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REVIEW

Role of Myofibroblasts in Fibrotic Changes of Oral Lichen Planus: A Narrative Review

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Abstract

Background: Fibrotic changes of Oral Lichen Planus (OLP) are a possible underlying cause of trismus in OLP patients and might have a role in malignant progression of OLP as well. Research relates the fibrotic change in tissue to myofibroblasts. Thus, this study aimed to review the published articles regarding the role of myofibroblasts in fibrosis of OLP lesional tissues.

Methods: PubMed Central search engine and Google Scholar were used to gather information from full-text articles published between 2000 and 2025 on "myofibroblast and oral lichen planus and fibrosis." The most relevant articles were selected and studied.

Results: A total of 153 articles were identified. The authors reviewed articles with the most relevant topics and available full texts to determine the possible role of myofibroblasts in OLPFCs.

Conclusion: Based on information gathered from previous studies, it can be concluded that myofibroblasts play a role in the fibrotic changes associated with oral lichen planus. But further studies are required in order to make precise conclusions.

Keywords: Lichen Planus, Oral; Myofibroblast; Interleukins; fibroblasts; fibrosis

Introduction

Oral lichen planus (OLP) is a chronic inflammatory condition. It is characterized by the presence of white keratotic, red erosive or a combination of white and red lesionswhich are commonly found bilaterally on the buccal mucosa (1). The exact etiology of OLP is still not fully understood, but it is believed to involve an autoimmune response in which T lymphocytes are involved (2). Diagnosis typically requires a thorough clinical examination, and in clinically complex cases, a biopsy may be performed to rule out other conditions (3). Treatment options focus on managing symptoms and may include topical corticosteroids, immunosuppressive agents, or other therapies aimed at reducing the inflammation (4).

It is believed that his chronic inflammatory condition can lead to significant changes in the mucosal lining and may result in complications such as mucosal fibrosis, a phenomenon, a newly evolved subject, known as Oral lichen planus-induced fibrotic changes (OLPFCs) (5). OLPFCs and the subsequent reduced mouth opening can be challenging for patients as it has negative impact on the normal functions of the oral

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cavity and result in lower quality of life .Thus , a better understanding of the mechanisms involved in this process is essential (1, 5, 6).

The complex biological environment, including a variety of cytokines and chemokines produced in the OLP lesional tissues, can be responsible for the fibrotic process seen in OLP. We know that lymphocytes,a major component of OLP, are involved in the process of fibrosis in inflammatory lesions through producing fibroblast growth stimulating factors. Butstudies have proposed that only specific subtypes of Oral Lichen Planus (OLP) might be associated with submucosal fibrotic changes (7-9). However, a study showed that the thickness of the subepithelial fibrotic band was not related to clinical subtype and the severity of inflammatory infiltrate in OLP lesions (1).

Understanding the factors that regulate OLPFCs is crucial for developing preventive and therapeutic interventions for this condition (1, 5, 10). Fibrosis is usually characterized by an excessive accumulation of collagen in the connective tissue. It can result from various factors, including chronic infections, autoimmune reactions, allergic responses, radiation exposure, tissue damage, and natural aging (1, 10). Various cells and mechanisms are believed to be involved in this process, including mast cells and myofibroblasts. Research has shown that mast cells play a significant role in the initiation of fibrosis and are implicated in the pathogenesis of OLP. Tryptase, a substance released by mast cells, can lead to proliferation, chemotaxis, collagen synthesis, and migration in human fibroblasts (3, 7, 11). Myofibroblasts, which are specialized cells characterized by the presence of actin in their structure, play a crucial role in the body's response to injury. They may also contribute to pathological conditions associated with inflammation, such as fibrosis and cancer. Once formed, myofibroblasts act as the primary cells of connective tissue, responsible for collagen production (1, 12). Due to the unknown aspects of OLPFCs, this study aimed to review previous articles regarding the role of myofibroblasts in OLPFCs.

Methods

The PubMed Central search engine and Google Scholar were used to gather articles published within the period of 2000 to 2025 The keywords used were myofibroblast and fibrotic changes and oral lichen planus. A total of 153 articles were suggested. Articles with the most relevant topic and available full text were read by the authors in order to find an answer regarding the role of myofibroblasts in OLPFCs.

Discussion

The main goal of this study was to collect data on myofibroblasts and their possible role in the OLPFCs. This was achieved through the review of previously published research studies. It's important to highlight that there is currently limited research specifically focusing on the fibrotic changes in oral lichen planus and the role of myofibroblasts.

OLP Myofibroblasts

Interaction between epithelial cells and connective tissue plays a crucial role in various biological processes (6, 7). The typical histopathological features of OLP are defined as hydropic degeneration of the basal layer and band-like chronic lymphocytic inflammatory infiltrate in the subepithelial layer (13, 14). Research indicates that damage to epithelial cells triggers the release of various inflammatory mediators, including fibrogenic cytokines. A key characteristic of activated stromal cells is the adoption of smooth muscle features, particularly the formation of contractile fibers and the expression of alpha-smooth muscle actin, leading to their designation as

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myofibroblasts. The temporary acquisition of this phenotype is advantageous for normal tissue repair, as myofibroblasts contribute to remodeling that restores and preserves tissue integrity. However, if myofibroblasts persist, they can cause tissue stiffening and deformation (11, 15, 16) Jayaraj et al. (12) have demonstrated a phenotypic change in the stroma of oral squamous cell carcinoma, which is characterized by an increase in alpha-smooth muscle actin-positive myofibroblasts. They propose that the basement membrane typically acts as a barrier separating the epithelial and stromal components. However, invading tumor cells may breach this membrane, bringing the epithelial and stromal elements into proximity. This disruption leads to numerous stromal alterations, one of the most significant of which is the transformation of fibroblasts into myofibroblasts, facilitating tumor progression. Additionally, lymphocytes secrete factors such as TGF-β and interleukin-13, which enhance the activity of macrophages and fibroblasts, ultimately leading to fibrosis (17, 18). Fibroblasts have been identified as important contributors to various autoimmune diseases, including psoriasis, rheumatoid arthritis, and inflammatory bowel disease. These cells play a crucial role in the initiation, progression, and recurrence of these conditions by secreting inflammatory factors, presenting antigens, and facilitating immune memory. However, the specific subtypes of pathogenic fibroblasts and the underlying mechanisms related to oral lichen planus (OLP-fibroblasts) are still not well understood (19- 21).

An immunohistochemical study performed by Wang et al. (9) showed expression of α-SMA in CD31-negative spindle-shaped cells adjacent to the OLP mucosal epithelium, a feature which was not found in normal buccal mucosa. Although previous studies did not demonstrate the expression of α-SMA in the epithelium and subepithelial tissues of OLP mucosa, the presence of myofibroblasts in OLP lesions should be considered controversial (1). Shudo (8) reported a case of oral lichen planus associated with fibrotic changes, confirmed through Masson's trichrome staining. This article suggests that histopathological examination with specialized staining techniques can help evaluate the fibrotic changes induced by OLP. In the case reported by Shudo (8), the microscopic evaluation (hematoxylin and eosin stain) showed the characteristic histopathological features of OLP, including hydropic degeneration of the basal layer, interface band-like lymphocytic inflammatory infiltrate, hyperkeratosis, sharply demarcated rete ridges of epithelial processes, and Civatte bodies. Additionally, some fibrotic changes were noticed in the connective tissue. To further investigate these findings, Masson's trichrome staining was performed, which effectively highlighted the progression of distinct fibrosis, particularly in the areas surrounding the infiltrated lymphocytes within the subepithelial layer. These fibers showed negative results for Elastica van Gieson staining confirming the collagenous nature of the fibers (10). Wu et al (22) showed a significantly higher frequency of serum SMA in OLP patients compared to healthy controls.

In 2020, Shteiner et al. (5) were the first to document the presence of submucous fibrous bands in patients diagnosed with OLP. Their findings indicated that approximately one-third of studied OLP patients exhibited clinically palpable fibrotic bands within the buccal submucosa, with the majority of cases demonstrating bilateral involvement. The authors introduce mast cells as the major cell involved in this phenomenon. They believe fibrosis is a known complication in non-oral manifestations of lichen planus, such as lichen plano-pilaris, a subtype of lichen planus characterized by cicatricial alopecia of the scalp.

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A recent study conducted by Foroughi et al. (1) investigated the relationship between subepithelial fibrosis and clinical characteristics in patients with oral lichen planus (OLP). The researchers discovered that the thickness of subepithelial fibrosis does not correlate with the specific clinical subtype of OLP, the overall severity of the inflammatory response and the number of blood vessels present in the affected tissues. This finding is particularly significant, as it suggests that the mechanisms underlying fibrosis in OLP may operate independently of the inflammatory processes typically associated with the condition. Furthermore, the results of the study propose that the development of fibrosis and subsequent trismus in patients with oral lichen planus may be linked to specific cellular components, particularly mast cells and myofibroblasts. Understanding the role of these cell types could provide insights into the pathophysiology of oral lichen planus and potentially guide therapeutic strategies aimed at managing fibrosis and improving patient outcomes.

Numerous studies have highlighted the critical role of myofibroblasts in the progression of tumors. These specialized cells contribute to cancer development in several ways. First, they facilitate angiogenesis, the formation of new blood vessels, which is essential for supplying nutrients and oxygen to growing tumors. Overall, the involvement of myofibroblasts in these processes underscores their importance in cancer biology and potential as therapeutic targets (22-25). Xu et al (25) and other researchers propose that myofibroblasts play a crucial role in the increased angiogenesis observed in oral lichen planus, potentially facilitating its malignant transformation (26-28). Research findings indicate that OLP myofibroblasts produce substantial quantities of interleukin-6 (IL-6) when exposed to inflammatory factors. Previous reports have indicated that chronic inflammation may provoke excessive cellular proliferation and the activation of various cellular processes. Research suggests that the application of anti-IL-6 receptor antibodies, along with targeted intervention against these myofibroblasts, may represent novel therapeutic strategies to effectively inhibit the malignant transformation associated with OLP (19, 29, 30). According to Wang et al. (9), myofibroblasts secrete pro-inflammatory cytokines, including interleukin (IL)-6, IL-8, and tumor necrosis factor-alpha (TNF-α), in response to stimuli such as Porphyromonas gingivalis lipopolysaccharides. Therefore, dentists are encouraged to educate and support OLP patients in maintaining proper oral health. Clinicians are encouraged to report cases of oral lichen planus that exhibit signs of reduced mouth opening or palpable fibrotic bands related to OLP lesions. Additionally, pathologists should document any instances of oral lichen planus accompanied by subepithelial fibrosis or hyalinization. This documentation will enhance our understanding of the OLP induced fibrotic changesin the future.

Conclusion

Based on previous studies, it can be concluded that myofibroblasts might play a significant role in the development of fibrosis and the formation of subepithelial fibrotic bands in oral mucosal tissues affected by lichen planus.

Conflict of Interests: The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial, in this article

References

1. Foroughi A, Aminzadeh A, Kamranzadeh M. Oral Lichen Planus-induced Fibrotic Changes. A pilot Retrospective Study. cofs 2025; 3 (4) :54-59
2. Aminzadeh A, Jahanshahi G, Ahmadi M. A retrospective comparative study on clinico-pathologic

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[DOI: 10.66224/cofs.4.3.2]

features of oral lichen planus and oral lichenoid lesions. Dent Res J (Isfahan). 2013;10(2):168-72.

3. Jahanshahi G, Aminzadeh A. A histochemical and immunohistochemical study of mast cells in differentiating oral lichen planus from oral lichenoid reactions. Quintessence Int. 2010;41(3):221-7.
4. Zoodashena P, Hoveida L, Aminzadeh A. A Comparative Study on the Prevalence of HPV16 Virus in Oral Lichen Planus and Oral Lichenoid Lesions Using PCR Technique (Persian). Jundishapur Journal of Medical Sciences. 2022; 21(5):628-637.
5. Shteiner M, Kleinman S, Shuster A, Raiser V, Ianculovici C, Rachima H, et al. Submucosal Fibrotic Bands in Oral Lichen Planus: A Clinico-Pathological Investigation of a Newly Described Phenomenon. Head Neck Pathol. 2021;15(2):395-401.
6. Scott B, Butterworth C, Lowe D, Rogers SN. Factors associated with restricted mouth opening and its relationship to health-related quality of life in patients attending a Maxillofacial Oncology clinic. Oral Oncol. 2008;44(5):430-8.
7. Hasegawa M, Fujimoto M, Takehara K, Sato S. Pathogenesis of systemic sclerosis: altered B cell function is the key linking systemic autoimmunity and tissue fibrosis. J Dermatol Sci. 2005;39(1):1-7.
8. Shudo A. Histopathological specialized staining of oral lichen planus-induced fibrotic changes and surgical treatment of associated restricted mouth opening: a case report. Bull Natl Res Cent 2021;45(1):56.
9. Wang L, Yang Y, Xiong X, Yu T, Wang X, Meng W, Wang H, Luo G, Ge L. Oral lichen-planus-associated fibroblasts acquire myofibroblast characteristics and secrete pro-inflammatory cytokines in response to Porphyromonas gingivalis lipopolysaccharide stimulation. BMC Oral Health. 2018;18(1):197.
10. Wynn TA. Cellular and molecular mechanisms of fibrosis. J Pathol. 2008 Jan;214(2):199-210.
11. Conti P, Caraffa A, Mastrangelo F, Tettamanti L, Ronconi G, Frydas I, et al. Critical role of inflammatory mast cell in fibrosis: Potential therapeutic effect of IL-37. Cell Prolif. 2018;51(5):e12475.
12. Jayaraj G, Sherlin HJ, Ramani P, Premkumar P, Natesan A. Stromal myofibroblasts in oral squamous cell carcinoma and potentially malignant disorders. Indian J Cancer. 2015;52(1):87-92.
13. Saharkhiz A, Aminzadeh A, Yahyaabady R. A Histomorphology Comparison of Saw-Tooth Shaped Rete Ridge Between Oral and Cutaneous Lichen Planus. Enviro Dental Journal 2022; 4(1): 20-24
14. Aminzadeh A, Razavi S M, Sabeti Sanat A. Immunohistochemical Evaluation of Expression of CK19 Premalignant Indicator in Oral Lichenoid Reaction (OLR) Compared to Oral Lichen Planus (OLP), Oral Squamous Cell Carcinoma (OSCC) and Normal Oral Mucosa. J Isfahan Dent Sch 2018; 14(1): 17-28
15. She G, Ren YJ, Wang Y, Hou MC, Wang HF, Gou W, et al. K_{Ca}3.1 Channels Promote Cardiac Fibrosis Through Mediating Inflammation and Differentiation of Monocytes Into Myofibroblasts in Angiotensin II - Treated Rats. J Am Heart Assoc. 2019;8(1):e010418.
16. Croft AP, Campos J, Jansen K, Turner JD, Marshall J, Attar M, et al. Distinct fibroblast subsets drive inflammation and damage in arthritis. Nature. 2019;570(7760):246-251.
17. Hewitt RJ, Pearmain L, Lyka E, Dickens J. Epithelial damage and ageing: the perfect storm. Thorax. 2025;80(9):668-675.
18. Burgoyne RA, Fisher AJ, Borthwick LA. The Role of Epithelial Damage in the Pulmonary Immune Response. Cells. 2021;10(10):2763.
19. Buechler MB, Pradhan RN, Krishnamurty AT, Cox C, Calviello AK, Wang AW, et al. Cross-tissue organization of the fibroblast lineage. Nature. 2021 May;593(7860):575-579.
20. Otranto M, Sarrazy V, Bonté F, Hinz B, Gabbiani G, Desmoulière A. The role of the myofibroblast in tumor stroma remodeling. Cell Adh Migr. 2012;6(3):203-19.
21. Zheng M, Hu Z, Mei X, Ouyang L, Song Y, Zhou W, et al. Single-cell sequencing shows cellular heterogeneity of cutaneous lesions in lupus erythematosus. Nat Commun. 2022;13(1):7489.
22. Wu KM, Wang YP, Lin HP, Chen HM, Chia JS, Sun A. Modulation of serum smooth muscle antibody levels by levamisole treatment in patients with oral

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[DOI: 10.66224/cofs.4.3.2]

lichen planus. J Formos Med Assoc. 2013;112(6):352-7.

23. Pourreyron C, Dumortier J, Ratineau C, Nejjari M, Beatrix O, Jacquier MF, et al. Age-dependent variations of human and rat colon myofibroblasts in culture: Influence on their functional interactions with colon cancer cells. Int J Cancer. 2003;104(1):28-35.
24. Malekzadeh H, Robati M, Yousefimanesh H, Ghafourian Boroujerdnia M, Nadripour R. Salivary Interferon Gamma and Interleukin-4 Levels in Patients Suffering from Oral Lichen Planus. Cell J. 2015;17(3):554-8.
25. Xu XH, Liu Y, Feng L, Yang YS, Liu SG, Guo W, et al. Interleukin-6 released by oral lichen planus myofibroblasts promotes angiogenesis. Exp Ther Med. 2021;21(4):291.
26. Karakasheva TA, Lin EW, Tang Q, Qiao E, Waldron TJ, Soni M, et al. IL-6 Mediates Cross-Talk between Tumor Cells and Activated Fibroblasts in the Tumor Microenvironment. Cancer Res. 2018;78(17):4957-4970.
27. Nagasaki T, Hara M, Nakanishi H, Takahashi H, Sato M, Takeyama H. Interleukin-6 released by colon cancer-associated fibroblasts is critical for tumour angiogenesis: anti-interleukin-6 receptor antibody suppressed angiogenesis and inhibited tumour-stroma interaction. Br J Cancer. 2014;110(2):469-78.
28. Liao YP, Schaue D, McBride WH. Modification of the tumor microenvironment to enhance immunity. Front Biosci. 2007;12:3576-600.
29. Cheng J, Liu J, Zhu Y, Yang J, Geng Y, Fan Y. Single cell dissection reveals SFRP2+ fibroblasts amplifying inflammatory responses in oral lichen planus. Front Immunol. 2025;16:1553963.
30. Kaur J, Jacobs R. Proinflammatory cytokine levels in oral lichen planus, oral leukoplakia, and oral submucous fibrosis. J Korean Assoc Oral Maxillofac Surg. 2015;41(4):171-5.

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