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ORIGINAL RESEARCH

A Clinicohistopathologic Study and Probable Mechanism of Pigmentation in Oral Lichen Planus

Rubina Anjum, Jasmin Singh, Shailesh Kudva

ABSTRACT

Aim: Probable mechanism of pigmentation in oral lichen planus which is associated with anxiety disorder and its relation to gamma aminobutyric acid whose imbalance in brain occurs during stress and strain.

Materials and methods: A cross-sectional study comprising of 33 cases of clinically diagnosed oral lichen planus was conducted. Ethical clearance and informed consent was obtained. Detailed history was recorded and clinical examination was conducted. All patients were subjected to thorough routine blood, urine and stool examination for any systemic conditions. Clinical photographs and biopsies were obtained. The biopsy specimens were subjected to hematoxylin and eosin and periodic acid Schiff's reagent staining.

Results: Histopathological features of lichen planus include hyperkeratosis, liquefaction degeneration of stratum basale and subepithelial band of chronic inflammatory cells. Lichen planus is related to anxiety as predisposing factor.

Conclusion: Due to excitation of melanocytes lichen planus are seen with pigmentation.

Keywords: Lichen planus, Pigmentation, Gamma aminobutyric acid, Histopathology.

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INTRODUCTION

Lichen planus is a relatively common inflammatory disease of the skin and mucous membrane. The mucosal surface most frequently involved is that of the oral cavity. Lichen planus was first described to some extent in 1869 by Erasmus Wilson[1] who also recorded oral lesions in three out of 50 patients, the first report of oral involvement in the disease. However, despite many subsequent studies the etiology and pathogenesis of lichen planus still evade elucidation.

Lichen planus has been reported to occur in the general population at a rate of 0.9 to 1.2%. Both the male and female are equally affected and majority of cases occur in patients between the age of 30 and 60 years. The disease usually occurs in males from the ages of 40 to 49 years, and in females from the age of 50 to 59 years and it is seen in all races.[2-8]

Its etiology is unknown but is considered as psychosomatic disorder. Stress and anxiety have frequently been mentioned as possible factors related to the development of oral lichen planus.[1,9,10]

Pigmentation is frequently observed in most of the lichen planus patient. Cawson[11] on pigmentation in lichen planus here stated the degenerative changes in the basal keratinocytes frequently lead to pigmentary incontinence. The melanin pigment is ingested by macrophages in the superficial corium and can result in an area of brownish pigmentation in the mucosa which persists long after the lichen planus has resolved.

Various authors[12] have said that pigmentation in mucosal lesion have got defence mechanism as melanin has the capability to bind to free radials and it has been observed that by virtue of this function it protect the mucosa from the harmful effect of toxic substances which penetrates the mucosa and that beyond the threshold level toxin can destroy the pigment system.

Our study is concerned with the probable mechanism of pigmentation in oral lichen planus which is associated with anxiety disorder and its relation to gamma aminobutyric acid (GABA) whose imbalance in brain occurs during stress and strain.

OBJECTIVES

1. To investigate the histopathological pattern of oral lichen planus.
2. To investigate the pattern of clinical involvement of lichen planus in the oral cavity.
3. To investigate the prevalence of premalignant changes.
4. To investigate the probable mechanism of pigmentation in oral lichen planus, which is associated with anxiety disorder and its relation to GABA whose imbalance in brain occurs during stress and strain.

MATERIALS AND METHODS

A cross-sectional study comprising of 33 cases of clinically diagnosed oral lichen planus was conducted. Ethical clearance was obtained from the institutional review board. Informed consent was taken from all the participants of the study.

Detailed history was recorded on a specially designed proforma. Clinical examination was conducted. All patients

were subjected to thorough routine blood, urine and stool examination for any systemic conditions.

The diagnostic criteria for oral lichen planus consisted of (Figs 1 and 2):

1. Lesions consisting of radiating white or gray velvety patches.
2. Lesions arrange in typical reticular patches or streaks.
3. Plaque-like lesions showing radiating striae at the periphery.
4. Frankly ulcerative or erosive lesions, irregular in size and shape, appearing raw and painful.
5. Surface of lesion smooth on palpation.

Clinical photographs and biopsies were obtained. The biopsy specimens were subjected to the following:

1. Hematoxylin and eosin (H&E) staining.
2. Periodic acid Schiff's (PAS) reagent staining.

All slides were examined under the light microscope using ×10, ×40 and ×100 powers.

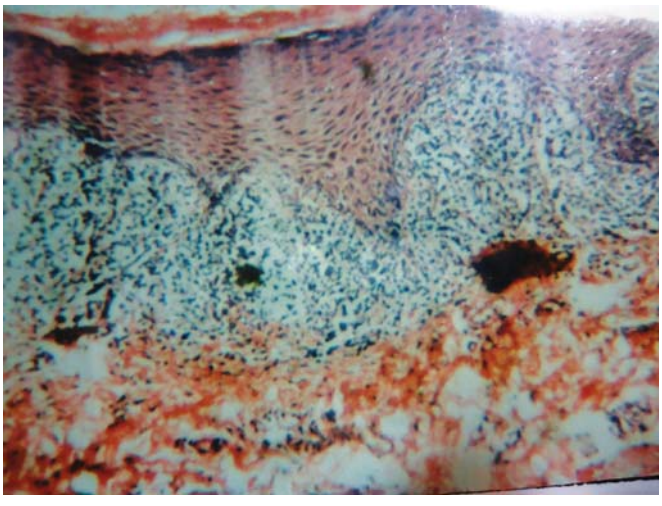

Fig. 1: Photomicrograph showing classical features of oral lichen planus showing hyperkeratosis, saw tooth rete pegs, subepithelial bands of inflammatory infilterate and basal cell degeneration (H&E ×10)

RESULTS

Majority of the patients were in the age group of 40 to 59 years followed by five patients each in the age group of 2nd and 3rd decade and three in the 6th decade. The youngest patient was 21 years old and oldest patient was 67 years.

Males and females are almost equally affected since 16 males were affected against 17 females and M:F ratio is 1:1.1.

The buccal mucosa was the site most frequency involved (81.8%). The oral lesions on the buccal mucosa (Fig. 3) reported here were bilateral in almost all the cases except few and were mostly confined to the middle part of the cheek along the occlusal plane. Linear pattern was seen maximally in 18 cases (54.5%). Four cases (12.12%) showed hyperorthokeratosis and six cases showed presence of both hyperparakeratosis and hyperorthokeratosis. The hyperplastic epithelium was seen in 18 cases, atrophy in eight sections, and both hyperplastic and atrophic in two cases and the epithelium was found to be normal in five cases. Focal degeneration of basal cell degeneration occurred in only 59% cases of oral lichen planus. Broad and Blunt rete-pegs were noticed in 10 section (30.3%) while generalized flattening was noticed in seven section (21.2%) and two sections showed normal rete-pegs. Plasma cells were noticed in great numbers within the inflammatory infiltrate.

The melanin pigmentation was seen in the basal layer 18 sections and its extension in the upper part of lamina propria was seen in 15 sections. Thirty-two patients out of 33 patients (16 males and 16 females) gave history of anxiety (96.97%). Only one female patient (3.03%) did not show anxiety disorder.

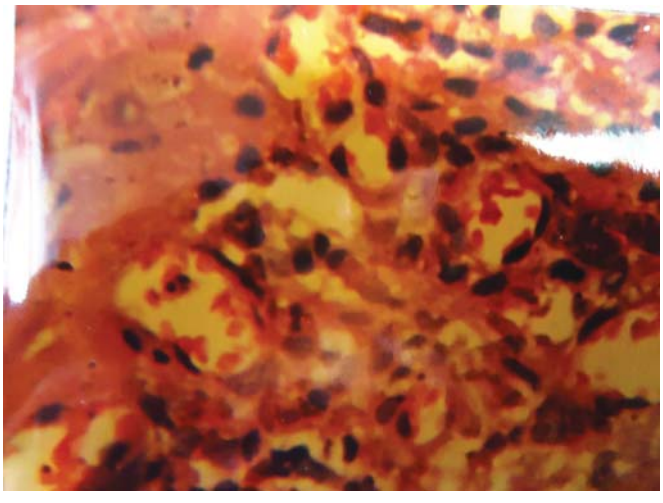

Fig. 2: Photomicrograph showing melanin pigmentation at the upper part of connective tissue

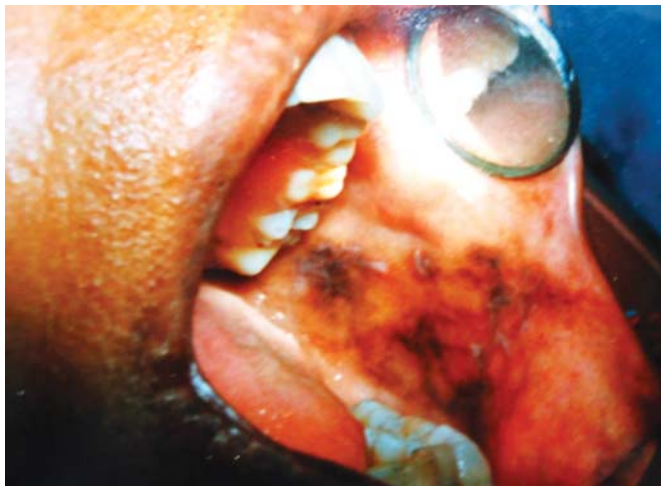

Fig. 3: Pigmentation at the area of buccal mucosa

DISCUSSION

It is well known that lichen planus is a chronic complex mucocutaneous disease of unknown etiology, uncertain pathogenesis and diverse histopathology.

A perusal of the medical and dental literature reveals that lichen planus may affect patients of any age from 6 months to 80 years. Pussey[13] has described a case of lichen planus in an infant under 6 months of age. Laufer and Kuffer[7] found that majority of patients involved were between the age of 30 and 60 years while Cooke[14] in his analysis of 50 cases of oral lichen planus reported his oldest patients to be a male aged 80 years and youngest, a female, aged 21 years. Shklar and McCarthy[15] in their study of 100 cases of oral lichen planus reported that the age of the patients varied from 13 to 78 years. Lichen planus has been reported by many workers like Tompkins et al,[16] Banoczy,[17] Lacy et al[5] who are also in agreement that lichen planus predominantly is a disease of the middle aged and elderly with ages ranging from 30 to 70 years. Tyldesley[18] in there study of 60 cases reported that the age of patients presenting with oral symptoms covers a wide range from 30 to 78 years. Our study is in agreement with these workers since majority of the patients were in the age group of 40 to 59 years followed by five patients each in the age group of 2nd and 3rd decade and three in the 6th decade. The youngest patient was 21 years old and oldest patient was 67 years.

In our study males and females are almost equally affected since 16 males were affected against 17 females and M:F ratio is 1:1.06. This finding of ours is in agreement with Moschella et al[8] and Shafer et al[19] who said that there is no dramatic sex predominance. Many[5,6,20,21] have reported female predilection, however, some investigators like Sehgal[22] and Shklar and McGrathy[15] found males to be affected more than females. Thus, there is contrasting evidence in the literature regarding the sex incidence of the disease.

From the accumulated data in the literature, it is evident that the buccal mucosa is the commonest site affected. This has been stated by workers like Jungell,[23] Andreasen,[9] Shklar and McGrathy,[15] Sehgal.[22] In our study too, the buccal mucosa was the site most frequency involved (81.8%). The oral lesions on the buccal mucosa reported here were bilateral in almost all the cases except few and were mostly confined to the middle part of the cheek along the occlusal plane. This may be due to the fact that the buccal mucosa in his region is subjected to trauma and irritation more often from the buccal cusps of the upper posterior teeth and thereby acting as a biologically fertile region for the development of lichen planus.

In this study, gingival was the second most affected site and was found to be in agreement with the finding of Shklar and Mcgrathy.[15]

The tongue was found to be involved in five cases (15.2%). This incidence is lower than studies by Andreasen[9] (72%), Shklar and McCarthy[15] (65%) but higher than that reported by Sehgal[22] (8.19%). The floor of the mouth was found to be involved in only one case (3.03%). This is an agreement with the finding of Andreasen[9] and Shklar and McGrathy[15] who reported an incidence of less than 10%.

Other sites involved in this study are retromolar areas (3.03%), hard palate (3.03%), labial mucosa (3.03%).

The oral lesion of lichen planus may take various clinical forms. Andreasen[9] in his extensive study of 115 cases observed reticular patterns of the disease to be the most common (49 cases) followed by atrophic variety (24 cases), ulcerative (23 cases), plaque (14 cases) and a few cases with other types.

Silverman and Griffith noted that the erosive form of the disease was the most common one. Cooke[14] classified the oral lesion of the lichen planus as linear, discrete-papular, confluent-papular, reticular, annular, pigmented, vesiculosus, bullous atrophic or erosive. Commonest was the linear pattern. The results of our study are in agreement with Cooke[14] study since linear pattern was seen maximally in 18 cases (54.5%).

Mild dysplastic epithelium is seen in lichen planus cases in our study. This is in agreement with various workers like Krutchkoff et al,[24] Katz,[25] Daftary et al,[26] Holmstrup.[27]

Heyden et al[28] in 1947 remarked that oral lichen planus lesion are characterized by increase in parakeratosis. McClatchey et al[29] (1975) reported the occurrence of parakeratosis in 60% of his cases while a high 86% was recorded by Andreasen.[30] The finding of this study is in agreement with these investigators since hyperparakeratosis was recorded in maximum number of cases (13 cases). While four cases (12.12%) showed hyperorthokeratosis and six cases showed presence of both hyperparakeratosis and hyperorthokeratosis.

Acanthosis has been reported in lichen planus by various workers like Andreasen,[9] Heyden et al,[28] Shklar and Meyer.[31] Mild to sever acanthosis was seen in 16 cases (48.5%).

The liquefaction degeneration of the stratum basale is said to be a consistent histological finding in oral lichen planus. It has been reported in cases of lichen planus by EL-Labban and Kramer,[32] Shafer et al[19] and Scully.[3] In this study, focal degeneration of basal cell degeneration occurred in only 59% cases of oral lichen planus.

Meyer and Shklar[31] (1961) had the opinion that the rete-pegs may present some elongation but the typical 'saw

toothed' configuration seen in skin lesions is usually absent in oral lesions. In this study four cases (12.1%) showed 'saw toothed' rete-pegs while five sections (15.2%) showed elongation of the pegs. Broad and blunt rete-pegs were noticed in 10 sections (30.3%) while generalized flattening was noticed in seven section (21.2%) and two sections showed normal rete-pegs.

Komori et al[33] (1986) noticed the extreme thinning for the basement membrane in area where the inflammatory cells infiltrated the subepithelial connective tissue. Hashimoto et al[34] have also observed disruption of the basement membrane by the immigrating inflammatory cells. In the present study, the changes in the character of the basement membrane have been clearly demonstrated by PAS technique. In few instances, it is presented as thick while in others it appears as a continuous thin linear configuration. Plasma cells were noticed in great numbers within the inflammatory infiltrate. Diffuse extension of the inflammatory and the presence of substantial amount of plasma cell within the infiltrate are said to be disqualifying feature of lichen planus according to Krutchkoff et al.[35]

Probable Mechanism of Pigment in Oral Lichen Planus which is associated with Anxiety Disorder

In this study, the melanin pigmentation was seen in the basal layer 18 section and its extension in the upper part of lamina propria was seen in 15 sections. Murti et al[36] reported lichen planus with pigment in 99 patients out of 117 in the Ernakulam district, Kerala, India. Ten out of the 11 oral lichen planus cases associated with pigmentation remained unchanged and they suggest that pigmentation may be reactive rather than suggestive of impending resolution of the lesion. In our study number of patients showing pigmentation are 23 (69.7%) out of 33 patients, 30.3% did not show any pigmentation.

A relationship of lichen planus with stress and anxiety has often been quoted and neurogenic basis suggested. Wilson[1] considered that lichen planus was associated with hysteria, anxiety or depression. Andreasen et al[9] found that 47% of patients gave a history reported that there is statistically significant difference in mental disturbance between oral lichen planus. McCartan[37] reported that the sample profile showed slight tendency toward anxiety. Our study is also in agreement with these workers as 32 patients out of 33 patients (16 males and 16 females) gave history of anxiety (96.97%). Only one female patient (3.03%) did not show anxiety disorder.

In our study, we are relating pigmentation of the oral lichen planus with the anxiety disorders. It has been reported that GABA imbalance occurs in brain tissue during stress and anxiety. The anxiety drugs potentiate the neural inhibition that is mediated by GABA. Although possible action that lead to increased release of GABA cannot be excluded but it potentiate the action of GABA on neuron at all levels of neuraxis. As a result of the detection and characterization of specific binding sites for antianxiety, a substance body of biochemical evidence has accumulated that suggest a close molecular association between the sites of action GABA and the antianxiety drugs. This imbalance of GABA which occurs in anxiety disorder in all probability pass through cranial nerve and excites the production of melanocytes, this results in excessive deposition of pigmentation in oral lichen planus.

Ralf Dammer et al[38] suggested that Schwann cells and melanocytes are both neural crest derived and are somewhat difficult to distinguish by means of immunohistochemistry. If there is severe reaction of GABA, then lymphocytes which are accumulated in the connective tissue destroy the melanocytes resulting into erosive planus. Hence, in erosive lichen planus there is no pigmentation. In case of bullous lichen planus the occurrence of which is about 0.5% of total oral lichen planus cases, the irritation of the acid is so severe that it destroys the nerve cell similar to neurotropic virus, resulting into bullae formation.

Further elaborate studies about pigmentation in oral lichen planus should be carried out to confirm our hypothesis.

CONCLUSION

Majority of the patients affected are in their 4th and 5th decade. The characteristic triad of histopathological features of lichen planus includes hyperkeratosis, liquefaction degeneration of stratum basale and subepithelial band of chronic inflammatory cells. Lichen planus is related to anxiety as predisposing factor. Due to excitation of melanocytes lichen planus are seen with pigmentation.

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ABOUT THE AUTHORS

Rubina Anjum

Associate Professor and Head, Department of Oral Pathology, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir India

Jasmin Singh (Corresponding Author)

Registrar, Department of Oral Pathology, Indira Gandhi Government Dental College, Jammu, Jammu and Kashmir, India, e-mail: jasmin.ravneet@gmail.com

Shailesh Kudva

Principal, Professor and Head, Department of Oral Pathology Rajasthan Dental College, Jaipur, Rajasthan, India