

Systemic Lupus Erythematosus: A Rare Case Report

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Abstract: Systemic lupus erythematosus (SLE) is a multiorgan autoimmune disease of unknown etiology with many clinical manifestations. The skin is one of the target organs most variably affected by the disease. Skin lesions in patients with lupus may be specific or nonspecific. This paper covers the SLE-specific cutaneous changes: malar rash and oral mucosal lesions as well as SLE nonspecific skin manifestations, their pathophysiology and management. A deeper thorough understanding of the cutaneous manifestations of SLE is essential for diagnosis, prognosis and efficient management. Thus, dermatologists should cooperate with other specialties to provide optimal care of SLE patient.

I. Introduction

The nosographic concept of lupus erythematosus (LE) includes 3 major subtypes: chronic cutaneous LE, subacute cutaneous LE, and systemic or acute cutaneous LE. Besides these 3 subtypes, other less frequent clinical varieties may occur.¹ Systemic lupus erythematosus (SLE) is a multiorgan autoimmune disease of unknown etiology that can have many clinical manifestations. The skin is involved in up to 85% of systemic lupus erythematosus (SLE) cases and may be the only organ involved in cutaneous lupus erythematosus (CLE).

The diagnosis of the cutaneous manifestations of LE is based on clinical, histopathology, and immunohistology of skin lesions. In addition, serum autoantibodies are considered immunologic markers for distinct clinical types of the illness. The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is used as a clinical tool that standardizes the way disease activity is described and provides guidelines for identifying a clinical change. This clinical tool quantifies disease activity and damage in cutaneous lupus erythematosus. The activity score is based on the erythema, scale, mucous membrane lesions, and nonscarring alopecia. A recent study gives us a foundation for the practical use of the CLASI in clinical trials as a tool to measure disease severity and responsiveness to therapy.² In 1982, the diagnosis criteria for SLE were published by the American College of Rheumatology (ACR) which were revised in 1997 and are currently used in clinical practice.³ Undoubtedly useful, mainly for differential diagnosis between systemic LE and other rheumatologic diseases, such criteria are commonly inadequate for some LE subsets. Concerning cutaneous manifestations, the ACR criteria include malar rash, discoid rash, photosensitivity, and oral ulcers. It must be pointed out that the immunologic study does not include the immunohistology of the skin (lupus band test).

Cutaneous manifestations of SLE.

- 1) Malar rash
- 2) Discoid LE (DLE)
- 3) Localized DLE
- 4) Generalized DLE
- 5) Photosensitivity
- 6) Mucosal DLE
- 7) Oral DLE
- 8) Conjunctival DLE
- 9) Nasal DLE
- 10) Genital DLE
- 11) Subacute cutaneous lupus erythematosus
- 12) Alopecia
- 13) Lupus panniculitis/lupus profundus
- 14) Lichenoid DLE (LE/lichen planus overlap)
- 15) Small vessel cutaneous leukocytoclastic vasculitis secondary to LE
- 16) Dependent palpable purpura
- 17) Urticarial vasculitis
- 18) Secondary atrophie blanche
- 19) Periungual telangiectasias
- 20) Livedo reticularis

- 21) Raynaud's phenomenon
- 22) Bullous lesions (BSLE)

II. Case Report

A 29 year old female reported to the dept. of periodontics a c p m dental college Dhule with chief complaint of generalized pain, burning sensation, difficulty in chewing food and drinking water since 8 months along with bright red discolouration of the skin involving the malar region bilaterally, bridge of nose. Patient also gave history of itching of the discoloured malar region (Figure 1) and hand (Figure 3).

There was no significant contributory medical and family history extra-oral eruptions on forehead, malar region and vermilion border of lips aggravated on exposure to sun rays with previous history of pain constitutional symptoms of fatigue, headache, fever, malaise and unsatisfying sleep since last 8 months. Patient also complained of reduced vision and dryness of eyes since last 1 year. Medical consultation sought by the patient from a physician 8 months back revealed a suspected case of "systemic lupus erythematosus" (SLE).

Intraoral examination revealed multiple oral ulceration on hard palate(Figure 3).

Therapy begins with the use of sun-protective measures, including sunscreens, protective clothing, and behaviour alteration. Ultraviolet A and B (UVA and UVB) radiations have been implicated in the initiation and exacerbation of skin lesions. As a result, current standard of care includes minimizing sun exposure, and the use of broad spectrum sunscreens. Despite sunscreens are widely used to photoprotect patients with photosensitive lupus erythematosus, standardized controlled studies that can prove their efficacy for this indication have been lacking. The regular use of sunscreens is beneficial to LE patients because it prevents the UV radiation-induced skin lesions. Effective protection, however, might vary considerably between different sunscreens.

Topical and intralesional corticosteroids were used for limited disease; however, long-term use may lead to significant side effects, especially on the face. For the treatment of oral ulcers hydrogen peroxide gargle, buttermilk gargle, or steroid impregnated gel was applied. Suspected infections were treated with antiviral agents after a swab has been taken for culture and microbial sensitivities.



Figure 1 Figure 2



Figure 3

III. Discussion

The first criterion of the ACR is malar rash (sensitivity 57%; specificity 96%), which is characterized by an erythematous rash over the cheeks and nasal bridge (Figure 1). Malar rash is a fixed erythema that typically spares the nasolabial folds. It is a butterfly-shaped or vesperilio rash that can be flat or raised over the cheeks and bridge of the nose. It lasts from days to weeks and is occasionally painful or pruritic.

The second criterion is photosensitivity (sensitivity 43%; specificity 96%). Exposure to ultraviolet light causes skin rash or other symptoms of SLE flareups. A macular or a diffuse erythematous rash occurs in sun-exposed areas, as the face, arms, or hands and that generally persists for more than 1 day. Sometimes erythematous papules or macules on the dorsal aspects of the hands classically sparing the knuckles are observed (Figure 2).

The impact of UV irradiation on initial triggering, and on perpetuation of the various cutaneous manifestations of LE, suggests that abnormal photoreactivity is one important

factor in LE. Photosensitivity shows a strong association with the manifestation of all CLE subtypes, and the abnormal reactivity to ultraviolet (UV) light is an important factor in the pathogenesis of both cutaneous and systemic disease. A potentially crucial role in the initiation of the autoimmune reaction cascade has been attributed to UV-induced keratinocyte apoptosis⁴. Interestingly, a significantly higher number of apoptotic nuclei in the epidermis has been described in primary and UV-induced skin lesions of CLE patients compared with normal donors⁵. This is in analogy with the evidence that impaired clearance of apoptotic cells may trigger the immune response in patients with autoimmune disorders. Apoptotic cells accumulate in the germinal centres of lymph nodes from patients with SLE, which might be due to impaired phagocytic activity or caused by the absence of tangible body macrophages⁶, indicating that apoptotic cells accumulate, and, subsequently, enter late stages of apoptotic cell death including secondary necrosis.

The chromatin nonhistone DNA binding protein high mobility group box one (HMGB1), released during cell activation and death, may also be involved in the inflammatory clearance of apoptotic cells, which justifies the release of HMGB1, detected in the serum of SLE patients as well as an increased expression of HMGB1, was demonstrated in skin lesions of lupus patients. HMGB1 makes easier interaction and uptake (followed by inflammation) by macrophages and dendritic cells through receptor for advanced glycation end products and Toll-like receptors 2, 4, and 9 due to the connection with nucleosomes and DNA released from apoptotic cells.

Apoptosis or clearance of apoptotic cells has been reported as an important pathophysiological characteristic in autoimmune diseases such as systemic lupus erythematosus, therefore targeting HMGB1 might have an important role on the inflammation control⁷.

Nitric oxide (NO), an important regulator of apoptosis, has been implicated in the course of various autoimmune diseases. Interestingly, NO has been shown to protect against UVA-induced apoptosis by increasing Bcl-2 expression and inhibiting UVA-induced upregulation of Bax protein in endothelial cells⁸. In addition, an antiapoptotic role for NO in keratinocytes was suggested after UVB irradiation. Furthermore, UV exposure has also been shown to modulate local production of NO by the constitutively expressed nitric oxide synthase (iNOS). It has also been reported that iNOS is expressed in human skin in the first 2 days after exposure to UVA and UVB⁹. In contrast, in CLE patients, an iNOS-specific signal appeared only 72 h after UV exposure and persisted in the evolving skin lesions up to 1 month, evidencing a delayed and prolonged expression of iNOS in the LE skin. It has further been studied that NO production is increased in patients with SLE, possibly due to the upregulated iNOS expression in activated endothelial cells and keratinocytes¹⁰.

Ultraviolet irradiation leads to release of interleukin-10 (IL-10) by keratinocytes, which may be related with increased autoantibody production and apoptotic damage in skin lesions of LE patients¹¹. An interferon- α (IFN- α) or "type I IFN signature" has been found in patients with SLE. Lesional skin from LE patients has shown a high number of plasmacytoid dendritic cells (pDCs) which are the primary cellular source of IFN- α in LE skin lesions¹². Interferon-inducible protein-10 (IP-10 or CXCL10), a monokine induced by gamma interferon (MIG or CXCL9) and interferon- α /p-inducible Mx 78 kDa protein (MxA), is downstream surrogate marker for IFN- α expression.

The next criterion of ACR is oral ulcers (including oral or nasopharyngeal ulcers)¹³. Lupus should be considered in all patients who experience painless or painful oral (or less frequently nasal or vaginal) ulcers. Palatal ulcers are most specific for SLE (Figure 3).

Erythematous lesions are often accompanied by oedema and petechial reddening on the hard palate, although they are usually found incidentally as flat macular areas with poorly defined borders¹⁴. Ulcers tend to occur in crops and are shallow. They are usually 1-2 cm in diameter and in about one-third of patients may extend into the pharynx¹⁵.

IV. Conclusion

Management of the dermatological disorders associated with oral involvement is often complex undertaking and requires a joint expertise and communication of clinician to provide the patient with the optimal treatment plan based on scientific rationale so a dentist should look into and treat accordingly.

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