500 cc/day
2. Azatioprine 2x50 mg IV
3. Dexamethasone 6 mg/day IV (4mg-0-2mg)
4. Ranitidine 2x50mg IV

2nd Visit one week later (inpatient)

History taking:

The lips and oral cavity still felt sore, pain in swallowing, it's hard to open her mouth because of the pain in the lips, but the pain when chewing has decreased since two days ago.

Extra oral examination:

Lips: dry (+), bleeding lesions (+)

Intra-oral examination:

Right and left buccal mucosa : Pseudomembrane white lesion, elevated (like plaque)

Upper and lower labial mucosa : Pseudomembrane white lesions, elevated (like plaques)

Hard palate : diffusely pale without elevation

Soft palate: erythema (+)

Tongue: pseudomembrane white lesions, there was is an elevation plaque-like



Hematology Test:

Hemoglobin 10,7g/dL
Hematocrit 32%
Leukocyte 7400/mm^3
Erythrocyte 3,77 million/uL
Platelet240.000/mm^3

Erythrocyte Index:

MCV 84,1 fL
MCH 28,4 pg
MCHC 33,8 %
Clinical Chemistry:
Ureum 20 mg/dL
Creatinine 0,54 mg/dL

Diagnosis: Pemphigus vulgaris and acute pseudomembranous candidiasis

Therapy (inpatient):

1. Oral hygiene instruction (OHI)
2. Compounded Prednisone mouthwash was discontinued
3. Candistatin therapy is discontinued
4. Fluconazole 50 mg tablets, two tablets once a day for 7day
5. Multivitaplex one tablet a day and a topical compounded ointment for the lips

Therapy for patients at home (the patient had been allowed to go home by the dermatologist a few days later), then the Oral Medicine gave the following prescription:

1. Gargling compounded Prednisone mouth wash three times a day for one week (grinded of 5 mg

tablet, one tablet every day dissolved in one spoon of water)

2. Candistatin oral suspension, 4 times 1 ml every day for a week

3. Continue to take multivitamins one tablet every day

3rd visit 3 weeks later (outpatient)

History taking:

The patient complained of dry lips, bleeding, soreness since ± 5 days ago, painful when eating, therefore she consumed porridge again. Since 2 days ago the patient was not brushing her teeth because it hurts if touched by a toothbrush. The compounded mouthwash (grilled green tablets and candistatin) was discontinued by the patient because she felt soreness and coughing.

Extra oral examination:

Lips: dry (+), bleeding lesions (+)

Intra-oral examination:

Right and left buccal mucosa : Pseudomembrane white lesion (+)

Lower labial mucosa : dental impression pseudomembrane white lesions

Dorsum of tongue: pseudomembrane white lesions (+)





Diagnosis: Pemphigus Vulgaris

Therapy :

1. OHI: brushing the teeth and cleaning of the tongue, using a toothbrush or gauze

2. Fluconazole tablets 50 mg No. XV, two tablets a day

3. Lip compounded ointment, 3-4 times a day

4. Gargling compounded prednisone mouthwash 3 times one tablet every day

4. Oral prednisone 2-0-2, for the second week will be given if the condition was not improved

4th visit 3 weeks later (outpatient)

History taking:

The Complaints in the mouth were decrease, but it still felt a little bit of sore. She could already chewing solid food (rice). Complaints on the lips had decreased but it still look dry/ cracked.

Extra oral examination:

Lips: dry (+), bleeding lesions (+)

Intra oral examination:

Right and left buccal mucosa : white granulomatous lesion (+)

Lower labial mucosa: tooth impression granulomatous white lesion (+)

Tongue: granulomatous white lesions (nodules, d = ± 1 cm)

Therapy:

1. OHI

2. Gargling compounded prednisone mouthwash twice a day (a grinded of one tablet 5 mg prednisone dissolved in one spoon of water) (the plan to give prednisone systemically was postponed because the patient showed improvement)

3. Candistatin oral suspension No. IV with a dose of 1 ml 4 times a day

4. Vaseline for lips

5th visit 5 weeks later (outpatient)

History taking:

Complaints in the mouth had decreased, patient could eat well without pain but sometimes it still hurts, especially at the tip of the tongue and under the tongue.

Extra oral examination:

Lips: slightly dry, corner of the lip fissure (+), bleeding (+) on the right lip

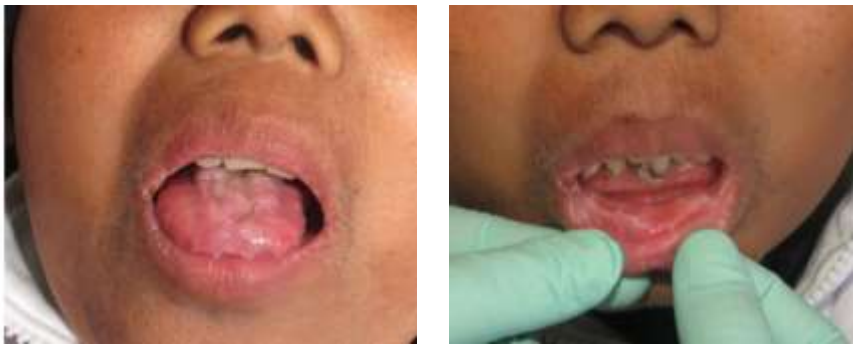
Face: moon face

Intra oral examination:

Buccal mucosa left, right and upper, lower labial: granulomatous tissue (healing).

Dorsum of the tongue: granulomatous tissue (nodules, d = ± 1 cm), there was hyperkeratin on the surface (healing)

Lateral of the tongue: squiggly because of the impression of the teeth (anterior part)



Diagnosis: Pemphigus Vulgaris (healing)

Therapy :

1. OHI: brush teeth at least 2 times a day

2. Suggestion for scaling

3. The dose of prednisone gargling was reduced to once a day for 2 weeks and then in the third

week the dose was tapering off alternate days

4. Surbex Z one tablet a day

DISCUSSION

History of the current disease, the patient is aware of the emergence of complaints in the mouth as a canker sore which was initially small after the patient ate anchovies which felt itchy in the mouth before finally becoming canker sores. The history taking showed that there was were other triggering factor which was strongly suspected to be the emotional stress factor experienced by the patient due to the collapse of the patient's house which was being renovated at that time. Canker sores at some time later grew bigger, extended to the lips and got worsened, until finally after about four weeks the complaints appeared on the skin, almost in all parts of the body experiencing skin peeling, the same condition as the previous two conditions that caused the patient to be hospitalized.

The stress factor is strongly suspected as the background for the recurrence of pemphigus disease in this patient. According to the theory that the meaning of stress varies widely but in simple terms it includes general adaptation and reaction patterns in dealing with stressors, both from inside and outside. If the adaptation process is successful and the stressor being faced can be adequately addressed, it will not cause stress. On the other hand, if it fails and becomes incapacitated, it will cause stress.[5] According to Dorland's Medical Dictionary, stress is a physiological or psychological tension caused by harmful stimuli, physical, mental or emotional, internal or external, which tend to interfere with the functioning of the organism and natural desires. the organism to escape. Another

definition according to Richard S Lazarus, stress is a feeling that is experienced when someone thinks that "the demands that exist exceed his ability to cope with them".[6]

Stress factors can trigger the hypothalamus to secrete corticotropin-releasing hormone (CRH). This CRH then stimulates the pituitary gland to secrete adrenocorticotropic hormone (ACTH) and causes the adrenal glands in the cortex to secrete cortisol which can increase up to 20 times.[7,8] Actually, physiologically, the body has a negative feedback effect mechanism on cortisol secretion which aims to return to its normal value, but in conditions of chronic stress like this patient, continuous cortisol expenditure can actually cause further damage to the body.

Another factor that triggers the onset of complaints in the patient's mouth was the food. Foods such as salted fish usually have undergone through a preservation process which did not rule out the possibility of being accompanied by the addition of chemicals as preservatives. The oral mucosa is more vulnerable than the skin so that it is more easily irritated if it is exposed to certain chemicals which can cause erosional lesions and can develop into ulcers, or due to physical trauma from the salted fish which is rough and hard which triggers friction with the oral mucosa. The mechanism of the pathogenesis of pemphigus as an autoimmune disease in this patient was probably initially triggered by environmental factors, namely emotional stress which had a very bad influence on the occurrence of disorders of the patient's immune system together with food triggers as local factors that came in direct contact with the oral mucosa causing lesions that were originally in the form of irritative lesion that develop into oral lesions mediated by impaired cellular immune response, which in the case of pemphigus, oral lesions are characterized by loss of contact between cells (acantholysis) accompanied by blisters that break easily releasing fluid and are covered by a layer that is easily removed (sloughing) like a membrane, white in color, in addition to clinical manifestations in the form of erosive and erythematous lesions that are widespread due to the ruptured bull. The working diagnosis was established from the dermatologist based on history taking showing a recurrent history of the disease, clinical examination, including a positive Nikolsky sign, positive Asboe Hansen sign, Tzanck showing acantolytic cells, and also Gram staining showing PMN cells, and negative for Gram (-) and (+), support the diagnosis towards pemphigus vulgaris.

The management of this patient was carried out by a multidisciplinary team, and the Dermatology and Venereology Department as the leader. The treatment provided by dermatologist was primarily the administration of corticosteroids and their adjuvants intravenously in addition to administering topical drugs. In line with the development of the patient's disease, corticosteroids were given orally, namely methylprednisolone with a tapered dose from the dermatologist.

The treatment given by the Oral Medicine department during the first visit was in the form of compounded mouthwash from grinding 5 mg prednisone tablets then dissolved in 2 tablespoons of water and gargling for 5 minutes and then discarding. For the initial dose of administration, was 3 tablets for one compounded mouthwash, three times a day. The consideration of giving prednisone because the condition of the oral lesions were erosive lesions accompanied by widespread sloughing which causing pain in the patient, making it difficult to eat and even talk. Prednisone is a mild to moderate acting corticosteroid drug which has anti-inflammatory and immunosuppressive effects which can provide satisfactory results according to many studies. The administration of corticosteroid drugs besides having an effect on the inflammatory process also has side effects due to its immunosuppressive properties which can facilitate the emergence of secondary infections, one of which is the growth of fungi, such as Candida spp. Therefore, she was also given candistatin oral suspension 4 times 1 ml every day, to be gargled for a few moments until it coated the entire oral mucosa and then swallowed.

Topical application of a compounded ointment for lips containing prednisone, avil, lanolin and vaseline was is expected to overcome the crusting lesions and bleeding that occurred by making the condition of the lips to be moist due to the content of lanolin and vaseline, as well as the anti-inflammatory effect of the prednisone content which aimed to improve tissue damage caused by the excessive inflammation, and avil as an antihistamine to minimize histamine release that may accompany severe inflammation. This compounded ointment was applied 3-4 times a day. The patient was also given multivitamins once a day containing of vitamins A, B1, B2, B6, B12, C, D, nicotinamide, and Ca pantothenate, to increase the intake of micronutrients needed for epithelial cell regeneration and tissue healing processes.

At the second visit, which was six days from the first visit, the patient's condition did not show significant improvement, in line with the patient's general condition which had decreased, with the results of routine hematological examinations leading to anemia which was influenced by impaired nutritional intake due to the condition of the oral cavity, but the condition the lips were better, with less crusting and bleeding, and they looked more moist. Inside the mouth there were thickening of the white coating in almost all part of the mucosa, and the patient complained of a burning feeling. This condition led to the diagnosis of pseudomembranous candidiasis which triggered by the patient's low immune system that was affected by the administration of long-acting corticosteroids, namely dexamethasone 6 mg/day intravenously plus the administration of compounded prednisone mouthwash with a relatively high dose of 45 mg for one day even though it was given as a mouthwash. , because it could trigger an increase in systemic absorption of the mouthwash corticosteroid drug on the mucosal surface that had large erosive lesions or ulcerated areas with the presence/absence of open blood vessels so that it had a tendency to cause large systemic adverse effects.[9]

Cortisol levels can also increase in the patient's body which supports the emergence of other conditions, is candidiasis. Cortisol is known to have an effect on blood cells and immunity, because cortisol can reduce the number of eosinophils and lymphocytes in the blood, so that the level of immunity to most foreign substances that enter the body will be reduced, which can eventually lead to fulminant infections and death from diseases that are actually not deadly.[10] Therefore, the compounded prednisone mouth rinse was discontinued, and the antifungal therapy which was originally in the form of nystatin (candistatin) was replaced with fluconazole 50 mg orally at a dose of 2 tablets once daily for one week. Administering fluconazole according to consideration as an antifungal drug with a more potent effect than nystatin, which can be given if there was resistance from nystatin, lip topical therapy was still continue because it had has shown an improvement in the lips, and multivitamins was also still continued to help the healing process.

On the next visit, the patient was not hospitalized, so the patient came for control for outpatient treatment at the Oral medicine clinic. The condition was still almost the same as before while as an inpatient. Before the patient went home (two weeks ago) she was given compounded prednisone mouthwash three times daily but only one tablet of 5 mg

prednisone which was grinded and dissolved in one spoon of water (lower dose compared to the initial administration). Prednisone was administered to prevent a severe erosive condition from recurring again, and with the consideration that the patient had been given systemic fluconazole for the previous week so that the candidiasis condition had been suppressed. The patient was also provided with candistatin oral suspension to be applied 4 times 1 ml while at home to overcome the side effects of giving back compounded prednisone mouthwash. The patient did not follow the instructions for using the given drugs because the patient's general condition had deteriorated, and she stopped using the mouthwash both prednisone and candistatin because of discomfort due to the patient's coughing complaint. She did not show any significant improvement at this outpatient control and on consideration of the last administration of fluconazole about 3 weeks ago, the patient was again given a prescription for fluconazole to be taken 2 tablets once a day for one week. She said that it was more comfortable if she took this drug compared to candistatin. Other treatments were being continued, including compounded prednisone gargling. The plan for the second week, she will be given oral prednisone 2 tablets in the morning and 2 tablets in the afternoon if the condition had not improved, with consideration that it had been approved by the dermatologist.

About 20 days later, the patient was only able to be controlled by reason of adjusting the time with the control schedule to the dermatology department, the complaints in the mouth had decreased, she was able to eat porridge. The results of clinical examination also showed significant improvement, the pseudomembrane white membrane had disappeared throughout the mucosa, but the buccal mucosa and tongue still showed granulomatous lesions which were the healing tissue. Therapy was still continued by administering compounded prednisone mouthwash, the dose was ~~is~~ reduced to one grinded tablet twice a day. Candistatin antifungal administration was continue with a dose of 4 times 1 ml every day to prevent the formation of candidiasis again. Topical therapy for the lips because they still look dry and in some locations still look prone to bleeding, it was recommended for patients to apply the bleeding lesions with compounded ointment and if there are was no crusting/bleeding lesions any more, she could apply the lips with vaseline.

The patient came for control approximately one month later, the patient said that she could not come for control on time because there were several matters. The patient's condition showed significant improvement, the condition of the lips that were not so dry, only fissures were still visible on the right side, and the condition in the mouth was getting better, there were only a few impressions of the teeth on the lower labial mucosa, and lateral tongue, and dorsum of the tongue showing granulomatous tissue with overlying hyperkeratin. At this visit the patient received therapy of compounded prednisone mouthwash with a lowered dose, one grinded tablet a day for two weeks and in the third week with alternate day doses and then discontinued. The patient was also given multivitamins containing vitamins E, C, B1, B2, B6, B12, niacin, folic acid, pantothenic acid, and zinc to help the tissue healing process.

CONCLUSION

Pemphigus vulgaris is a chronic mucocutaneous autoimmune disease with oral lesions that usually precede skin lesions. Pemphigus vulgaris can occur repeatedly as in this patient which has occurred three times with the strongest triggering factors due to emotional stress. Multidisciplinary management and patient compliance with doctor's instructions will support the success of therapy and patient recovery, including preventing relapse and ultimately improving quality of life.

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