Oral lesions as a clinical sign of systemic lupus erythematous

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ABSTRACT

Background: Oral lesions represent one of the most important clinical symptoms of systemic lupus erythematosus (SLE), an autoimmune disease with a high degree of clinical variability rendering it difficult to arrive at a prompt and accurate diagnosis. There are many unknown causes and multiple organ systems involved, with the result that permanent organ damage may occur before treatment commences. Purpose: The purpose of this case report is to discuss the importance of recognizing the lesions related to SLE which may help dentists to make an early diagnosis. Case: A 17-year-old female patient was referred by the Internal Medicine Department with a suspected case of SLE. Prior to admittance to the hospital, the patient was diagnosed with tuberculosis. A subsequent extraoral examination revealed ulceration with a blackish crust on the upper lip. An intraoral examination showed similar ulceration covered with a blackish crust on the labial mucosa accompanied by central erythema in the hard palate. Blood tests indicated decreased levels of hemoglobin, hematocrit and platelets, but increased levels of leukocytes. A diagnosis of oral lesions associated with SLE and angioedema was formulated. Case management: The patient was given 1% hydrocortisone and vaseline album for extraoral lesions, while 0.2% chlorhexidine gluconate and 0.1% triamcinolone acetonide was used to treat intraoral lesions. An improvement in the oral lesions manifested itself after two weeks of treatment. Conclusion: Early detection of oral lesions plays a significant role in diagnosing SLE. It is important for the dentist to recognize the presentation of diseases that may be preceded by oral lesions. A multidisciplinary approach and appropriate referrals are necessary to ensure comprehensive medical and dental management of patients with SLE.

Keywords: Early detection; oral lesions; systemic lupus erythematous

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INTRODUCTION

Systemic lupus erythematous (SLE) is a systemic autoimmune disorder with a broad spectrum of clinical manifestations, multi-organ inflammation and a multitude of laboratory and immunologic abnormalities. Depending on the body part involved, clinical SLE courses are characterized by relapse and remittance that can be mild, moderate or severe. The difficulty in identifying SLE patients in the early stages of the disease stems from its complexity. The production of pathogenic autoantibodies directed against nucleic acids and their binding proteins is one symptom of the disease, reflecting global loss of self-tolerance. Immune dysregulation disorder with reduced tolerance results from a combination of genetic factors, the regulation of environmental triggers and stochastic events. Recent research has produced data that more than 30 genetic loci are involved in the pathogenesis of the disease.1-4

SLE has an incidence rate that varies between ethnic groups and geographic locations, genders and age groups. A prevalence of approximately 20 to 150 cases per 100,000 people within the general population has been reported.4 Women are estimated to be six to ten times more likely to develop SLE than men with double X chromosomes and different estrogen levels which modulate the immune response possibly being associated with this event. SLE mainly affects young women, with a peak incidence rate occurring between the ages of 15 and 40. The annual incidence rate of SLE in adults is estimated to be 2-7.6 cases per 100,000 individuals, while that in children in the US is estimated to be 0.53-0.60
SLE has a far greater impact than that in adults due to its following the clinical course of a more severe disease. A worse prognosis is also often associated with male and elderly patients. A tendency to lower photosensitivity, more serious serositis, older age at the time of diagnosis and a higher 1-year mortality rate compared to women are all characteristics of SLE in men. The mortality rate of SLE patients remains two to four times higher than that of healthy people.

The etiology of SLE remains unknown. However, genetic, hormonal and environmental factors, in addition to immune disorders, have been identified as elements in its pathogenesis, with SLE being linked to a single gene defect. Indeed, genetic factors exert a fundamental influence on disease progression, as do exposure to environmental stimuli in the form of ultraviolet light, dietary factors, certain infections and drugs, smoking, DNA demethylation, and infectious or endogenous viruses or elements similar to viruses. Certain gene products that interact with environmental stimuli are etiological factors that will produce a deregulated immune response. Various organ system damage will be caused by SLE, as a consequence of the formation and deposition of autoantibodies and immune complexes.

The prevalence of mucosal involvement is present in approximately 9-45% of cases and accompanied by a systemic form of the disease. According to the literature, oral lesions occur more frequently in women with a female to male ratio that is 2.7 times greater. This report describes the case of a patient who presented early clinical features of oral lesions that constitute an important symptom in the diagnosing of SLE. Dentists have an important role in the early detection of SLE since oral lesions represent one of the clinical symptoms of the condition.

CASE

A 17-year-old female patient was referred by the Internal Medicine Department to the Oral Medicine Department in the emergency unit at RS Hasan Sadikin Bandung, the chief complaint being bleeding and blood clots on the left upper lip and labial mucosa. These caused difficulties when eating and drinking with patients also complaining of problems swallowing accompanied by general physical weakness. The first complaint manifested itself approximately four months before admittance to hospital with patches of reddish spots accompanied, at times, by itching on both arms and neck after patients had been administered with the drug. This was described as a pulmonary medicine consisting of red and yellow tablets which had been prescribed by a general practitioner.

After three months of following the drug regime, the patient was referred to Rotinsulu Hospital and treated with five different forms of anti-tubercular medication (unfortunately, the family of the patient was unable to recall the name and shape of the drugs in question). Since less than three weeks earlier, patches of reddish spots were present on both arms and the neck extending to the chest, abdomen and back, while blackish spots were visible on the skin. The presence of similar complaints or a history of allergies or recurrent stomatitis aphthous in patients and their families were denied. However, there was a history of joint pain and hair loss commencing approximately two weeks before admittance to hospital.

An examination adhering to American College of Rheumatology (ACR) criteria was conducted and produced four positive results in 11 criteria including: arthritis, malar rash, renal disease and hematologic abnormalities. Multidisciplinary management was performed by the Oral Medicine, Internal Medicine, Dermatology and Venereology departments. The patient is suspected of suffering from SLE with renal involvement, mucocutaneous candidiasis (CMC), hematology, acute kidney injury (AKI), superimposed chronic kidney disease (CKD) et causa lupus nephritis with metabolic acidosis, uremic gastropathy, moderate dehydration et causa gastrointestinal (GI) loss and hyponatremia et causa GI loss. Hematological examination showed a decrease in hemoglobin, hematocrit, platelets, and an increased in leukocytes. The thorax x-ray examination confirmed cardiomegaly, rather than active pulmonary TB. The results of hematological, blood urea and creatinine examinations performed during the patient’s treatment at Hasan Sadikin Hospital (RSHS) Bandung can be seen in Figure 1 and 2.
The patient was hospitalized for eight days during which period an initial regimen was applied by the Department of Internal Medicine including: systemic treatment with 3-4 liters of oxygen per minute, infusion of 0.9% sodium chloride (NaCl) 1800 cc every 24 hours, topical treatment of the entire body using 10% urea lotion, the application to the lips and buttocks of open compresses with 0.9% NaCl three times a day and 0.1% gentamicin sulfate cream to the buttocks twice a day.

Extraoral clinical examination of the patient revealed a pale conjunctiva with painful ulceration covered by a blackish crust on her left upper lip accompanied by a reddish edema on her upper lip (Figure 3a). An intraoral examination revealed painful ulceration covered by a blackish crust on her upper labial mucosa (Figure 3b), while central erythema was present in the hard palate (Figure 3c). Intraoral assessment is limited because of the condition of those patients who experience pain when opening their mouths. Based on anamnesis and clinical findings, a clinical diagnosis of oral lesions associated with SLE and angioedema was made. Such lesions can be differentiated from other oral lesions, for example, erythema multiforme, oral lichen planus and erythematous candidiasis.

CASE MANAGEMENT

The oral lesions were treated with 1% hydrocortisone for those on the lips, 0.2% chlorhexidine gluconate was compressed on the labial mucosa and the palate three times a day. A 0.2% chlorhexidine gluconate was compressed on lesions in the oral cavity due to the inability of the patient to open her mouth fully or rinse it with mouthwash. On the second visit three days after the first, the patient complained of less pain and there was an accompanying improvement in the lesions on the lip, labial mucosa and palate during inpatient treatment. However, a blackish crust on the lips and ulceration of the labial mucosa were still evident. The central erythema of the palate, although showing signs of healing, was present (Figure 4). The previous therapy was continued and, given the dryness of the patient’s lips, vaseline album was added three times a day and she was instructed to rinse the mouth thoroughly with 10ml of 0.2% chlorhexidine gluconate three times a day.

On the third visit seven days after the initial visit, the oral lesions had largely healed, except for the ulceration of the labial mucosa (Figure 5). Consequently, 0.1% triamcinolone acetonide in orabase was applied to the lesions on the labial mucosa three times a day. Those patients who had previously tested positive for antinuclear antibody (ANA) with a homogeneous pattern were discharged from hospital. A week later, the lesions were observed to have completely healed. The pain within the oral cavity was eradicated, while the crust on the lips, ulceration on the labial mucosa and central erythema of the palate were all healed (Figure 6). Nevertheless, the patient was instructed to continue rinsing her mouth with 10ml of 0.2% chlorhexidine gluconate three times a day.

DISCUSSION

On examination of the patient in question, oral lesions were found on the lips, labial mucosa and hard palate. Based on ACR criteria, oral lesions are one of the clinical symptoms in the diagnosis of SLE. More than 40% of patients suffering from the condition experience ulceration...
in the oral mucosa. Another study reported the prevalence of oral lesions in patients with SLE to be approximately 7-52%. Early management of SLE must be initiated due to the several clinical manifestations of oral lesions present when the disease is active. According to ACR classification criteria, LE-specific and non-LE specific are typical oral lesions.

The specific oral lesions associated with LE consist of palatal erythematous ulcers, oral discoid lupus erythematosus, honeycomb plaques and verrucous LE. The LE nonspecific oral ulcers comprise aphthous ulcers, lupus cheilitis and other types of oral lesions. Within the ACR criteria, a typical oral ulcer which is the most specific for an SLE, is a palatal erythematous ulcer usually located on the hard palate with single/multiple lesions that are painless in masticatory or mucosal keratinization. When the disease is active, this constitutes an acute symptom of the disease and is occasionally the first evidence of SLE unaccompanied by skin lesions. Haemorrhaging usually occurs before the early lesion develops into an ulcer. The progression of the lesion into a reticulated restricted ulcer will be preceded by the appearance of solitary erythema and a patch of hemorraghing which is a lupus-specific lesion. Non-painful lesions located on the hard palate are typical of this type. Oral DLE is an atrophic plaque accompanied by white radiating keratotic striae and telangiectasia located in the lining layer, covering the buccal mucosa and soft palate. A honeycomb plaque is classified as chronic and well-circumscribed with white lacy hyperkeratosis and buccal erythema. Intense keratotic and raised plaques that are usually found in the mucosal lining, such as in the buccal mucosa, lips and hard palate (e.g. alveolar ridge) are characteristic features of LE verrucosa that may be involved.

In contrast, lesions on the buccal mucosa, lips and nasal septum, which are usually painful and tend to bleed, are characteristic of nonspecific aphthous ulcers more common in juvenile than adult SLE patients and usually occur when the disease is active. Lupus cheilitis may turn into a painful ulcer which presents clinically as inflammation of the buccal lips including small or diffuse erythematous and edematous plaques. Ulcers, usually shallow and 1-2 mm in diameter and present in approximately one third of patients, may extend to the pharynx. Lower lip vermillion is often related to cheilitis (typical of lupus cheilitis). Labial lesions are very common, possible affected areas being the upper and lower lips. Erosion, crusting and necrosis often occur in addition to the onset of erythema and edema. A rare clinical manifestation is bullous SLE whose lesions typically have clinical features which include multiple tense bullae on the face, neck and trunk.

According to the results of examinations conducted by the Internal Medicine Department, the patient recorded four positive results in 11 ACR criteria including arthritis, malar rash, renal disease and hematologic abnormalities. The clinical symptoms of this patient included those of arthritis with joint pain being experienced in the two weeks before admission to hospital. Nonerosive arthritis is a hallmark of SLE, often being the earliest manifestation, recorded in up to 53–95% of patients suffering from the condition. The clinical symptoms may be misinterpreted as another type of inflammatory arthritis, rendering diagnosis of SLE difficult.

Other observable clinical symptoms in these patients included irregular shaped, 0.1 x 0.1cm to 20 x 35cm sized, hyperpigmented macules with partially clear boundaries on the face, both arms, chest, abdomen and back. This complaint was first experienced less than four months ago with the
appearance of occasionally itchy red spots on both arms and the neck after the taking of medicine prescribed by a general practitioner who declared it to be for the treatment of lung conditions. Approximately three weeks before admission to hospital, the existing red spots spread to the chest, abdomen and back turning blackish in colour and sometimes feeling itchy. One of the worst affected organs in SLE patients is the skin, which may actually be the sole organ involved, as in cutaneous LE. A study reported that the prevalence of malar rash among SLE patients was high (73.5%).

Examination by the hematology laboratory following initial treatment of the patient revealed low levels of hemoglobin, hematocrit, erythrocytes and platelets, but high levels of leukocytes. The examination results also revealed anemia that was classified as normocytic-normochromic in nature based on the mean corpuscular volume and mean corpuscular hemoglobin concentration. Hematologic abnormalities in SLE can constitute a symptom of the presentation of SLE that is common, varied and affects each cell. Anemia, leukopenia, thrombocytopenia and antiphospholipid syndrome are the main clinical manifestations of SLE.

Anemia is found in approximately half of SLE patients. It is common and correlates to disease activity with pathogenesis including: chronic anemia, hemolysis, (autoimmune or microangiopathy), blood loss, renal insufficiency, medications, infection, hypersplenism, myelodysplasia, myelofibrosis and aplastic anemia. The high levels of blood urea and creatinine indicated a problem with the patient’s kidney. Renal involvement is common in SLE patients, with an incidence rate of 40-70%, together with significant rates of morbidity and hospitalization. An extremely common characteristic of lupus-related renal disease is the occurrence of proteinuria at various levels. All patients who experience oral disease, be it painful or painless, must be considered to have lupus, rather than the condition being automatically associated with systemic disease. Oral lesions may be the initial symptom of lupus. 57% of the mucosal lesions studied proved painful, while other observations confirmed 82% of oral ulcers to be painless. The contrasting findings of these two studies may be due to differences in the types of lesions studied. Erythematous lesions are usually painless, whereas discoid lesions often cause considerable discomfort. Careful examination of the oral cavity in all lupus patients must be undertaken because of the significant proportion of asymptomatic oral lesions. At the active stage of the disease, discoid and ulcer lesions are often observed and subside with remission of the disease. Oral lesions and the duration of the disease are closely associated, the duration of the prolonged disease being associated with fewer oral mucosal lesions. For the duration of the most active period of the disease the greatest number of oral mucosal lesions can be encountered. Treatment of the disease confirms that it is under control and in an inactive phase.

Specific genes that interact with environmental stimuli can initiate the onset of systemic lupus erythematosus resulting in a deregulated immune response. Environmental stimuli include: ultraviolet light, diet, certain infections and drugs, smoking, demethylation of DNA and infection or endogenous viruses or viral-like elements. One suspected cause of SLE might be that of drug use where the patient had previously been prescribed the aforementioned drug (red and yellow tablets) as pulmonary medicine for TB approximately eight months before hospitalization (five months with a general practitioner and three months in Rotinsulu). Various drugs have been identified as, possible, probable or definite causes of lupus. Patients without a diagnosis or history of SLE should be suspected of having drug-induced lupus (DIL) following a positive ANA examination and at least one clinical feature of lupus after the appropriate duration of a drug regime, with symptoms disappearing after discontinuation of the drug’s use. When the clinical and serologic manifestations of SLE appear in patients with historical use of certain medications, a diagnosis of DIL must be made. Certain drugs can certainly induce autoantibodies in a large number of patients, a condition referred to as drug-induced lupus. More than 100 drugs that cause DIL have been reported, including a number of new biological and antiviral agents. The best known of these drugs are procainamide, hydralazine, quinidine, phenytoin and isoniazid. The pathogenesis of DIL is not fully understood, but genetic predisposition plays an important role in the case of certain drugs. Gene expression in CD4+ T cells is altered by drugs with the inhibitory mechanisms of DNA methylation and induction of over-expression of lymphocyte function related to antigen-1, causing autoreactivity.

The patient’s management in this case involved the Departments of Internal Medicine, Dermatology, Venereology and Oral Medicine. While hospitalized, her intraoral lesions gradually healed following two weeks of treatment. Oral lesions associated with SLE are often difficult to resolve. The same regimen used to treat the overall LE process is also applied in the treatment of oral LE lesions. The treatment of oral ulcers in SLE includes the use of topical anti-inflammatory agents. Some of the most common drugs used in SLE patients are topical corticosteroids (e.g., 0.1% triamcinolone oral paste). Intraleisional applications of corticosteroid may also be considered. The severity of symptoms is related to the duration of corticosteroid use. If the treatment of oral lesions is refractory or there is no appropriate response to topical steroids within two weeks, then a more potent agent (for example, betamethasone or clobetasol in oral preparation) or the use of antimalarial agents and systemic drugs, including steroids, thalidomide, clofazimine and methotrexate may be needed.

The oral lesions were treated with 1% hydrocortisone, 0.2% chlorhexidine gluconate and 0.1% triamcinolone acetonide in orabase which promoted healing after a 2-week period of treatment. Chlorhexidine gluconate was used to disinfect the skin and cleanse traumatic wounds, being an antiseptic capable of eliminating bacteria by combining the mechanical action of an inert liquid and producing active chemical antimicrobial effects without damaging the host tissue. Chlorhexidine gluconate produces an effect on the
prokaryotic cell membrane rendering it active against a broad spectrum of microbes including: gram-negative and gram-positive bacteria and fungi through its effect on prokaryotic cell membranes, while exhibiting low toxicity to mammalian tissue.\(^\text{23}\)

SLE is a fatal disease requiring complex management because it involves multiple organs and, therefore, necessitates a multidisciplinary approach.\(^\text{4}\) While the symptoms of SLE can be controlled, the condition itself cannot be cured. Consequently, SLE treatment is primarily associated with improved disease control and patient survival. The management objectives of SLE are those of reducing inflammation, before planning SLE treatment is mandatory. Protection from ultraviolet light can prevent an eruption of lupus skin lesions.\(^\text{23}\)

High blood pressure, limited real function, low blood count and low levels of serum protein are associated with a poor prognosis.\(^\text{18,24}\)

An important role is played by the dentist in arriving at a diagnosis with the aid of clinical and histopathological findings before the cutaneous lesions become apparent. To avoid infection, a thorough clinical examination is required. Patients with SLE can rapidly develop infection due to disease or therapy-related immunosuppression. Before surgery, the results of the latest laboratory tests can be analysed to determine platelet counts, prothrombin time and international normalization ratio for blood clotting time. Local measures may also prove essential to maintain hemostasis.\(^\text{15,20}\)

In conclusion, oral lesions are one of the important clinical symptoms in the diagnosing of SLE which are frequently found in patients suffering from the condition. A painless erythematous palate ulcer in the masticatory or keratinized mucosa, especially the hard palate, is a typical lesion. An appropriate understanding of the complex clinical features and locations of SLE is very important in order that effective dental management can be provided by a dentist. Detection of oral lesions plays a significant role in diagnosing SLE. It is important for the dentist to recognize the symptoms of diseases to enable the definitive diagnosis and appropriate treatment to be identified, thereby enhancing the prognosis for patients. A multidisciplinary approach and appropriate referrals ensure complete dental and medical management of patients with SLE.

REFERENCES