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Oral Manifestation of Systemic Lupus Erythematous: A Review

Fitria Mailiza[1*]

[1]*Oral Medicine Department, Baiturrahmah University, Padang, Indonesia*
[*]*Corresponding author. Email: fitriamailiza_drg@yahoo.com*

ABSTRACT
Systemic Lupus Erythematosus (SLE) is a chronic multisystem autoimmune disorder characterized by the development of autoantibodies and immune complexes in association with a wide variety of clinical manifestations and tissue damage including oral mucosa. Oral lesions were non-spesific in SLE, may be present as erythematous areas, ulceration and white striae. Oral lesions are found in over 40% of patients with SLE. This study aim was to recognize the clinical manifestation of oral lesions associated with SLE. The clinical of SLE is variable and may be characterized by episodes of recurrent acute or chronic inflammation. Oral lesions which typically consist of erythematous areas, erosions or white patches, are fairly symmetrically distributed and resemble lichen Planus. The diagnosis of SLE requires several compatible clinical features and supportive laboratory studies. A wide spectrum of autoantibodies can be found in patients with SLE and are often associated with specific clinical features. The presence of anti-double-stranded DNA (dsDNA) is highly specific for SLE and it can be a marker to differentiation with other diseases. Patients with SLE may present a variety of oral manifestations. Histological investigation plays an important role in the definitive diagnosis of oral lesions when clinical doubt exists.

Keywords: *Oral Lesions, Systemic Lupus Erythematosus*

1. INTRODUCTION

Systemic Lupus Erythematous (SLE) is an immune complex-mediated multisystem autoimmune condition in association with a wide variety of clinical manifestations and tissue damage with multifactorial etiology which mainly affects in women their 30s and 40s. The clinical of SLE is variable and may be characterized by episodes of recurrent acute or chronic inflammation. Prevalence of SLE ranges between 12 and 50 per 100.000. Knowledge of this condition facilitates understanding of most other autoimmune diseases [1].

The etiology of SLE is still not fully understood, the varied penetrance and lack of concordance of the disease among genetically and environmental triggers are likely inducing the onset of the disease and disease flares. Environment factors such as cigarettes smoke, alcohol, occupationally, viruses and vaccines have been advocated induced lupus and disease flares [2].

SLE often presents in a non-specific, vague fashion, frequently with periods of remission and exacerbation. Cutaneous manifestations are erythematous patches on the face that coalesce to form a roughly symmetrical pattern over the cheeks across the bridge of the nose in a butterfly distribution. The skin over the neck, arms, shoulders and fingers are also affected. The patient may complain of itching or burning sensation. Some may present with areas of hyperpigmentation. Oral lesions of SLE develop in 20-50% of patients. The oral mucosa may be involved either prior to or following the development of skin lesions or even in the absence of skin manifestations. Oral lesions begin as erythematous areas, without induration and with white spots. The margins of the lesions are not sharply demarcated but frequently show the formation of a narrow zone of keratinization. In this review, we present SLEwith oral manifestations [3,4].

2. REVIEWS

The patient with SLE may present with various systemic manifestations. Lupus is known as “the great mimic”. The general symptom include fever, malaisea, arthralgias, myalgias, mucocutaneous lesion headache and loss of appetite and weight. Musculoskeletal sign and symptom are predominant in present and is often the earliest

manifestation. Oral lesions such as desquamative gingivitis, marginal gingivitis or erosive mucosal lesion have been reported in up to 40% of patient Oral lesions which typically consists of erythematous areas, erosions or white patches, fairly symmetrically distributed and resembling lichen planes, may be seen in 10-20% of patients with SLE. Slit like ulcers may also be seen near the gingival margins (Fig.1) [3,4,5].

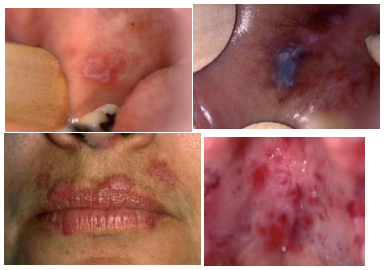

Figure 1. Different oral manifestations of LE. Discoid lesion, (B) white plaques on a pigmented mucosa, (C) red plaques on the lips and (D) various erythematous maculae on the palate.

The diagnosis of SLE requires several compatible clinical features and supportive laboratory studies. A wide spectrum of autoantibodies can be found in patients with SLE and are often associated with specific clinical features. Antinuclear antibodies (ANA) are found in 98% of SLE patients but are non-spesific. The presence of anti-double-stranded DNA (dsDNA) is highly specific for SLE but they only present in around 70% of cases. Other autoantibodies reported in patients with SLE include anti-Smith, anti-ribosomal P and anti-proliferating cell nuclear antigen (PCNA). The SLE requires several compatible [5,6] clinical features and supportive laboratory studies. A wide spectrum of autoantibodies can be found in patients with SLE and are often associated with specific clinical features. Antinuclear antibodies (ANA) are found in 98% of SLE patients but are non-spesific. The presence of anti-double-stranded DNA (dsDNA) is highly specific for SLE but they are only present in around 70% of cases. Other autoantibodies reported in patients with SLE include anti-Smith, anti-ribosomal P and anti-proliferating cell nuclear antigen (PCNA) [5,7].

Histopathological diagnosis of the oral lesion in LE should also be confirmed with Direct Immunofluorescence (DIF), which is a useful tool to rule out other oral lesions such as lichen Planus and non-specific white lesions. The characterization of the inflammatory infiltration by immunohistochemistry showed that inflammatory cells in all specific lesions of LE are mainly composed of T lymphocytes, while B lymphocytes CD 20 positive, macrophages and Langerhans cells are minor components of the infiltrate, regardless of the clinical aspect of the lesion. These findings are in accordance with studies that analyzed the quality of the inflammatory component in biopsies of cutaneous and mucosal lesions of LE which report the predominance of T cells (about 75%) [6,7].

Histopathologically lichen Planus and SLE are the same. Five histologic criteria to distinguish both are: vascularization of keratinocyte, subepithelial presence of patchy PAS-positive deposits, oedema in upper lamina propria, PAS-positive thickening of blood vessel walls, and severe deep or perivascular inflammatory infiltrate [7,8]. OLP usually presents bilaterally on the oral mucosa and has various patterns, with reticular, erythematous with striae and ulcerative being the most common. These patterns may coexist in the same region or may alternate in time. On our patient, the oral lesion pattern that we found are the reticular and the erythematous [1,2,9].

The classic histopathologic features of OLP include liquefactive degeneration of the basal cell accompanied by apoptosis of the keratinocytes, a dense band-like lymphocytic infiltrate at the interface between the epithelium and the connective tissue, focal areas of hyperkeratinized epithelium (which give rise to the clinically apparent Wickham's striae) and occasional areas of atrophic epithelium where the rete pegs may be shortened and pointed (a characteristic known as sawtooth rete pegs). Eosinophilic colloid bodies (Civatte bodies), which represent degenerating keratinocytes, are often visible in the lower half of the surface epithelium. Degeneration of the basal keratinocytes and disruption of the anchoring elements of the epithelial basement membranes and basal keratinocytes (e.g. hemidesmosomes, filaments, fibrils) weaken the epithelial connective tissue interface. As a result, histologic clefts (Max–Joseph spaces) may form and blisters on the oral mucosa (bullous LP) may be seen at clinical examination. (Fig.2). B cells and plasma cells are uncommon findings [10,11].

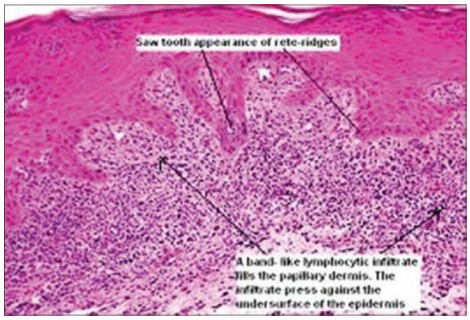

Figure 2. Histological appearance of oral lichen planus

Pathogenesis SLE disease is characterized by a humoral immune response exhibited by the production of autoantibodies against many components of intracellular particles. On exposure to environmental stimulus in the form of ultraviolet light, dietary factors, infection and certain drugs, demethylation of DNA occur rendering it antigenic. Patients with SLE have poor clearance mechanisms for cellular debris and these induce the immune system. Immune complexes from intravascularly are deposited in the glomeruli. Alternatively, autoantibodies may bind to antigens already located in the glomerular basement membrane, forming immune complexes in situ. Immune complexes promote an inflammatory response by activating complement and attracting inflammatory cells, including lymphocytes, macrophages and neutrophils [12,13].

The pathobiology of systemic lupus erythematosus (SLE) probably involves complicated and multifactorial interaction among various genetic and environmental factors. Multiple genes that contribute to disease susceptibility include genes encoding complement and other components of the immune response in addition to major histocompatibility complex class I and II genes. Interaction sex, hormonal and the hipothalamopituitary-adrenal axis modifies this susceptibility and the clinical expression of the disease. A defective immune regulatory mechanism such as clearance of apoptotic cells and immune complexes are important contributors development of SLE. The loss of immune tolerance increased antigenic load, excess T cell help, defective B cell suppression and the shifting of T helper (Th1) to Th2 immune responses leads to B cell hyperactivity and the production of pathogenic autoantibodies. In addition, environmental factors such as chemicals and drugs, ultraviolet light, dietary factors, viruses and environmental estrogen are probably required to precipitate the onset of the disease (Fig.3) [13,14].

Many autoantibodies are produced in systemic autoantibodies within the nucleus of the cell, these antinuclear antibodies (ANA's) have been useful in the differential diagnosis of such as Scleroderma, Sjorgen's Syndrome and mixed connective tissue disease. A wide spectrum of autoantibodies can be found in patients with SLE and are often associated with spesific clinical features.

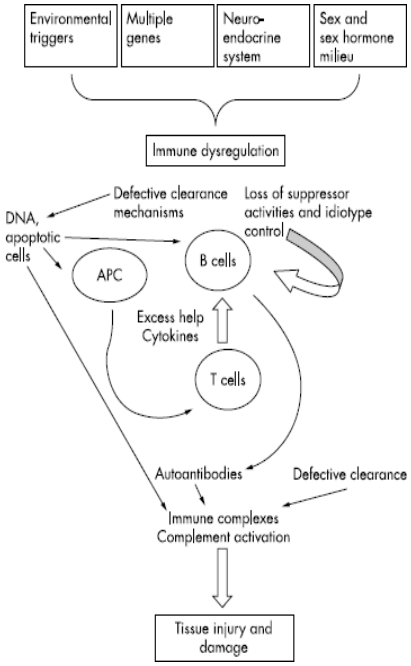

Figure 3. Pathogenesis of SLE

Antinuclear antibodies (ANA) can be found in 98% of SLE but are non-spesific. The presence of anti-double-stranded DNA (dsDNA) is highly specific for SLE but they are only present in around 70% of cases. Other autoantibodies reported in patients with SLE include anti-Smith, anti-ribosomal P and anti-proliferating cell nuclear antigen (PCNA) [5,6].

Constitutional symptoms of SLE, such as complaints of fatigue, malaise, arthralgia, myalgia and mucocutaneous lesions are common. Musculoskeletal signs and symptoms predominate in SLE. Arthralgia, asymmetric and migratory, is usually present and is often the earliest manifestation. The joints of the hands are most often affected. The arthritis is moderately painful and nondestructive. Deformities observed are usually due to tendon inflammation (Jaccoud-type arthropathy), rather than degeneration [7,8].

Microscopic features of lupus mucosal lesions are quite similar to those of lichen planus and erythema multiforme. A common microscopic feature of these lesions is the band-like subepithelial inflammation. However, in patients with SLE and erythema multiforme, the inflammatory infiltrate extends deeper into the underlying connective tissue and shows a perivascular pattern. Deep submucosal vesicles may also be apparent. Lupus lesions will exhibit periodic acid-Schiff staining in the basement membrane zone. Direct immunofluorescent testing will show immunoglobulin and complement deposition along the basement membrane zone in a granular pattern that is characteristic of type III hypersensitivity reactions [8,9,10].

SLE can run a varied clinical course, ranging from a relatively benign illness to a rapidly progressive disease with fulminant organ failure and death. Most

patients have episodic relapsing and remitting course that may be managed with high-dose steroids during severe flare-ups. SLE is probably the most difficult of all autoimmune rheumatic disorders to control, putting prevention of infections at the forefront of disease management. For patients with SLE, emphasis is therefore placed on the dental team's continuous reinforcement of good oral hygiene, provision of close monitoring for and aggressive treatment of dental and oral infections, and assistance with the diagnosis of mucocutaneous lesions of the head and neck [9,11].

Several diseases mimic the initial course of SLE and make its differentiation from other conditions difficult. The onset of symptoms of many rheumatic disorders often overlap. Lupus-related mucocutaneous lesions can mimic those of erythema multiforme, lichen planus and other vesiculobullous lesions. Clinical differentiation will depend on the morphology of the lesion analyzed. The main differentiation diagnoses for keratotic diagnoses are lichen planes, lichenoid reaction to dental fillings, traumatic and smoker's keratoses and verrucous carcinoma. Histologic and immunohistochemical confirmation of intact tissue adjacent to a given lesion remains the criterion standards for definitive diagnosis [10,11].

The goals of SLE management are based on prevention, reversal of inflammation, maintaining states of remission and alleviation of symptoms. Avoidance of flare-ups of lupus and skin lesions consists of protection from ultraviolet sunlight. The best management of erosive lesions of SLE in the intraoral mucosa is uncertain but corticosteroids often in high doses may be the only effective treatment. Biopsies of oral lesions show irregularly distributed chronic inflammatory infiltrates [11,12].

SLE is usually treated by a rheumatologist who specializes in treating diseases that affect the joint and muscle. Topical creams are often prescribed for a rash. For more serious problems, anti-inflammatory drugs, antimalarial, and steroids such as cortisone, prednisone, are reserved for patients with morbid symptoms associated with significant organ involvement, particularly renal, central nervous system and systemic vascular diseases [12,13].

B.12 Vitamin and folic acid are important in intra-cells metabolism. Both of these vitamins play roles in DNA synthesis and reepithelization. SLE have disturbance in synthesis DNA and with giving this vitamin we can recover the problems [14]. Dentists must enforce preventive dentalcare and monitor patients with SLE closely for head and neck infections because they are predisposed to severe infections. Theseinfections are often silent and difficult to detect because of a paucity of pain and swelling. A multidisciplinary approach medical consultation and appropriate referrals ensures comprehensive medical and dental management of patients with SLE.

3. CONCLUSION

Patients with SLE may present a variety of oral manifestations. Histological investigation plays an important role in the definitive diagnosis of oral lesions when clinical doubt exists.

REFERENCES

[1] Mangla, P. Goyal, H.P. Singh, Oral Manifestation of Systemic Lupus Erythematous: A case Report, International Journal of Applied Dental Sciences, 2018.:4(3):69-71, 2018.

[2] A. Mak, S.H. Tay, EnvironmentalFactors, Toxicants and Systemic Lupus Erythematosus. A Review, *International Journal of Molecular Sciences*, 15, 16043-16056, 2014. www.mdpi.com/journal/ijms.

[3] L.S. Bichile, V.C. Chewoolkar Lupus Flare: How to Diagnose and Treat. *Medicine Journal Update.* p: 281- 286, 2011

[4] J.A Reynolds, I.N. Bruce. Overview of the Management ofSystemic Lupus Erythematosus,Report on Rheumatic Disease/series7/Spring 2013/Topical Reviews No. 2. *Journal of Arthritis ResearchUK*.2013.

[5] M. Cojocaru, T. Masaryk. Manifestation of Systemic Lupus Erythematosus, A Journal of Clinical Medicine.Vol. 6 No. 4. 2011.

[6] H.S. Shilpashree. Systemic Lupus Erythematosus in a 12 years-old Boy: A Rare Entity in Childhood. International Journal of Clinical Pediatric Dentistry,;3(3):199-202, 2010

[7] C. Scully, Medical Problem in Dentistry, 7th Edition. Ch.18.. Elsevier.p.467-470, 2014.

[8] M. Hammoudeh M et al, OralManifestation of Systemic LupusErythematous Patirnt in Qatar. A Pilot Study, Hindawi International Journal of Rheumatology, Vol.2018. Accesed July, 27th 2021.

[9] [9] G.C. Tsokos.. Mechanisms of Disease Systemic Lupus Eryhematosus. *The New England Journal of Medicine*, Dec 1, 365:2110-21, 2011

[10] K. Sriram , S . Mahadevan. Systemic Lupus Erythematous : Recent Concepsr in Genomics, Pathogenetic Mechanisms, and Therapies, Review Article. *International*

Journal ScholarlyResearch Network, Vol. 2011.

[11] J.C, Crispin, G. Tsokos G.C, IL-17 in Systemic Lupus Erythematosus. Journal of Biomedicine and Biotechnology.2010.

[12] E.K, Munthe, I. Sufiawati , Oral Lesions as a Clinical Sign of Systemic Lupus Erythematous, Dental Journal, 5(3):147-152, 2018.

[13] I.L, Cardoso I.L, M.F. Leal M.F, Regis R.C.D. Systemic Lupus Erytematous and Implication for the Oral Cavity, Journal of Medical Care Research and Review.Sept 22th .2020.

[14] Conclutions of a WHO Technical Consultation on Folate and Vit.B.12 deficiencies, Food and Nutritional Bulletin 29(2), 2008.