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ORIGINAL ARTICLE

Lichen sclerosus of the oral mucosa: clinical and histopathological findings. Review of the literature and a case report

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ABSTRACT

Objectives: Lichen sclerosus (LS) is a rare, chronic mucocutaneous disease that most frequently affects the female genital area. Oral manifestations are seldom detected; only 36 well-documented and histopathologically verified oral LS cases have been published.

Materials and methods: Here we describe one patient affected by oral (LS) and review of the literature 1957–2017.

Results: Findings in our review suggest a female to male ratio of 1.64:1. It is most commonly diagnosed at the age of 10–29 years (46%). Oral LS can appear as symptomless, irregular-shaped, porcelain-white and flat lesions situated asymmetrically. Lesion is commonly sole, well-demarcated area and its size varies from 2 mm (small macula) to 7 cm (large plaque). The most common sites in the oral cavity include the labial mucosa, lips and gingiva. The histopathological criteria include atrophy and sometimes hyperkeratosis of the epithelium, hydropic degeneration of basal cells, hyalinization of the lamina propria, lymphocyte infiltration beneath the zone of hyalinization and scantiness of elastin. Surgical excision is an effective treatment for small lesions; intralesional triamcinolone or corticosteroid injections are used for larger lesions.

Conclusions: Oral LS may be under-recognized due to its asymptomatic nature and rarity.

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Gingiva; histopathology; lichen sclerosus; lichen sclerosus et atrophicus; mouth diseases

Introduction

Lichen sclerosus (LS) is a rare, chronic, inflammatory mucocutaneous disease of unknown aetiology. LS can involve any part of skin or mucosa, but mostly it affects the anogenital mucosa of women. LS has autoimmune characteristics and the cause seems to be multifactorial. Autoimmune mechanisms, genetic and local factors, trauma, hormones and infections are suspected to play a role. Pathogens such as Epstein–Barr virus and *Borrelia burgdorferi* have also been explored as triggers [1,2].

Hallopeau first described LS in the vulva in 1887 [3]. LS was earlier called lichen sclerosus et atrophicus, lichen albus and white spot's disease. As atrophy is not always present in the lesions, the name was changed to LS in 1976 [4]. The prevalence of LS is 0.1–0.3% [5] and is more frequent among women. Women are 6–10 times more often affected by genital LS compared to men. 15–20% of patients with genital LS also have extragenital manifestations, while only 6% of LS patients have extragenital lesions exclusively [1,2]. While LS can appear at any age, LS is most commonly diagnosed among pre-pubertal or post-menopausal women [1]. The mean age of girls at the time of diagnosis is 6.7 years and of women 60 years [6,7]. Men are usually diagnosed between the ages of 30–40 years [1]. Approximately 10–15% of LS patients are children, and most are girls with genital-area lesions [8]. However, the typical LS patient is a postmenopausal Caucasian woman between the ages of 50–60 years.

Genital LS typically affects the vulva and appears as hypopigmented, porcelain-white smooth papulas and maculas that unite into plaque-type areas. There may be hyperkeratosis or atrophy, fissures, purpura, teleangiectasy and blisters linked into changed morphology in connective tissue and epidermis; this is partly due to scratching and scarring. Genital LS seldom affects the vagina in contrast to lichen planus. Symptoms of genital LS often include pain and pruritus. Without treatment, severe LS may cause significant changes in vulvar architecture, inducing dysuria and dyspareunia. Genital LS is associated with a higher risk of vulval squamous cell carcinoma; a 4–5% risk has been reported. According to Halonen [9], in addition to the increased risk of vulvar carcinoma, genital LS also increases the risk of vaginal cancer [1,2,7,8].

Cutaneous LS is characterized by firm, hypopigmented white papulas or larger plaques [1]. Lesions are flat or slightly raised. Cutaneous LS is generally found on the neck, upper back, breasts, axillaes, flexor sides of the wrists, abdomen and thighs. The scalp, face and nails are rarely affected [2,7]. Cutaneous LS can be completely asymptomatic or pruritus may be present.

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Oral LS is a very rare condition and thus far only 36 histopathologically proven and well-documented oral LS patient cases have been reported. The first histopathologically verified oral LS cases were reported in 1957 by Miller [10] and Ravits [11] in the same publication. Histopathological changes were described to be similar in cutaneous and mucosal LS. Oral LS can occur with or without skin or genital (or both) involvement. Oral LS can appear in different sites of the mouth, including lips, buccal and labial mucosa, tongue, palate, gingiva and anterior tonsillar pillars [12]. Here, we describe one patient with oral LS and summarize the data on the histopathological and clinical features, diagnostics and treatment options of this rare form of LS.

Case presentation

Anamnesis

A 70-year-old Finnish woman was referred to the Department of Oral and Maxillofacial Diseases, Helsinki University Hospital for symptomless oral white lesions in the upper attached gingiva. The lesions were present for one year. She had diagnoses of hypertension, diabetes and cutaneous and genital LS. Skin and genital lesions appeared two years before oral involvement. Current medications at the time of examination were metformin hydrochloride (Metforem®), simvastatin (Simvastatin®), calcium and D vitamin (Calcichew D3 forte®), enalapril (Linatil®) and asetylsalisylic acid (Primaspan®). She had a history of smoking a couple of small cigarettes daily for years.

Oral health was good and there were no signs of 4 mm or deeper periodontal pockets at the time of examination. She had regular visits to a periodontist every six months. However, gingival recessions were found. Laboratory exams (full blood count, glucose levels and TSH) were performed and only glucose levels were elevated; HbA1c was 55 mmol/mol (reference range 20–42 mmol/mol) and fasting blood glucose level was 7.7 mmol/l (4–6 mmol/l). An oral specimen of the mouth was obtained and *Candida albicans* was detected in small amounts. She had no marks of candida infection or associated symptoms; she was assumed to be an asymptomatic carrier of *C. albicans*. A subgingival plaque sample was collected but no periodontal pathogens were found in the gingival pocket sample.

Intraoral examination

Porcelain-white, well-demarcated, non-scrapable, smooth lesions were found on the buccal side of the upper and lower canine and incisor area (dd. 13–23 and 33–43). In the upper jaw gingiva, the lesion was 4 × 1 cm and in the lower jaw 3 × 0.5 cm. Lesions were symmetrically affecting the keratinized attached gingiva. The marginal 1–2 mm of the gingiva was normally coloured except in region dens (d)11. Gingival recessions were also seen at the same location. The palatal side and the remaining oral mucosa appeared normal. Lesions were symptomless, but the patient was worried about the recessions that appeared during the year (Figures 1–3).

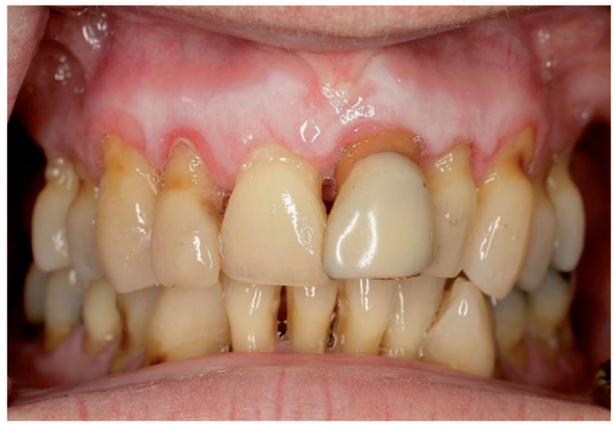

Figure 1. Upper teeth and porcelain-white lichen sclerosus lesion in the attached gingiva.

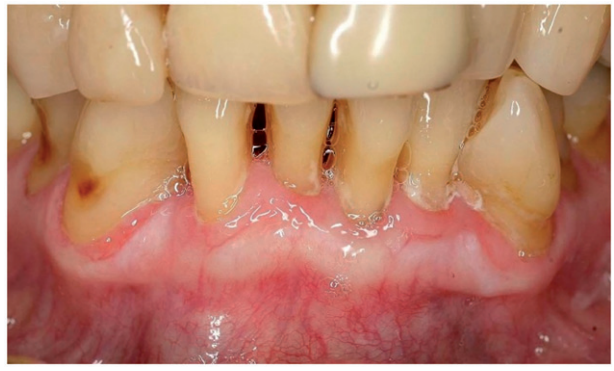

Figure 2. Lower teeth and gingiva: the marginal gingiva has normal colour and the attached gingiva is white.

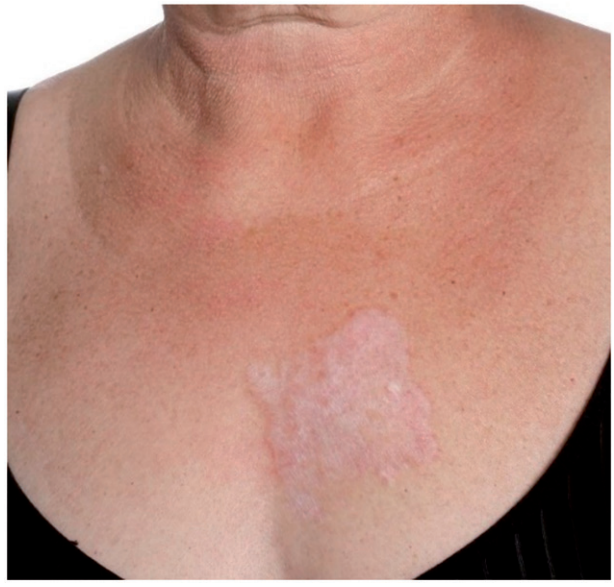

Figure 3. Three years ago, a pruritic, white lesion of 5 cm appeared on the skin of the breast. Several of smaller lesions appeared on the back. Genital LS was diagnosed at the same time.

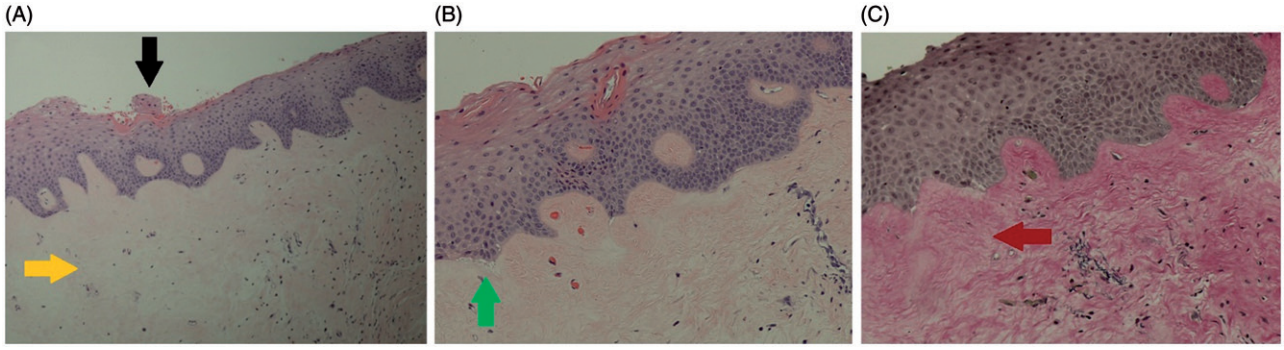

Figure 4. (A) Oral mucosa at 200 x magnification, upper arrow marking hyperparakeratosis and lower arrow hyalinization and hyposellularity in lamina propria. (B) 400 x magnification, arrow marking hydropic degeneration of basal cells. (C) van Gieson's staining, arrow marking loss of elastic fibres.

Histopathological findings

The diagnosis was confirmed with biopsy. An incisional biopsy of 3×2 mm was taken from the labial mucosa and gingiva region of dd.21–22 under local anaesthesia. Microscopic examination of sections stained with haematoxylin and eosin revealed focal areas of hyperparakeratosis in the epithelium. The epithelium was connected to the lamina propria with sharp rete ridges. Hydropic degeneration of the basal cells was occasionally noted. The upper part of the underlying connective tissue revealed a zone of hyalinization and hypocellularity. Chronic inflammatory cells were detected focally. Gieson's staining showed scantiness of the elastic fibres in the superficial connective tissue. Oral LS diagnosis was confirmed based on histopathologic features and clinical appearance (Figure 4).

Materials and methods

A PubMed database search was performed using the keywords 'oral lichen sclerosus' and 'oral lichen sclerosus et atrophicus'. Only 36 well-documented and histopathologically confirmed oral LS case reports between January 1957 and July 2017 in English were found; all papers describing at least one patient case of oral LS were selected. All cases, including the present case (patient number 36), are listed in Table 1.

We did not include case reports with insufficient clinical or histopathological documentation. Kaminsky's report [36] was published in Spanish and the case report was excluded. Although not all relevant information was reported, we were able to include most case reports. Missing data typically concerned the site, presence of extraoral disease, symptoms and treatment. Attili and Attili [37] documented 27 histopathologically confirmed oral LS manifestations in the lip, but the exact clinical and histopathological features and site were not reported.

Review

Epidemiology

Although oral LS patient cases were documented worldwide, the patients were mostly Caucasian, but also Asian and Hispanic. No patients of African descent were reported. The majority of patient cases were documented in the United States and Brazil.

Among women, the prevalence of genital LS is 0.1–1.7% [7]; oral LS is much rarer. The incidence of oral LS is unknown. The majority of reported oral LS patients were women, with a female to male ratio of 1.64:1. This differs from genital LS, where the female to male ratio is much higher (6–10:1). The mean age at the time of diagnosis in oral LS patients was 35.7 years (7–70). However, nearly half of the patients were between the ages of 10–29 years (Figure 5).

About 71% (24/34) of patients had only oral manifestations of LS. In four cases (12%), LS was detected as a mucocutaneous disease affecting the oral cavity, genital areas and skin. Patients with oral LS had cutaneous LS in four (12%) cases and only two (6%) patients had OLS and genital LS without skin involvement. In three cases (patients 4, 19 and 33) no genital or skin involvement was reported.

There is a genetic component; HLA DQ7 is most commonly found among LS patients [38]. LS is strongly associated with other autoimmune diseases including vitiligo, autoimmune thyroid disease, alopecia areata, pernicious anaemia and diabetes [1,8]. Autoimmune diseases were not reported among oral LS patients and the majority were healthy.

Clinical presentation

Oral LS lesions are porcelain-white, well-demarcated, sharp-bordered maculae or larger plaques. Colour can also be greyish white. In addition, reticular strias, ulcerations, telangiectasia and petechiae have been reported [14,15,18,31,32]. The lesion surface tends to be flat or slightly elevated with firm consistency.

Over 60% of reported cases are asymptomatic. However, a third of the patients reported symptoms including difficulties opening the mouth, burning sensation, discomfort during teeth brushing, soreness, tightness and cosmetic concerns due to white colour or marginal gingiva recession.

Oral LS can affect any part of the oral cavity. The most common sites are labial mucosa (20/37, 54.1%), lips (19/37, 51.4%), gingiva (14/37, 37.8%) and buccal mucosa (11/37, 29.7%). Lesions can also appear on the dorsal side of the tongue (9/37, 24.3%) and on the palate (6/37, 16.2%). No

Table 1. Case reports of oral LS 1957–2017.

Histopathologically confirmed case reports of oral lichen sclerosus 1957–2017									
Reference	Patient number	Author	Year	Patient age and sex	Oral site	Size, amount of lesions and asymmetry (A = asymmetric, S = symmetric)	Symptoms	Exclusion	Extraoral site G = genitalia C = cutaneous
[10]	1	Miller et al.	1957	48 F	Right buccal mucosa Left buccal mucosa	2 × 2 cm, 2 lesions, symmetric	No		G = Yes C = Yes
[11]	2	Ravits et al.	1957	24 M	Right buccal, upper labial mucosa and upper gingiva Palate	Size*, 2 lesions, asymmetric	*		G = No C = No
	3			42 M	Palate, buccal mucosa and anterior tonsillar pillars	Size*, amount*, symmetry*	*		G = Yes C = No
				32 M	Right buccal mucosa	Size*, one lesion, asymmetric		X	
[13]	4	de Araujo et al.	1985	26 F	Maxillary gingiva midline reg. 11–22, labial mucosa, upper lip and skin in the subnasal sulcus	Size*, 1 lesion, asymmetric	*		G =* C = No
[14]	5	Siar et al.	1985	25 M	Right buccal mucosa and retromolar areas Palatal mucosa, Tongue Lips and labial mucosa	Size*, ≥4 lesions, asymmetric	Yes		G = No C = Yes
[15]	6	Macleod et al.	1991	57 F	Dorsum of the tongue Hard palate	Size*, 2 lesions, symmetric (tongue)	Yes		G = No C = No
[16]	7	Schulten et al.	1993	59 F	Upper right labial mucosa Left commissure and lip Right side of the tongue	0.5 cm, 1.5 cm, 0.2 cm, 3 lesions, asymmetric	No		G = No C = No
	8			12 M	Left lower lip	0.8 cm, 1 lesion, asymmetric	No		G = No C = No
[17]	9	Brown et al.	1997	18 M	Right lower lip and vermillion	Circa 1 × 1 cm, 1 lesion, asymmetric	No		G = No C = No
	10			44 M	Soft palate midline	1 × 1.5 cm, 1 lesion, symmetric	No		G = No C = No
[18]	11	Buajeeb et al.	1999	22 F	Right lower lip, vermillion border and labial mucosa, right buccal mucosa and buccal gingiva of dd.43–47	2 × 7 cm, 1 lesion, asymmetric	Yes		G = No C = No
[19]	12	Kaur et al.	2002	16 M	Right upper lip, vermillion and labial mucosa, buccal gingiva of dd.11–12	Circa 1.5 × 3 cm, 1 lesion, asymmetric	Yes		G = No C = Yes (nose)
[20]	13	Jensen et al.	2002	10 F	Left buccal mucosa and lower buccal sulcus	1 cm round, 2 lesions, asymmetric	No		G = No C = No
[21]	14	Jimenez et al.	2002	19 F	Buccal gingiva of dd. 12–11, right upper labial mucosa and frenulum	1 cm, 1 lesion, asymmetric	Yes		G = No C = No
[22]	15	Mendonca et al.	2004	20 F	Right side of lower lip and vermillion extending to labial mucosa	2 × 7 cm, 1 lesion, asymmetric	No		G = No C = No
[23]	16	Rajlawat et al.	2004	14 F	Right lower lip, vermillion, labial and buccal mucosa	3 × 1.5 cm, 1 lesion, asymmetric	No		G = No C = No
[24]	17	Chaudhry et al.	2006	60 F	Dorsum of the tongue	Circa 0.5 cm and 1 cm, 2 lesions, symmetric	Yes		G = Yes C = Yes
[25]	18	Kelly et al.	2006	10 F	Right lower lip, vermillion and labial mucosa	1.5 × 1.2 cm, 1 lesion, asymmetric	No		G = No C = No
[26]	19	Walsh et al.	2008	16 M	Right upper lip, vermillion and labial mucosa, buccal gingiva of d.11	Circa 1 × 3 cm, 1 lesion, asymmetric	No		G =* C = Yes (nose)
[47]	37	Wakamatsu et al.	2008	54 F	Lower lip	Circa 1 × 1 cm	No		G = No C = No
[27]	20	Jimenez et al.	2008	31 F	Dd.21–25 buccal gingiva, sulcus, left upper labial mucosa and lip	Circa 3 × 2 cm, 1 lesion, asymmetric	Yes		G = No C = No
[28]	21	Azevedo et al.	2009	19 M	Buccal and lower labial mucosa	Size*, 2 lesions, asymmetric	No		G = No C = No
	22			34 F	Vermillion, upper lip extending to labial mucosa and buccal sulcus	Size*, 2 lesions, symmetry*	Yes		G = No C = No

(*continued*)

Table 1. Continued

Histopathologically confirmed case reports of oral lichen sclerosus 1957–2017									
Reference	Patient number	Author	Year	Patient age and sex	Oral site	Size, amount of lesions and asymmetry (A = asymmetric, S = symmetric)	Symptoms	Exclusion	Extraoral site G = genitalia C = cutaneous
	23			11 F	Vermillion, upper lip, extending to labial mucosa	Size*, 1 lesion, symmetry*	No		G = Yes C = No
	24			38 F	Buccal mucosa and lower labial mucosa extending to vermillion lip	Size*, 2 lesions, asymmetric	Yes		G = No C = Yes
	25			31 F	Lower labial mucosa extending to vermillion lip and lateral marginal tongue	Size*, 2 lesions, asymmetric	No		G = No C = Yes
	26			28 F	Dorsum of the tongue, buccal and lower labial mucosa	Size*, 3 lesions, symmetry*	Yes		G = No C = No
[12]	27	Sherlin et al.	2010	60 M	Buccal gingiva of dd.14–16 Buccal gingiva of dd. 35–37 Buccal mucosa bilaterally	2 × 2 cm buccal mucosas and 2 × 3 cm gingiva, 4 lesions, asymmetric	No		G = No C = No
[29]	28	Kim et al.	2010	7 F	Left lower lip, vermillion and labial mucosa	2.5 × 1.5 cm, 1 lesion, asymmetric	Yes		G = No C = No
[30]	29	Louvain et al.	2012	70 F	Dorsum of the tongue, Upper left gingiva, Right buccal mucosa	Size on the tongue 3–4 mm, 5 lesions, asymmetric	No		G = Yes C = Yes
[31]	30	Liu et al.	2013	54 F	Dorsum of the tongue	2–3 cm^2, 1 lesion, symmetric	No		G = No C = No
	31			58 F	Dorsum of the tongue	2.5–3 cm^2, 1 lesion, asymmetric	No		G = No C = No
[32]	32	De Aquino Xavier et al.	2014	47 M	Upper alveolar mucosa reg. 21–23, labial mucosa and frenulum	2 × 1.5 cm, 1 lesion, asymmetric	No		G = No C = No
[33]	33	George et al.	2014	20 M	Upper labial mucosa Upper gingiva contacting the labial lesion	1 × 1 cm, 2 lesions, symmetry*	*		G =* C =*
[34]	34	Tupsakhare et al.	2016	67 M	Soft palatum on the right side	0.8 × 0.8 cm, 1 lesion, asymmetric	No		G = No C = No
[35]	35	Marangon et al.	2016	44 M	Upper left labial mucosa and lip	3.5 × 2 cm, 1 lesion, asymmetric	*		G = No C = No
	36	Matela et al.	2017	70 F	Buccal gingiva of dd.13–23 and 33–43	4 × 1 cm, 3 × 0.5 cm, 2 lesions, symmetric	No		G = Yes C = Yes
[36]		Kaminsky et al.	1974	26 F	Upper lip, labial mucosa and gingiva			X	
[37]		Attili et al.	2010	27 cases	Lower lip =*/27 Upper and lower lip =*/27	Size*, lesions*, symmetry*	*	X	G =*/27 C =*/27

X: excluded from review; not in English, insufficient information or biopsy was not performed.
*Not mentioned in report.

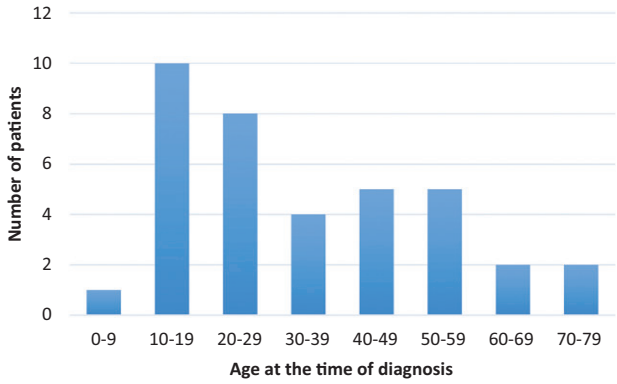

Figure 5. Age at time of oral LS diagnosis.

reports of OLS affecting the floor of the mouth or the ventral surface of the tongue have been published.

Lesions were mostly asymmetrical (81% of case reports). In over half of the patients, only one lesion was present. Oral LS also appeared as two or three separate lesions, and in three cases (8.1%) as four or more lesions.

The size of the lesion ranged from a small macula of 2 mm on the dorsal side of the tongue to 2×7 cm, affecting the vermillion, labial mucosa and gingiva. The average size of the lesion was 3.1 cm^2 (Figure 6).

Histopathological features

Classical histopathological features of well-developed genital or cutaneous LS lesions include hyperkeratosis and epidermal atrophy, flattening of rete ridges, acanthosis (especially in vulvar lesions), vacuolar or hydropic degeneration of basal cells, hyalinization of the superficial part of the lamina propria, band-like lymphocyte infiltration under the hyalinisated zone, dilated blood vessels and loss of elastic fibres [1,2,8,39,40]. Hyalinization is due to fragmentation of elastic fibres and collagen and can be explored with special staining. Histopathological features may change depending on disease duration [8]. Hyperkeratosis always exists in skin lesions [12]. In the early phase, oedema, homogenisation, elastin degeneration and collagen fragmentation lead to hyalinization and later to sclerosis [17]. Hyalinization appears as hypocellarity and an oedematous zone [16]. In younger lesions, the infiltrate is more superficial and the hyalinization zone is thinner; inflammatory cells may be located next to the epithelium [28]. The hyalinized zone pushes the lymphocyte infiltrate and vascular plexus deeper into the middle part of the lamina propria [17]. Changes in the lamina propria give the typical porcelain-white clinical appearance [17].

Histopathological findings of oral LS case reports are summarized in Table 2. In addition to haematoxylin-eosin staining, orcein staining (Weigert, Verhoeff and van Giesons) was used in 20 case reports to observe elastic fibres. Histopathological features in oral LS are similar to genital and cutaneous LS, with the exception of hyperkeratosis, which was absent in many cases. Atrophy (and in some cases, hyperkeratosis) was seen in the epithelium. Basal cells

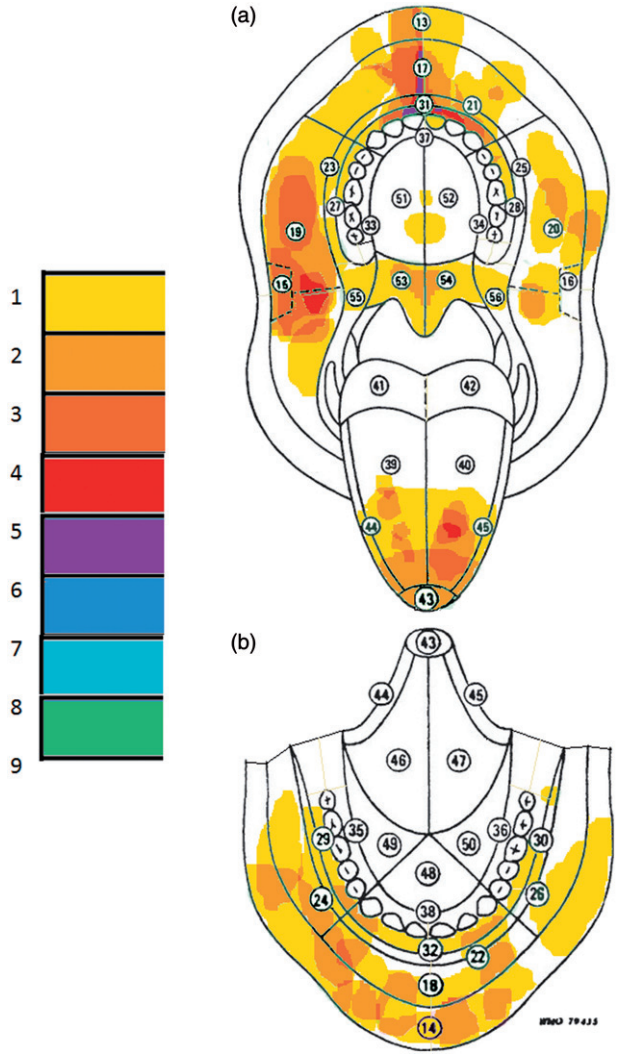

Figure 6. Sites of oral LS lesions in modified WHO topography picture.

were degenerated mostly by liquefaction and seldom by vacuolar degeneration. Loss of rete ridges and subepithelial clefting was occasionally seen. In the connective tissue stroma just beneath the epithelium, the main features were hyalinization of the superior part of the lamina propria and lymphocyte infiltration situated deeper under the hyalinized zone. Inflammatory infiltration was often band-like but also focal, sometimes situated perivascularly. Dilatation and telangiectasia were observed in vessels; in one case narrowing of vessels was reported. Orcein staining revealed fewer elastic fibres in the hyalinization zone.

Diagnosis

Diagnosis of oral LS is based on clinical and histopathological features and anamnestic data. Oral LS can resemble other more frequently encountered non-scrapable white, flat lesions in the mouth cavity. Accordingly, histopathological examination is a cornerstone for accurate diagnosis. As the histopathological picture in some disorders share similar findings, clinical features are needed to confirm the diagnosis.

Table 2. Histopathological features of reported oral LS biopsy specimens.

Histopathological features			
	N (*n* = 36)	%	Patient number
Epithelium			
Hyperkeratosis	12	33.3	1, 5, 6, 7, 8, 9, 11, 12, 15, 34, 35, 36
Atrophy	26	72.2	1, 5, 6, 9, 11, 12, 15, 16, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 37
Loss of rete ridges	5	13.9	4, 12, 14, 33, 34
Degeneration of basal cells (not specified)	7	19.4	10, 21, 22, 23, 24, 25, 26
Vacuolar degeneration of basal cells	3	8.3	12, 29, 34
Hydropic degeneration of basal cells	15	41.7	4, 6, 7, 8, 11, 13, 15, 27, 28, 30, 32, 33, 34, 36, 37
Subepithelial clefting	3	8.3	16, 32, 34
Acanthosis	2	5.6	1, 6
Lamina propria			
Homogenisation of collagen	23	63.9	1, 2, 4, 5, 7, 8, 9, 10, 13, 14, 19, 20, 21, 22, 23, 24, 25, 26, 30, 31, 32, 35, 37
Hyalinization of the lamina propria	28	77.8	4, 5, 6, 7, 8, 9, 11, 12, 14, 15, 16, 17, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 34, 35, 36, 37
Sclerosis of papillary dermis	2	5.6	18, 33
Hypocellularity, acellularity	1	2.8	32
Oedema	3	8.3	4, 12, 37
Lymphocyte infiltration			
Focal	17	47.2	4, 5, 6, 9, 11, 12, 13, 14, 16, 18, 20, 27, 28, 29, 34, 36, 37
Band-like	22	61.1	2, 6, 7, 8, 10, 13, 15, 16, 17, 19, 21, 22, 23, 24, 25, 26, 30, 31, 32, 33, 34, 35
Vessels			
Telangiectasia	4	11.1	11, 13, 30, 35
Dilated and haemorrhagic capillaries	7	19.4	9, 14, 20, 21, 22, 23, 29
Obliterative vasculitis	1	2.8	32
Gieson's, Verhoeff's staining	(*n* = 20)		
Scantiness of elastin fibres	20	100.0	4, 5, 9, 11, 12, 13, 15, 16, 17, 21, 22, 23, 24, 25, 26, 27, 32, 34, 35, 36

Exact histopathological features were absent from patient number 3 [11].

Table 3. White lesions in the oral cavity resembling oral LS.

Clinical differential diagnosis of oral LS
Oral lichen planus
Lichenoid reactions
Leukoplakia
Candida infection
Vitiligo
Localized scleroderma
Fibrous scar
Submucous fibrosis
White sponge nevus
Sideropenic anaemia
Discoid lupus erythematosus

Thorough anamnestic information consisting of medications, systemic diseases, allergies, dental treatments and use of tobacco, betel nut and alcohol products should be acquired. Oral white lesions of the patient with LS elsewhere on the body should be suspected as manifestations of oral LS. The symptomless nature of oral LS makes under-diagnosis very likely.

Lichen planus, lichenoid reactions, candida infection and leukoplakia are more frequently found as white lesions in the oral cavity. White lesions that may mimic oral LS are listed in Table 3.

When oral lichen planus appears as a white reticular form or as white plaques, it may appear similar as oral LS. Clinically, lichen planus usually exhibits a bilateral and symmetrical manifestation in the oral cavity. The histopathological picture changes depending on the form of the lichen planus lesion and the site of the biopsy. Atrophic, ulcerated and reticular forms have different histopathological features. In lichen planus, hyperkeratosis is detected in sections of white reticular areas (Wickhams striae) between areas of atrophy. Liquefaction degeneration of basal cells and a band-like, dense lymphocyte infiltration (primarily T cells and macrophages) are seen next to the basal cells. Mature oral LS differs from lichen planus regarding hyalinization, loss of elastic fibres and lymphocyte infiltration situated deeper in lamina propria [35,39].

The lichenoid lesion clinically and histopathologically resembles lichen planus. This lesion usually appears as reticular, atrophic or ulcerative forms. The manifestation is often asymmetrical, as in oral LS. Anamnestic data is important, as a lichenoid reaction is often caused by medication, dental restorative materials or may be a graft-versus-host reaction in a bone marrow transplantation patient. White lesions situated in contact with amalgam restoration suggest a lichenoid reaction. Histopathologically, lichenoid reactions have the same features as lichen planus, but the lymphocyte infiltrate may consist of eosinophils and is situated deeper in the lamina propria [39].

Leukoplakia is a clinical term defining a white plaque that cannot be categorized as any other disease. They are premalignant lesions, especially proliferative verrucous leukoplakia. Oral hairy leukoplakia has a viral aetiology and is seen in immunosuppressed patients. It is not associated with the malignancy. In leukoplakia, histopathological findings include hyperkeratosis, dysplasia, acanthosis, atrophy and inflammation. Basal cell liquefaction, bands of lymphocyte infiltration

Table 4. Medication options and their efficacy in oral LS.

Treatment	Efficacy	*n*	Patient number
No treatment	No efficacy	5	7, 10, 27, 35, 36
	Lesion enlargement	1	9
	Partial improvement	2	3, 15
Excision	Recurrence	1	25
	Improvement	5	8, 13, 22, 32, 34
Vitamins (A, D2)	No efficacy	2	2, 3
Pantothenyl alcohol	No efficacy	1	3
Solcoseryl	Improvement	1	5
Griseofulvin	Partial improvement	1	6
Topical testosterone	Improvement	1	9
Topical corticosteroid	No efficacy	1	6
Topical triamcinolone	No efficacy	1	11
	Improvement	1	5
Topical clobetasol propionate	No improvement	1	28
	Partial improvement	2	9, 16
	Improvement	1	18
Intralesional depo-medrol	Improvement	1	11
Intralesional triamcinolone	No efficacy	1	25
	Improvement	2	14, 20
Intralesional triamcinolone and prednisolone po	Improvement	1	12
Intralesional triamcinolone and colchicine po	Improvement	1	24
Colchicine po	Improvement	1	25
Betamethasone sodium phosphate and benzydamine in oral rinse	Improvement	1	17
Pimecrolimus 1% cream	Improvement	1	28
Topical tacrolimus	Partial improvement	1	29
Tacrolimus ointment 0.1%	Improvement	1	37
Not reported		9	1, 4, 19, 21, 23, 26, 30, 31, 33

and scantiness of elastic fibres are not seen in oral hairy leukoplakia as in oral LS [18,40].

In oral submucous fibrosis, there are variable changes in mucosa depending on the lesion stage. In the advanced stage, epithelial atrophy, flattening of rete ridges, epithelial atypia and pyknotic changes in basal cell layer nuclei, collagen hyalinization, inflammatory infiltration and obliteration of blood vessels are observed. The major aetiological factor for submucous fibrosis is areca nut chewing. This is related to the brown staining of teeth and trismus caused by tightening of oral tissues. Oral submucous fibrosis s histopathologically suggestive of LS, but differs in terms of epithelial atypia and vessel obliteration [18,41].

Localized scleroderma is an inflammatory disease leading to the sclerosis of the skin and subcutaneous tissues. Localised scleroderma is subdivided into morphea, generalized morphea, linear scleroderma and en coup de sabre [42]. Collagen fibre thickening, collagen hyalinization, disappearance of perivascular inflammatory infiltration and blood vessel obliteration were observed in histopathological specimens. Positive ANA autoantibodies may be found in serological samples. In localized scleroderma, elastic fibres exist and collagen synthesis is increased; the converse is observed in LS [18,43].

Vitiligo affecting the oral cavity is a very rare disorder. In vitiligo differential diagnosis, lamina propria hyalinization and lymphocyte infiltration are absent. Melanocyte reactivity can be tested by S-100 antibody; inactivity confirms vitiligo [17,44].

Discoid lupus erythematosus consists of usually atrophic, round lesions with white keratotic striae. Ulcerations are common and erythematous areas are usually seen. Histopathologically, the same features exist in oral LS such as hyperkeratosis, atrophy of rete pegs, liquefaction degeneration of basal cells, lamina propria oedema and deep diffuse inflammatory infiltration. Direct immunofluorescence is positive and IgA, IgG, IgM and complement components are found at the basement membrane [39].

There are currently no serological tests to confirm LS [7]. Serological immunoreactivity against extracellular matrix protein 1 (ECM1) has been reported in 74% of women with genital LS but only in 7% of healthy controls [45]. Additionally, autoantibodies against the basement membrane zone have been found in 33% of LS patients; the most common IgG subclasses were IgG1 and IgG2 that differ from those found in bullous pemphigoid [46].

Treatment

Treatment of oral LS depends on the symptoms, aesthetic concerns and possible later complications without treatment. During the last 60 years, topical medications primarily have been used. These include vitamins (A, D2, and E), griseofulvin, testosterone, topical corticosteroids, rinses and injections and calcineurin inhibitors. Systemic treatment such as colchicine and prednisolone have also been used in combination with topical treatment. The results of our literature review concerning oral LS medication are summarized in Table 4.

All lesions may not need therapy depending on the site and the symptomless nature of the lesion. During follow-up, some lesions remained unchanged without therapy and in some cases improvement was reported without therapy. When left untreated, gradual spreading of the lesions (especially on the lip to the surrounding skin, or vice versa) may occur. In the gingiva, oral LS is not only an aesthetic concern. Due to gingival recessions, loss of keratinized gingiva and even loss of alveolar bone, periodontal surgery, or in the

worst cases, tooth extractions were performed. When keratinized gingiva disappears around the tooth, this causes discomfort in tooth brushing, soreness and marginal gingivitis. Gingival recessions do not heal spontaneously and periodontal surgery is necessary.

The choice of the therapeutic option depends on the site and size of the lesion. In case of small lesions, surgical excision is an effective treatment and only one tongue recurrence has been reported. Some larger lesions on lips, buccal or labial mucosa have been treated successfully using primarily intralesional corticosteroid injections (ranging from two to seven times between 10 and 28 days). Topical corticosteroids as ointments have yielded variable results. Saliva rinses medication away from gingiva and customized trays may be useful to lengthen the time of contact between the ointment and the gingiva. Single case reports of improvements with local testosterone, pimecrolimus and betamethasone sodium phosphate as a mouth rinse have been described.

Due to disease rarity, no treatment guidelines for oral LS exist. Therapy efficacy is based only on individual case reports. Although recommendations are absent, excision of small lesions and topical ointments or intralesional injections (by moderate-potency corticosteroids, such as triamcinolone acetonide) could be first-line treatment. Topical calcineurin inhibitors (e.g. tacrolimus and pimecrolimus) may be used if topical corticosteroids have failed. Additional oral LS case reports of treatment efficiency and duration are needed to standardize therapy guidelines.

Conclusions

The present case report and literature review describes a rare gingival manifestation of LS. Clinical and histopathologic examination of oral and skin lesions and biopsy specimens is crucial for diagnosis. There may be aesthetic concerns in the treatment of oral LS. The nature of oral LS in the gingival area and periodontium is currently poorly understood and more information is therefore needed regarding alveolar bone loss when oral LS affects gingival margins.

There are only a few reports in English on oral LS. It is for this reason that each oral LS patient should be carefully documented clinically, histopathologically and photographically to spread knowledge of this rare form of LS. Descriptions of symptoms, treatment and therapeutic results are needed in long-term follow-ups.

Patients with LS should have an intraoral examination. Oral LS may be under-recognized due to its asymptomatic nature and rarity. An association between LS in the vulval area and squamous cell carcinoma has been reported. While malignancies in oral LS have not been reported, due to the small number of case reports this association cannot be completely excluded.

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