

VULVOVAGINAL GINGIVAL LICHEN PLANUS: REPORT OF TWO CASES AND REVIEW OF LITERATURE

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SUMMARY

Purpose. Oral Lichen Planus (OLP) is a chronic inflammatory disease of skin and mucous membranes. Approximately 20% of women with oral lichen planus develops lesions in the genital mucosa. In 1982, Pelisse described a special form of lichen planus (LP), which consists of a triad of symptoms: vulval, vaginal and gingival (VVG)-LP lesions. Aim of the present report is to report two new cases and review the international literature.

Material and methods. Two cases of VVG-LP are reported and a review of recent literature is performed.

Results. The onset of erosive or ulcerative mouth lesions may precede or follow by months or even years the onset of vulvovaginal lesions. Vaginal agglutination is associated with the postmenopausal state in conjunction with a dermatologic condition. Intra-lesional corticosteroids have a role in localized chronic ulceration, while systemic therapies such as corticosteroids, azathioprine, mycophenolate mofetil, hydroxychloroquine, ciclosporin, methotrexate, retinoids, thalidomide and photo chemotherapy have been used in more severe cases with varying success.

Conclusions. VVG-LP is rather a rare condition and has been documented in the literature mainly in the form of case reports. Lack of a precise diagnostic criteria of VVG-LP depends on the specialists.

Key words: oral lichen planus, vulvovaginal gingival syndrome, vaginal agglutination, peno-gingival lichen planus, and oral diseases.

Introduction

Oral Lichen Planus (OLP) is a chronic inflammatory disease of skin and mucous membranes, and is rather common in the general population: the prevalence being between 1 and 2% in the people over the age of 15 years (1, 2). It is more common in women than in men, and the most prevalent age is the 5th and 6th decades of life (3). Lesions are symmetrical and bilateral and the buccal mucosa is frequently involved. The risk of malignant transformation is extremely low. This disease can affect mucous membranes of the genitals also (4, 5). In fact vulvar involve-

ment of LP has frequently been reported. Lichen planus of the mucous membranes may affect buccal or gingival mucosa and the vulvar vestibule and vagina (4).

Its etiology is still uncertain whilst an autoimmune mechanism has been hypothesized. In recent years there have been numerous reports suggesting an association between hepatitis C-induced liver damage and lichen planus (1).

Although its exact etiology is unknown (1, 2, 4-6), numerous studies support the hypothesis that it is a complex immunologic disease mediated by cytotoxic T cells directed against basilar keratinocytes (6). However, in keeping with other autoimmune disorders, it is thought a strong as-

sociation with other autoimmune diseases (4). This finding might suggest common genetic or pathogenic factors (4). A potential association with the DQB1*0201 allele was reported (6). The DQB1*0201 allele has, for example, been associated with celiac disease, dermatitis herpetiformis, insulin-dependent diabetes mellitus, vitiligo, Graves' disease (7). There are very few cases in medical literature reporting the association of the syndrome with celiac disease (8).

Since the clinical presentations for oral erosive lichen planus, pemphigoid, and pemphigus vulgaris are similar; biopsy is the best way to establish the diagnosis (1). The diagnosis of VVG-LP requires histopathology confirmation from at least one involved site, coupled with analysis for direct or indirect immunofluorescence to exclude immunobullous disorders (9). Microscopic features considered to be diagnostic of oral lichen planus (OLP) include hyperorthokeratosis and parakeratosis, degenerative changes of basal cells, and a band-like subepithelial infiltrate of lymphocytes (1). The erosive form of the disease was the predominant type (9).

In patients with oral lichen planus, 6% will manifest simultaneous involvement in three or more sites, thus highlighting the importance of thorough evaluation and the need for a multidisciplinary approach to these patients (4, 5). In addition oral lichen planus may be associated with other oral diseases such as periodontal disease, mucosal atrophy, mucositis or lesions of gastroesophageal reflux (10-14).

Not uncommonly, patients with severe oral lesions displayed mild genital disease (1). Approximately 20% of women with oral lichen planus develops lesions in the genital mucosa (15).

In 1982, Pelisse identified a small subgroup and described it as vulvovaginal gingival syndrome (15). Pelisse stated a special form of lichen planus (LP), which consists of a triad of symptoms: vulval, vaginal and gingival LP lesions (15). A counterpart of this disease in men is termed peno-gingival LP (15). Vulvo-vaginal-gingival syndrome is a unique variant of mucosal LP characterized by erosions and desquama-

tion of the vulva, vagina and gingiva (16, 17). The VVG syndrome comprises an uncommon subgroup of mucosal LP associated with significant long-term sequelae (16). The main sequelae are scar formation, mucous stenosis, impact on specific functions and risk of malignant change (16). Complications were related to fibrosis and stricture formation in a variety of sites (16). However, it is unclear why this variant of LP in comparison with other subgroups of mucosal LP has such a marked propensity for scarring (16, 17).

Among the patients with VVG-LP, there were many additional sites of involvement. In the majority of patients chronic inflammation resulted in vaginal stenosis (4, 5). Vulval involvement results in loss of the normal architecture with loss or fusion of the labia minora, loss of the interlabial sulci, burying of the clitoris and vaginal stenoses and a florid generalized desquamative gingivitis (4-6). Cutaneous, nail, and scalp involvement are more frequent in VVG-LP (18). There is a striking association with scarring or stricture formation of other mucosal sites such as esophagus and the eye (18).

In the oral cavity vulvovaginal gingival lichen planus (VVG-LP) manifests as classical oral manifestations of lichen planus. Fibrous banding across the buccal mucosae and loss of buccal sulcular depth may also be evident (4, 5). Because scarring is present in 90% of patients with VVG and is uncommon in other types of LP, we considered this possible association.

Eisen concluded that this variant of LP was more likely to be underreported than represent a rare subgroup (17). Oral lesions may be poorly symptomatic or present with pain, burning, discomfort and bleeding during brushing of teeth. Genital lesions usually cause burning, pain, pruritus and bleeding. Some patients complain of dyspareunia and seropurulent discharge (5).

The onset of erosive or ulcerative mouth lesions may precede or follow by months or even years the onset of vulvovaginal lesions (1). Vaginal agglutination is associated with the postmenopausal state in conjunction with a dermatologic condition, such as lichen planus or epidermoly-

sis bullosa or a comorbid inflammatory process, such as chronic graft-versus-host disease (GVHD) (19).

Several diseases must be considered in the list of differential diagnoses for vulvovaginal-gingival syndrome, including idiopathic desquamative vaginitis, idiopathic erosive vulvitis and vulvar lichen sclerosis (5).

Idiopathic desquamative vaginitis is described as a noninfectious, idiopathic, erosive condition which frequently leads to vaginal adhesions and stenosis. Idiopathic erosive vulvitis has been described as erythroplasia and as plasma cell vulvitis. Erosive vaginitis with development of adhesions has been noted in several patients with GVHD after bone marrow transplantation (4, 5). An erythroplastic form of vulvar lichen sclerosis has also been described, and these patients demonstrate inflammatory erosive vulvitis, vulvar atrophy, labial fusion, and other changes that could be observed with either LP or with lichen sclerosis.

Diagnostically, lichen planus may be identified by the presence of immunofluorescent activity on biopsy (4). VVG-LP has usually a chronic course and requires more aggressive therapy than other types of LP (5). Topical corticosteroids appear to be the mainstay of therapy (20, 21). In recalcitrant cases, such as in many VVG-LP patients, systemic steroids and other modalities of immunosuppressive therapy may be implemented (22).

We considered the more frequent and earlier use of systemic immunosuppression mycophenolate mofetil substituted in those patients intolerant to azathioprine (23). Mycophenolate mofetil would normally be considered in this situation but has a potentially higher risk of life-threatening infection (23). Intralesional corticosteroids have a role in localized chronic ulceration, while systemic therapies such as corticosteroids, azathioprine, mycophenolate mofetil (MMF) (23), hydroxychloroquine, ciclosporin, methotrexate, retinoids, thalidomide and photo chemotherapy have been used in more severe cases with varying success (24, 25).

105 genes were found up- or down-regulated,

both in the oral and the genital mucosae, so it may be hypothesized that oral LP and genital LP are distinct clinical manifestations of the same disease (5). Therefore, as previously referred, it might be a specific disease association between the DQB1*0201 allele and the VVG syndrome (6). Stratified epithelium-specific antinuclear antibodies (SES-ANA) are a marker of VVG-LP (5). It is also known that oral lichen planus may be related to diseases like oral dysplastic lesions, and burning mouth syndrome (1, 26, 27).

It should be emphasized that the prevalence of VVG-LP is probably underestimated and that patients may be treated separately for their vulvitis and vaginitis by a gynecologist and for their oral lesions by a dermatologist or a dentist (26-32).

Case report 1

A 78-year-old woman presented with simultaneous oral and vaginal ulcerative lesions. Her medical history was significant for chronic hepatitis C and hypertension. Cutaneous examination of head revealed scarring alopecia, and characteristic violaceous papules on the flexor surfaces of the wrists, with more atrophic lesions in the axillary folds bilaterally, while skin of feet presented nail dystrophy with longitudinal ridging and splitting (Figure 1). Examination of the oral cavity revealed erythematous lesions along the gingiva and white, lace like striations of the right mandibular labial mucosa, extending posteriorly onto the right buccal mucosa (Figure 2). A biopsy was performed and revealed focal loss of basal epithelial cells, scattered Civatte bodies, degeneration at the epithelial connective tissue interface, and a band like infiltrate of lymphocytes in the subepithelial connective tissue. Direct immunofluorescence for IgG, IgA, and C3 were negative. Fibrinogen staining interstitially, however, was positive. She was referred to her gynecologist for vulvovaginal discomfort. Gynecologic examination revealed generalized vulvar erythema and tenderness but no vulvar or



Figure 1
Scarring alopecia in patient of case report 1.



Figure 2
Erythematous lesions of OLP along the upper gingiva (case 1).

vaginal lesions, and wet preparation microscopic examination was negative. These findings supported the diagnosis of lichen planus and the vulvovaginal-gingival syndrome.

Her initial management consisted of continuing corticosteroid therapy. The systemic corticosteroid dosage was gradually tapered to a maintenance dose of 5 mg daily over 6 months. She has continued to use intermittent topical clobetasol propionate 0.05% ointment and cyclosporine 0.1% rinses intermittently to manage her oral symptoms. The superimposed candida infection was treated with nystatin suspension (2 rinses daily). She takes cleansing and corticosteroid creams for skin lesions treatment. Topical estrogen cream was prescribed for presumed atrophic vaginitis.

Case report 2

A 64-year-old woman presented with oral lichen planus. Her medical history was significant for hepatitis B and hypertension in therapy with telmisartan and idroclorotiazid (80 mg telmisartan/12,5 mg idroclorotiazid daily), atenolol (50 mg daily), acetylsalicylic acid (100 mg daily). Cutaneous examination revealed scarring alopecia, hand nails dystrophy with longitudinal ridging and splitting (Figure 3), and characteristic violaceous papules on the flexor surfaces of arms. The patient also complained of oral ulcers on the buccal mucosa and gingival surfaces. Examination of the oral cavity revealed erosive, erythematous ulcerations alternates to white, lacy, keratotic striations (Figure 4). A biopsy of



Figure 3
Scarring alopecia in patient of case report 2.



Figure 4
Erosive, erythematous ulcerations alternating with white, lacy, keratotic striations of oral mucosa (case 2).

her oral lesions showed the changes described for lichen planus, with more atrophic lesions in the maxillary folds bilaterally. Direct immunofluorescence was negative for both immunoglobulin G (IgG) and IgA basement membrane zone antibodies, and in combination with clinical features, excluded mucous membrane pemphigoid. Gynecological examination revealed complete agglutination of the vaginal cavity with superficial erosion, purulent discharge, and desquamative vaginitis (Figure 5). A biopsy was performed and tissue was submitted from the vaginal vault apex, vestibule, and posterior vaginal wall. Sections showed focal loss of basal cells; basal layer degeneration at the epithelial-dermal interface; plasma cells, lymphocytes, and eosinophils in the submucosal fibrous connective tissue. Topical clobetasol propionate 0.05% ointment and cyclosporine 0.1% rinses were prescribed for oral lesions treatment, while topical corticosteroids were prescribed for genital use (clobetasol propionate 0.05% ointment daily).



Figure 5
Complete agglutination of the vaginal cavity.

Discussion

The data about the associations between OLP and vulvo-vaginal are diversified according to different studies. LP might manifest with coexisting lesions in various locations: skin, oral mucosa, and genital areas. It is believed that oral mucosa is often involved in patients with cutaneous LP. Bhattacharya et al. (24) reported mucosal lesions in 16.8% and genital ulcers in 5.2% of patients with cutaneous LP. Other Authors found that genital LP is present in approximately 25-50% of women and 5-25% of men with cutaneous LP lesions (24, 25). Kirtschig et al. (25) reported that mucosal vulval LP is more frequently associated with oral lesions than skin manifestations. Ebrahimi et al. (29), in a study of 120 patients affected by OLP, found the coexistence of oral and genital lesions in 40% of men and 53% of women. Scalp and nail lesions are rarely observed in patients with OLP; on the contrary, in a study of 584 patients with OLP the percentage of patients with coexisting scalp LP was 1.02% and nail involvement was 1.88% (30). There are also reports in the literature on LP lesions in the esophagus, the conjunctiva and the larynx (31-33).

The vulvovaginal-gingival syndrome is not a common form of LP. Erosive genital lesions can particularly be chronic, persistent and even painful. Epidermoid carcinoma might occur in longstanding genital lesions (34).

Accurate diagnosis and follow-up of any vulvar lesion is important, so it is recommended a multidisciplinary approach to the patient with VVG-LP, particularly when symptoms of vulvovaginitis are persistent. Knowledge of the impressive clinical spectrum of VVG-LP might help the clinician to recognize this common disease in its uncommon variations.

Other studies stated the correlation between OLP and periodontal disease. In fact it is known that periodontal therapy may improve clinical manifestation and patient discomfort related to OLP. Randomized clinical trials are needed to establish a two-way relationship between peri-

odontal disease and OLP. VVG-LP seems to be an autoimmune disease and may affect of prosthetic (35-38) and endodontic (39, 40) clinical outcomes.

Conclusions

VVG-LP is rather a rare condition and has been documented in the literature mainly in the form of case reports. Lack of a precise diagnostic criteria of VVG-LP depends on the specialists. Gynaecologists and dentists rarely exchange information in case of erosive lesions of genital and oral mucosa. On the other hand, patients seldom associate oral symptoms with cutaneous or genital lesions and are uncomfortable when talking about these with the doctor.

All this, taken together with the development of specific therapeutic protocols for OVVL, might certainly improve the quality of life of affected women and potentially avoid some neoplastic complications observed in our outpatients clinics.

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