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ORIGINAL PAPER

Submucosal Fibrotic Bands in Oral Lichen Planus: A Clinico-Pathological Investigation of a Newly Described Phenomenon

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Abstract
Fibrosis is a recognized complication of chronic inflammatory conditions, which has not yet been described in oral lichen planus. To describe characteristics of submucosal fibrotic bands in oral lichen planus. Prospective study. Patients with biopsy confirmed lichen planus were included. Clinical examination recorded fibrotic bands, mouth opening, vestibular depth loss, gingival recessions adjacent to band, lichen subtypes, areas of affected mucosa, extra-oral manifestations. Patients completed the Chronic Oral Mucosal Disease Questionnaire, with additional questions regarding stiffness, restricted opening, symptom frequency, time from diagnosis of lichen, co-existing medical conditions. 73 patients were included, 14 M, 59 F, age 28–84 (mean 61) years. Buccal fibrous bands were palpated in 22 (30.1%), 13 (59%) were bilateral. Self-reported restricted opening/stiffness were significantly associated with fibrous bands (36% Vs. 11% in controls, p = 0.02). Mouth opening less than 40 mm was recorded in only 2 (9%) with bands, none in controls. Reduced vestibular depth was significantly associated with bands (11 (50%) Vs 3 (6%) in controls, p = 0.0001).Gingival recessions adjacent to bands were recorded in 3 (13.6%). No association was demonstrated between fibrous bands and erosive lesions, extra oral involvement, smoking, age, visual analogue scale, quality of life questionaire and disease duration. Histological evaluation of one case each with and without band and control showed increased mean width of connective tissue. Submucous fibrous band is first described in the present study. It is common in oral lichen planus, may lead to feeling restricted mouth opening, stiffness, loss of vestibular depth and adjacent gingival recession.

Keywords Oral lichen planus · Fibrosis · Quality of life

Introduction

Lichen planus is a T cell-mediated chronic inflammatory mucocutaneous disease. The exact cause of which is still undetermined [1].

It is a common condition, with a mean prevalence of 1.5% [2].

Clinical manifestations of OLP include reticular, atrophic and erosive lesions [3].

The presence of fibrosis in the form of submucosal fibrotic bands (SFB) in the buccal mucosa of OLP patients has not yet been reported in the literature, although it has been the author's impression that it is a common finding.

The study aims to present the clinical and histologic features of SFB in OLP, its frequency, characterization of the patients, and its clinical significance.

Subjects and Methods

In this prospective study, subjects were recruited between December 2012 and May 2013 at the department of oral and maxillofacial surgery, in Tel-Aviv Sourasky Medical Center.

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The institutional ethics committee reviewed and approved the study (0587-12-tlv). Eligible patients signed written informed consent forms.

Inclusion criteria included oral lesions clinically consistent with OLP, biopsy confirmation of the diagnosis according to the modifications for WHO 2003 criteria [4], and age above 18 years.

The exclusion criteria included medical conditions that may present with features similar to OLP (graft versus host disease, systemic or discoid lupus erythematosus).

A licensed oral pathologist (IK) was responsible for both the microscopic diagnosis in all cases, as well as clinical treatment and follow-up.

Clinical examination was conducted to record the presence of fibrotic bands, mouth opening, loss of vestibular depth, presence of gingival recessions in proximity to the bands, subtype of OLP, areas of the mucosa affected and extra-oral manifestations of lichen planus.

Patients also completed the Chronic Oral Mucosal Disease Questionnaire (COMDQ). Several additional questions added to the original questionnaire included subjective feeling of stiffness or restriction in mouth opening, a visual analogue scale (VAS), frequency of symptoms, demographic information, co-existing medical conditions, and the time from diagnosis of OLP.

The COMDQ is a new oral mucosal disease quality of life (QOL) instrument containing 26 items. The items are grouped according to clinical judgment into four domains: pain and functional limitation, medication and treatment, social and emotional status and patient support. For each questionnaire, patients answered by using a Likert-type response coded scale. Response options were: not at all = 0, slightly = 1, moderately = 2, considerably = 3, extremely = 4. Responses were added to give a total potential score of 104.

Histological analysis of one specimen of a fibrotic band from a single patient was performed, from an area in which the patient complaint was of local discomfort.

Statistics

The statistical analysis was performed by a medical statistician. The continuous variables were tested for normality using the Kolmogorov–Smirnov test, the difference between the groups was tested using t-test for normality or Mann–Whitney test. The association between categorical variables was tested using Fisher's exact test or Chi squared test (SPSS version 15).

Fig. 1 Submucosal fibrotic band in left buccal mucosa (arrowes), Wickham's striae present

Fig. 2 Submucosal fibrotic band in left buccal mucosa (arrowes), hyperkeratotic OLP lesions present

Results

The study population included 73 consecutive patients, recruited during regular follow up appointments at the oral and maxillofacial surgery department. There were14 males and59 females, age: 28–84 years (mean 61).

SFB in the buccal mucosa were palpated in 30.13% (22) of study participants (Figs. 1, 2, 3, 4), more frequently in a bilateral (59% than a unilateral presentation.

The SFB group included two males and 20 females, with a mean age of 66 years.

The reported feeling of restriction in mouth opening was significantly associated with SFB in comparison to patients without SFB (36% Vs 11%, respectively, p = 0.02). Reduced measured mouth opening of less than 40 mm was

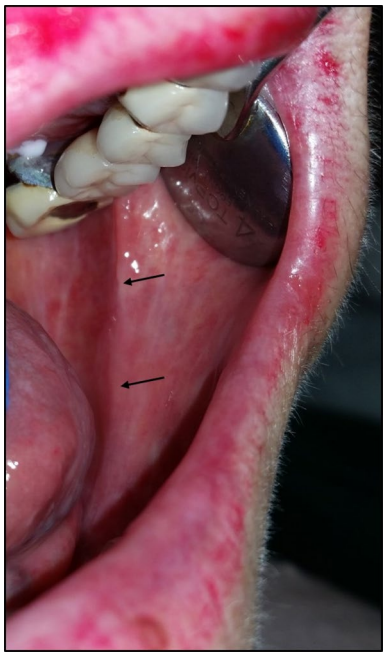

Fig. 3 Left buccal mucosa with submucosal fibrotic band

Fig. 4 Two fibrotic bands are present in left buccal mucosa (arrowes), an atrophic OLP lesion (dotted arrow)

recorded in only two patients (9%) with SFB, and in none of the patients in the control group (Table 1).

A significant difference in the frequency of flattening of the vestibule in dentate areas (reduced vestibular depth) was recorded in 11 (50%) of the SFB patients, in comparison with 3 (6%) in the control group ($p = 0.0001$).

Gingival recessions in the areas adjacent to the SFB were recorded in 3 (13.6%) subjects.

No association was found between SFB and the following parameters: erosive lesions, extraoral involvement, smoking, age, VAS, COMDQ, and duration of the disease since first diagnosed (Table 2).

Histological findings from 2 cases with and without SFB are presented in (Figs. 5, 6). Since the inclusion criteria for the study required that patients have both a clinical and a histological diagnosis of OLP, and because removal of the bands (to perform microscopic analysis) was not considered clinically justified, this study only presents histopathological results for 2 cases, one with and one without band formation, both from the buccal mucosa.

In the control case fibrotic band was not present and the biopsy was performed for diagnosis. In the case with SFB the biopsy was done in the band area since the patient pointed to the band area as a source of significant discomfort when opening wide. Using the image analysis function (Olympus, Cellsens), measurement of the width of the connective tissue (basement membrane to adipose tissue layer) in three locations along the lining was obtained. The mean width of connective tissue in the case with SFB (Fig. 5) and the control case (Fig. 6) was 586 µm and 444 µm, respectively. These findings suggest there may be some increase in width of the fibrous tissue adjacent to the mucosa in the band area; however, biopsies from the band area were not routinely performed, as there was no clinical indication to do so, thus, information is limited.

Discussion

Approximately a third of randomly selected consecutive OLP patients exhibited clinically palpable fibrotic bands in the buccal submucosa. Involvement was bilateral in the majority, but not in all cases. Mast cells, which have a recognized role in the pathogenesis of OLP, also have a recognized role in initiating fibrosis in various diseases in various organs, thus this pathway provides a possible biological explanation for the clinical finding of SFB described in the present study [5, 6].

Fibrosis is a known complication in non-oral areas of the body in lichen planus patients. Genital lichen planus has been known to cause vulval scarring and vaginal stenosis that has an impact on sexual function [7]. Lichen plano-pilaris is considered a form of lichen planus, and is characterized by cicatricial alopecia of the scalp [8–10]. Esophageal stricture [11], cicatricial conjunctivitis and obstruction of the lachrymal canal have also been reported in lichen planus patients [12]. SFB, the oral equivalent of fibrosis in OLP has never been described before in the literature, although it seems to be a common finding in the present study group. The finding of SFB was strongly associated with the reported feeling of restriction in mouth opening, causing some dysfunction, and with the observation of loss of vestibular depth in these patients. However, using the COMDQ quality of life instrument, no significant differences were found between OLP patients with or without SFB. This can be explained by the lack of specific questions in the COMDQ related to the presence of SFB. Further investigations may be required

Table 1 Clinical characteristics of oral mucosal findings in the study population

Patient no.	Age/gender	*Presence of SFB*[a]	Uni/bilateral SFB[a]	Restricted mouth opening[a]	Reduced vestibular depth[a]	Gingival recessions
1	74,F	N		N	N	
2	69, F	N		N	N	
3	51,F	N		N	Y	
4	62,F	N		N	N	
5	42,F	y	Bilateral	Y	Y	N
6	54,F	y	Unilateral	N	Y	y
7	61,F	N		N	N	
8	75,F	N		N	N	
9	66,F	N		N	N	
10	72,M	N		N	N	
11	49,M	Y	Bilateral	N	N	N
12	54,F	N		N	N	
13	80,F	N		N	N	
14	76,F	Y	Bilateral	Y	Y	N
15	60,M	N		N	N	
16	72,M	N		N	N	
17	73,M	N		N	N	
18	65,F	N		N	N	
19	72,F	N		N	N	
20	41,M	N		Y	Y	
21	43,F	N		N	N	
22	61,F	N		N	N	
23	63,M	N		Y	N	
24	28,F	Y	Bilateral	Y	N	N
25	83,F	Y	Bilateral	N	N	N
26	38,M	N		N	N	
27	62,F	Y	Bilateral	N	Y	N
28	60,F	Y	Unilateral	N	N	N
29	67,F	N		Y	N	
30	43,M	Y	Unilateral	Y	N	N
31	60,F	N		N	N	
32	40,F	N		N	N	
33	62,F	N		N	N	
34	65,F	N		N	N	
35	53,F	N		N	N	
36	57,F	N		N	N	
37	38,F	N		N	N	
38	32,F	Y	Bilateral	N	N	N
39	74,F	Y	Bilateral	N	Y	N
40	51,F	Y	Unilateral	Y	Y	N
41	75,F	N		N	N	
42	35,M	N		N	N	
43	74.F	Y	Unilateral	Y	Y	N
44	80,M	N		N	N	
45	66,M	N		N	Y	
46	53,F	Y	Bilateral	N	Y	N
47	56,F	N		N	N	
48	41,F	N		N	N	
49	69,F	N		N	N	

Table 1 (continued)

Patient no.	Age/gender	*Presence of SFB*[a]	Uni/bilateral SFB[a]	Restricted mouth opening[a]	Reduced vestibular depth[a]	Gingival recessions
50	73,F	Y	Unilateral	N	Y	N
51	56,F	N		N	N	
52	57,F	Y	Unilateral	N	Y	N
53	68,F	N		N	N	
54	48,F	N		Y	N	
55	65,F	N		Y	N	
56	84,F	N		N	N	
57	67,F	Y	Bilateral	N	Y	y
58	75,F	Y	Bilateral	Y	N	N
59	74,F	N		N	N	
60	62,F	N		N	N	
61	57,F	N		N	N	
62	35,F	Y	Unilateral	N	N	N
63	51,F	N		N	N	
64	83,F	Y	Bilateral	N	N	N
65	57,F	N		N	N	
66	65,F	Y	Unilateral	Y	Y	y
67	74,M	N		N	N	
68	74.,F	N		N	N	
69	57,F	N		N	N	
70	53,M	N		N	N	
71	79,F	Y	Bilateral	N	N	N
72	36,F	N		N	N	
73	60,F	N		Y	N	

[a]*y* yes, *N* no

Table 2 Comparison of clinical characteristics between OLP cases with and without SFB

Group	M/F	Smoking	Restriction in mouth opening	Reduced vestibular depth	Duration of the disease (Years)	Presence of erosive lesions	Extra oral lesions	VAS	COMDQ
Cases with band (22)	0.1 (2/20)	4% (1)	0	54% (12)	6.25	50% (11)	50% (11)	4.3	28
cases w/o band (51)	0.23 (12/51)	23% (12)	11% (6)	6% (3)	4.24	31% (16)	39% (20)	3.9	28
P	0.2	0.32	0.024	0.00001	0.51	0.15	0.39	0.53	0.98

to address the impact of SFB on QOL. In the present study, histological examination was performed in a single patient, in which the biopsy was taken from an area of OLP overlying the band area (Fig. 5), and compared to a pre-existing diagnostic biopsy from an OLP patient without band formation, both cases located in buccal mucosa. There seems to be some increased width of connective tissue in the patient with SFB. In view of the fact that justification for surgical intervention to remove and biopsy such bands exists in only rare circumstances, in which the sensation of restriction in mouth opening becomes a significant complaint, biopsy material for analysis is extremely rare, and there are limited conclusions that can be drawn from histological analysis of a single case with SFB. Within these limitations, the clinical finding of palpable SFB seems to be histologically supported by the presence of the increased width of sub-epithelial fibrous tissue. The lack of significant impact of the SFB on quality of life parameters, further supports our reluctance to recommend surgical intervention to remove these bands, although from a purely scientific point of view it would have been interesting to be able to analyze the tissue removed.

The most significant finding in the present study was the established frequency of clinically palpable fibrous bands in approximately a third of OLP patients. Further

Fig. 5 Histologic specimen from an OLP patients with SFB, connective tissue width in three locations was measured (basement membrane to adipose tissue layer), the mean width was 586 µm. (Hematoxillin and Eosin, original magnification X200

Fig. 6 Control histology specimen of an OLP patient without clinical SFB, the mean width of connective tissue was 444 µm

investigation of the microscopic features may be considered in selected cases in the future, depending on the degree of discomfort associated with the bands.

While the clinical presentation of OLP typically changes over time, with fluctuations in signs and symptoms [13], the presence of SFB was present in the study group irrespective of the clinical type of oral lesions, thus the study hypothesis that SFB would be more frequent in the erosive OLP patients could not be supported in the present study group.

Fibrosis is characterized by the presence of an excess of fibrous connective tissue in an organ. Hyper-proliferation of fibroblasts results in excessive extracellular matrix synthesis and secretion, particularly deposition of collagens. It can be the result of a reparative or reactive process that can occur in many organs, including lung, liver, heart, and kidney. Under chronic pathological situations, fibrosis may cause increased tissue stiffness and progressive organ dysfunction. Fibrosis can also be considered as the end result of chronic inflammatory reactions induced by a variety of stimuli, including persistent infections, autoimmune reactions, allergic responses, chemical insults, radiation, tissue injury and normal ageing [14–18]. OLP falls in this recognized group of factors associated with fibrosis, as it is a chronic state of mucosal inflammation, which often persists for years, possibly with a particular role for mast cells in this process (as discussed above).

Although the link between chronic inflammation and fibrosis is well established in several organ systems, the particular form of band-like fibrosis in the buccal mucosa in OLP patients is documented and reported here for the first time.

When the insertion of the bands is in proximity to the gingival mucosa, some cases present with gingival recession. The fibrotic band may create an effect of pulling and "striping" of the gingiva with every mouth opening. This phenomenon, coupled with a loss of vestibular depth in the area, often results in significant difficulty with hygiene procedures, and additional burden on gingival tissues, which can aggravate recession and inflammation.

Conclusions

SFB are a common clinical finding in OLP patients. Sensations of restricted mouth opening/stiffness are frequently reported by these patients. SFB is associated with gingival recession and loss of vestibular depth, and therefore recognition of SFB should lead to more intense periodontal care, specifically in areas affected by SFB. Using COMDQ failed to detect differences between OLP patients with or without SFB in issues of quality of life. Further research is needed in order to determine the clinical significance of SFB.

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Compliance with Ethical Standards

Conflict of interest No conflict of interest to disclose.

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