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Case Report

Oral Lichen Planus: A Case Report and an Update on the Role of Mast Cells in its Pathogenesis

Bibin Thomas George[1], Prabu Mahin Syed Ismail[2], Siddique Ahmad Syed[2], Sitansu Sekhar Das[3], Debkant Jena[4], Gopi Krishna Moosani[5]

Contributors:

[1]Associate Professor, Department of Periodontia, IBN SINA National College for Medical Studies, Jeddah, Saudi Arabia; [2]Assistant Professor, Department of Conservative Dentistry, IBN SINA National College for Medical Studies, Jeddah, Saudi Arabia; [3]Professor, Department of Prosthodontics, Siksha O Anusandhan University, Bhubaneswar, Odisha, India; [4]Reader, Department of Conservative Dentistry, Siksha O Anusandhan University, Bhubaneswar, Odisha, India; [5]Professor, Department of Conservative Dentistry, G Pulla Reddy Dental College, Kurnool, Andhra Pradesh, India.

Correspondence:

Gopi Krishna Moosani, Professor, Department of Conservative Dentistry, G Pulla Reddy Dental College, Kurnool, Andhra Pradesh, India. Contact: 9493870068, E-mail: gopi.moosani@gmail.com

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Abstract:

Lichen planus (LP) is a common chronic mucocutaneous disease of the skin and mucous membranes. It affects about 0.1-4% of the general population. Here, we present a case report of a 36-year-old female patient who presented with burning sensation and a white lesion bilaterally on the buccal mucosa along with a mixed red and white lesion on the tongue. The histopathological features were suggestive of oral LP (OLP). In this article, we try to evaluate the histopathological features of OLP and stress the eminence of mast cells (MCs) in the occurrence of OLP. We also try to review the literature behind the role of MCs, their significance and their effects on the histological picture of LP.

Key Words: Lichen planus, mast cells, pathogenesis

Introduction

Oral lichen planus (OLP) is a chronic red, white, or mixed lesion of the mucosa with unknown etiology. It is believed to be a T-cell mediated autoimmune inflammatory mucosal disease. T-lymphocytes which are the chief inflammatory cells accumulate within the basement membrane (BM) of OLP lesions by extravasation from the regional blood vessels. They are the main cells which result in the basal cell degeneration of the basal keratinocytes of the epithelium. Recently, there is increased intentness toward the role of mast cells (MCs) in the pathogenesis of OLP. MCs are now being termed liable for the increased surveillance of inflammatory cells, especially T-lymphocytes into the connective tissue that results in advancement and sustenance of OLP. OLP lesions usually contain few B-cells or plasma cells and minimal deposits of immunoglobulin or complement.[1] This article describes a case of OLP and reviews the role of MCs in OLP.

Case Report

A 36-year-old female patient came to our department with the chief compliant of burning sensation of the buccal mucosa bilaterally since 2 months. On inspection, the right side of the buccal mucosa showed fine white radiating network like striae, surrounded by a discrete erythematous area (Figure 1). The left side of the buccal mucosa also showed white radiating striae, but it was not as significant as it was on the right side (Figure 2). Along with these, the lateral side of the tongue on the left side showed an oval erythematous area which was painful (Figure 3).

Her intraoral examination revealed she had poor oral hygiene with Grade 2 calculus and Grade 3 stains. All teeth were present. Dental caries in relation to 37. There were generalized periodontal pockets with bleeding on probing. Her systemic health was normal, and she had no other lesions on the body.

Histopathological features

An incisional biopsy was taken from the right buccal mucosa and stained with hematoxylin and eosin for histopathological examination. The sections showed hyperparakeratinized stratified squamous epithelium with thin and elongated rete ridges. The epithelium was hyperplastic with saw tooth shaped rete ridges. A sub-epithelial band of the dense chronic inflammatory cell infiltrate was present. Lymphocytes formed the predominant group of the inflammatory infiltrate. Focal areas showed basal cell degeneration, with the inflammatory cells predominantly lymphocytes extending into the basal layers of the epithelium. The stroma also showed collagen fibers with moderate vascularity (Figure 4). All these features were favorable toward a diagnosis of OLP.

Discussion

LP is a relatively common mucocutaneous lesion but, in many ways is a conundrum both to the clinician and pathologist. The oral (OLP) lesions usually have a characteristic clinical appearance and attributable features, but OLP may also exist in a perplexed number of patterns and forms, and mimic other disorders which may clinically appear as OLP. Lesions may affect cutaneous and/or mucosal surface.[1] OLP affects from

0.1 to about 4% of individuals, with a female predominance.[2] The pathogenesis of OLP is based on a self-antigen present on the keratinocytes of the epithelium which provokes an inflammatory response which is autoimmune and directed against the keratinocytes themselves. The sub-epithelial band of inflammatory infiltrate forms a predominant feature of OLP which is made up mostly of T-lymphocytes and their complimentary products which appear in a synchronized fashion. While there is sizeable literature on the T-cell population 3, 4 in the OLP, other immunocompetent cells have attracted less attention.

OLP is a T-cell mediated autoimmune disease in which the auto cytotoxic CD8+ T-cells trigger apoptosis of the basal cells of the oral epithelium.[3] T-cells and macrophages comprise the dense sub-epithelial mononuclear infiltrate in OLP, and also there is an accentuation of T-cells within the epithelium. CD8 + T-lymphocytes which are activated by the major histocompatibility complex (MHC) complex form the predominant population of cells both within the epithelium and beside the damaged keratinocytes. Therefore, early in the formation of OLP lesions, T-lymphocytes appear in the lesional site either as a chance encounter on routine surveillance or direct immune activation by MHC complex. These MHC activated CD8 + T cytotoxic cells may recognize an antigen associated with the MHC class I on keratinocytes.[4] After antigen recognition, the CD8 + cytotoxic T-cells may trigger keratinocyte apoptosis under the influence of perforin, granzyme B, or by tumor necrosis factor-α (TNF-α). Activated CD8+ T-cells (and possibly keratinocytes) may release inflammatory mediators such as interleukins, cytokines that magnetize increasing numbers of lymphocytes into the lesional area thereby resulting in the progress of the lesion.[5] OLP lesions contain accentuated levels of the cytokine TNF-α[6,7] especially the basal keratinocytes and T-cells in the sub-epithelial area also express TNF-α *in situ*.[8,9] These combined systems result in an array of events beginning from T-cell accumulation in the superficial lamina propria, BM disruption, intra-epithelial migration of T-lymphocytes, and keratinocyte apoptosis resulting in OLP.[10]

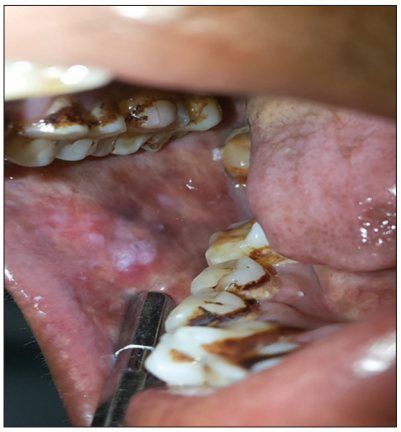

Figure 1: White lacy network on the right buccal mucosa surrounded by an erythematous zone.

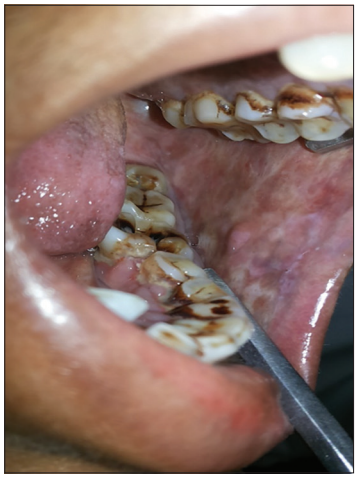

Figure 2: White radiating striae on the left buccal mucosa.

Several studies have focused that MCs have a prominent role to play in the pathogenesis of OLP. After more than 100 years

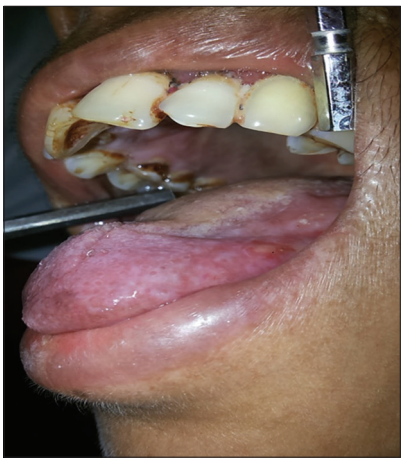

Figure 3: An oval erythematous are on the left lateral border of the tongue.

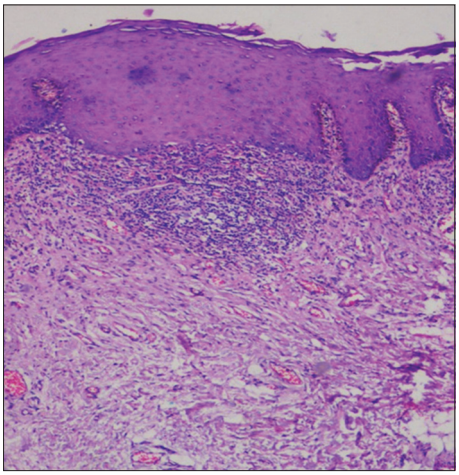

Figure 4: H and E picture showing sub-epithelial band of inflammatory cells. Note the basal cell degeneration of the epithelium (×20 magnification).

of its discovery by Paul Ehrlich, the MC continues to remain a cell of paradox. It is found widely distributed in the body particularly associated with connective tissues.[11] MCs are found ubiquitously in the oral cavity, including the dental pulp.[12,13]

MCs are the chief secretary histamine granule containing cells that are distributed predominantlyin the micro vascular endothelium of oral mucosa and pulpal tissue. The enzymatic secretion of oral MCs matches to the cutaneous MCs. Both of them secrete the serine proteases tryptase and chymase. Oral MCs along with histamine contain the pro-inflammatory cytokine, TNF-α in their granules. This TNF-α plays a key role in the inflammatory processes both in health and disease. TNF-α mediates inflammatory processes by promoting leukocytic crowding by stimulation of endothelial-leukocyte adhesion molecules.[12,13] This mechanism is seen in many oral conditions such as pulpitis, lupus erythematosus, periapical inflammation including LP.

Zhao *et al.* proposed that MCs play a potential role in the development of OLP. The interactions between MCs and T-cells, which are related to the disease process, are relevant to both the initiation, vaso-induction, and effector phases of OLP. They observed a mast cell count (MCC) of 151.5 mm^2 in LP. They considered MC as the offender in the BM destruction seen in OLP. These MCs are the culprits behind the array of inflammatory events occurring in OLP. TNF-α released from MCs resulted in accentuated production of matrix metalloproteinase-like collagenase, which cause the BM destruction and consequently resulted in the production of adhesion molecules such as E-selectin and intercellular adhesion molecule. Thus, these chain of events finally resulted in an increased output of leukocyte migration and infiltration in and around the BM.[14]

According to Zhou increased numbers of MCs were seen in OLP (59.75/mm^2) as compared to 25.50/mm^2 seen in normal oral mucosa. These results are similar to the studies carried out by Xijing *et al.*, who observed the MCC of 151.5/m^2 Zhou *et al.*, suggest a role for MCs in T-lymphocyte mediated BM degeneration occurring in OLP. CD8 + T-cells may then travel through BM breaks to enter the OLP epithelium.[15]

They considered MCs as the offenders in keratinocyte degeneration. Apart from TNF-α released from the MCs, another important substance is Heparin, which is known for its allergic stimulus. The part played by histamine in the pathogenesis of OLP is increased vasopermeability leading to sub-mucosal edema and antigen-induced T-cell proliferation. This thus explains the unique stuffing of lymphocytes in OLP. The cytotoxic lymphocytes thus initiated by the MCs end up causing keratinocyte apoptosis, and thus the characteristic civette bodies which are nothing but the degenerating keratinocytes seen in the epithelium.[15]

TNF-α also up-regulates CCR1 (cell surface receptors 1) expression by a variety of inflammatory cells (including T-cells and MCs). It also stimulates RANTES secretion by lesional T-cells. The RANTES attracts CCR + MCs and inflammatory cells into developing OLP lesion and triggers further MC degranulation.[16] Both TNF-α and chymase stimulate secretion of RANTES by T-lymphocytes, which end up activating MCs to release TNF-α and chymase. This cyclical activity may result in the chronicity of OLP.[10]

Conclusion

The current data supports the part played by MCs in the pathogenesis and progression of OLP and also provides proof for the interconnected action between MCs and T-lymphocytes in OLP. Moreover, OLP lesional T-cells have a dual role of both producing and secreting RANTES, which again acts on MCs, resulting in its degranulation. MC degranulation in OLP releases mediators such as TNF-α which up-regulates lesional T-cell and RANTES production. Thus, a cyclical mechanism may underlie the chronicity behind LP. Thus, the future treatment strategies should target RANTES, TNF- α and, of course, the MCs.

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