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Oral Lichen Planus

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Idiopathic oral lichen planus is a chronic inflammatory disease that affects stratified squamous epithelium. It occurs within 1-2% of the population and has a higher incidence in women than men. Most patients with a form of oral lichen planus are over 40 years of age, although cases are seen in younger patients. Paediatric cases of OLP have been reported in the literature [Laeijendecker, Van Joost et al 2005, Alam and Hamburger 2001].

The clinical presentation of OLP can be broadly divided into three main categories:

1. The reticular form is the white lace-like pattern called 'Striae of Wickham' which may also have plaque or papular appearance. This is the most common variant seen clinically and is usually asymptomatic. [photograph 1]
2. The erythematous form (atrophic) is a diffuse erythematous change within the oral mucosa that is usually symptomatic. It is often reported by patients as having a burning or stinging quality, especially during eating of spicy or hot foods.
3. The erosive form (ulcerative) of OLP is the second most common clinical presentation. It is uncomfortable for the patient and is the usual reason a patient will seek treatment. The erosions vary in size, but have irregular margins and are shallow or superficial in depth. They often have adjacent tissue margins that are admixed with striae and erythematous regions. [photograph 2]

The most common intra-oral sites for OLP are the posterior buccal mucosa, gingiva, lower labial mucosa/vermillion border and ventral-lateral margins of tongue. It is seen as bilateral and symmetrical in most cases. Much less common sites for OLP are the floor of mouth and hard/soft palate. Approximately 10% of patients with OLP have only a gingival site involvement [Scully and el Kom 1985] which may present as either desquamative gingivitis or white/striae pattern admixed within an erythematous background.

In some cases, OLP can lead to post-inflammatory oral pigmentation within the affected sites, caused by melanin incontinence or the increased release of melanin into the affected epithelium/lamina propria.

There are also much less common associated inflammatory disorders in which lichen planus is seen in conjunction with other mucosal disorders such as lichen planus-pemphigoides disorder in which both the histopathological features of OLP and bullous

pemphigoid are seen following biopsy of a patient.

Lichen planus is also seen as a skin lesion in which 33% of patients will have both OLP and skin lesions. It presents as purple-violaceous papules that are often non-raised and may have associated striae of Wickham. Most skin sites can develop lesions, such as patient limbs and abdomen but a common site is the flexor surfaces of their wrists. They are pruritic (itchy) and it is not uncommon to confuse their appearance with the broken skin healing from patient scratching at the regions affected. [photograph 3]

The duration of lichen planus on the skin may well be self-limited over a period of 1-2 years, however the OLP form is chronic in nature and duration is unknown. The time frame in excess of 20 years is not uncommon, and the disorder varies both in its intensity relating to patient discomfort and the extent of oral site involvement.

Other extra-oral sites for lichen planus include the following:

1. Genital lichen planus in which annular striae or red papules are seen on the penis/scrotum areas or within the vulva/vagina. The affected vaginal mucosa sites are desquamated leading to vaginal bleeding in a lot of cases. A typical case of mucosal genital lichen planus the erythematous areas are surrounded by a lacy border, the striae of Wickham as seen in oral lichen planus [Kirtschig G et al 2005]. An association between the vulva, vagina and gingival lichen planus has been described in the literature as the (Vulvo-Vaginal-Gingival syndrome) [Pelisse 1989].
2. Ungual lichen planus is the longitudinal grooving and/or splitting of the distal or free end of the nail in either the patients' finger or toe nails [photograph 4].
3. Actinic lichen planus is the clinical presentation of blue-purple-brown papules on sun-exposed areas of skin. These sites may also include the face, scalp or forehead regions. They are non-pruritic and non-scaly. The sunlight is immunogenic, acting as a trigger for the chronic inflammatory reaction as seen in other muco-cutaneous disorders such as lupus erythematosus.
4. Lichen planopilaris is lichen planus affecting the scalp and hair follicles with resultant scarring alopecia.
5. Oesophageal lichen planus most commonly seen

in patients also with OLP. The major clinical presenting features are pain on swallowing and dysphagia. The untreated form of oesophageal LP may lead to strictures.

Histopathology of oral lichen planus

There are several distinguishing histological features [photograph 5] that permit the diagnosis of lichen planus. These are:

1. 'Saw tooth rete pegs' which is more often seen in skin LP rather than OLP. The rete pegs have a pointed or saw-tooth pattern with adjacent papillary lamina propria arching.
2. The epithelium can vary from severe thinning/atrophy as in the atrophic form of OLP to Hyperkeratinized and acanthotic (thickened epithelium) as in the plaque/reticular forms of OLP.
3. The features of liquefactive basal epithelial cell degeneration and adjacent eosinophilic (pink staining to the eosin dye) representative of fibrinogen deposits (inflammatory exudate). In addition, Civatte bodies which are well defined, apoptotic basal keratinocyte cells are also seen, but this phenomenon is not specific to lichen planus. No significant degree of epithelial atypia or dysplasia should be present for a diagnosis of OLP. In cases where a superimposed Candida infection is noted, treatment with an antifungal agent and repeated biopsy should confirm the absence of epithelial atypia for the diagnosis of OLP to stand.
4. The dense band of predominately T-cell lymphocytes within the adjacent lamina propria. The predominate T-cell population of CD-8 (confirmed by the expression in infiltrating lymphocytes of the chemokines CCR5 and CCR3 and their respective ligand RANTES/CCL5 and IP-10/CXCL) [Iijima et al 1993].

Aetiology of Idiopathic OLP

The term 'idiopathic' denotes the unknown cause or trigger for the development of OLP. The literature has over many years speculated on the basis of associations between different patient populations and potential aetiological causes such as:

Genetics:

In the Chinese population a weak association between patients with OLP and HLA-DR9 [Scully et al 1998]

Infective agents:

Bacteria such as gram negative anaerobic bacilli within dental plaque, has been shown to improve OLP when improved plaque control is implemented, such as in gingival OLP adjacent to restorations/cervical tooth margin [Holmstrup P et al 1990].

An hypothesis for the role of bacteria as a possible superantigen was discussed by Kawamura, E et al (2003) in which OLP lesional T cells were predominantly stimulated by nominal antigens and in minor T-cell populations stimulated by superantigens. These superantigens postulated by this research group were

bacterial antigens such as staphylococcal and streptococcal toxins and Mycoplasma-derived protein. The accumulation of T cells, which are located just below the basal membrane in OLP lesions, could indicate that the potential antigen is associated with the basal epithelial cells in OLP lesions.

Hepatitis C (HCV) association with OLP and active liver disease appears partially dependent on the geographical regions patients are studied. Patient groups reviewed from United States [Eisen 2002], Britain [Ingafou et al 1998] and Germany [Friedrich et al 2003] found no significant association between liver disease secondary to the HCV and OLP, whereas in both a Spanish study [Bagan 1999] and Japanese study [Tanei R et al 1995] a statistically significant number of patients with erosive OLP onset also had hepatitis C conversion and raised liver function test enzymes compared to patient control group. This lack of association with hepatitis C may be due to the low incidence of HCV in these populations. The HCV and OLP association is supported by the fact that HCV viral sequences have been found in OLP patients serum (suggestive of active viral replication/liver disease), and HCV was shown to occasionally replicate in oral lichen planus tissue, possibly contributing to the pathogenesis of mucosal damage [Carozzo et al 2003]. A study of 7 patients with both hepatitis C and OLP demonstrated that HCV-specific T-lymphocytes (CD8+ T-cells) were found in larger numbers within the mucosa of biopsied OLP lesions than in the peripheral blood of the same patients [Pilli et al 2002]. One hypothesis for this association is that HCV specific T cells are attracted into OLP lesional tissue by local antigen presentation, namely the hepatitis C virus.

Psychological disorders:

Few studies published. Patients with OLP may present with co-morbid anxiety, cancer phobia or depression which is also commonly seen in patients with other chronic pain disorders rather necessarily as an aetiological agent. Associations however between patient mood and clinical expression of OLP have been published [Chaudhary 2004; Ivanovski K et al 2005].

Essentially the diagnosis of OLP can be considered as:

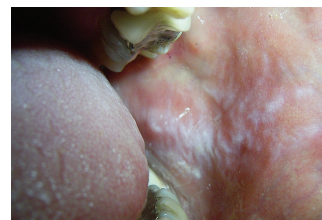
1. Idiopathic oral lichen planus
2. Oral lichenoid reaction
3. Idiopathic oral lichen planus exacerbated by a drug/or other trigger

Oral Lichenoid Reactions (OLR)

The diagnosis of an oral lichenoid reaction is where the cause for the oral mucosal changes which clinically and histologically are resemble OLP are identifiable with a known cause such as a medication.

The histological appearance between OLP and OLR can be difficult to discern, however OLR may have a more diffuse lymphocytic infiltrate which is more poorly defined, and contain eosinophils and plasma cells [Raghu A et al 2002].

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Photograph 1:
Reticular pattern of OLP with classic striae of Wickham only. This patient was asymptomatic



Photograph 2:
Erosive OLP involving both the attached and unattached gingiva. Note the subtle striae of Wickham and the superficial ulcer with an irregular margin adjacent tooth 22



Photograph 3:
Skin lichen planus lesions



Photograph 4:
Ungual Lichen Planus. Note the grooved surface of the nails and the splitting of nails towards the distal end.

An often described method of discerning a potential casual agent (e.g. a medication) is to withdraw the drug from the patient, and then observe the patient should any resolution of mucosal disease occurs. This might take up to a six month period. The drug is then re-commenced to observe if the OLR returns. This method is often fraught with problems and often impractical.

Aetiological agents associated with producing an OLR within the literature are:

Beta-Blockers	Dapsone
Angiotensin converting enzyme inhibitors	Cyclosporine
Calcium channel blockers	Levamisole
Thiazide diuretics	Simvastatin
Methyl dopamine	Tetracycline
Non-steroidal anti-inflammatory drugs	Acyclovir
Sulphenylurea	Ethambutol
Allopurinol	Isoniazid
Phenothiazines	Hydroxychloroquine
Carbamazepine	Penicillamine
Gold salts	Tamoxifen
Amalgam	Gold

Treatment

Patients with the reticular form of OLP and are asymptomatic, do not require active treatment, however regular review of their mouths is recommended.

Topical therapy is the mainstay treatment for symptomatic OLP. In particular is the use of topical steroid application. Patients are instructed in its frequency of use and varying potency creams or aerosolised steroid sprays can be used. The essential criterion for successful management of any OLP patient is to ensure the patient expectorates excess steroid after several minutes of its application and that they are applying it correctly. The use of betamethasone dipropionate 0.5mg/gm is the most frequently used cream, however selection of less potent creams may be warranted, or steroids applications as in intra-lesional injection of triamcinolone (e.g. Kenocort-A10) or customized oral rinse of dexamethasone (4mg/10mL) for more significant mucosal ulceration.

Side-effects such as mucosal atrophy is rare (unlike the skin) and essentially once the OLP is well controlled, a gradual reduction in frequency of application is recommended dependent if there is any relapse of patient discomfort. The use of a topical antifungal agent is often used given the possible increase in oral Candida loads while using the steroid therapy for prolonged periods (months/years).

Tacrolimus, a steroid free agent is a potent immunosuppressive agent and has been used in patients with recalcitrant OLP to topical steroids. Several uncontrolled studies have demonstrated effectiveness in the use of tacrolimus [Olivier et al 2002; Hodgson et al 2003], and also highlighted the variable degrees of systemic absorption

of this immunosuppressant drug. A recently issued US Food and Drug Administration public health advisory publication warned of the potential for tacrolimus as a carcinogenic drug and to be used in minimum amounts for a short period of time only. The studies linking squamous cell carcinoma of the skin and tacrolimus use was reported in paediatric patients.

Topical retinoids (Vitamin A) have been reported to be effective in the treatment of OLP [Sloberg et al 1979]. This treatment is particularly useful in the treatment of the plaque form of OLP because of its anti-keratinization role. Unfortunately its use can produce unpleasant burning within the site used, and in most cases cessation of drug will often result in the recurrence of the hyperkeratinized plaques.

Elimination of local trauma factors within the regions of OLP sites does help reduce the intensity of patient discomfort. The Koebner phenomenon is where mechanical (denture prosthesis rubbing on tissue sites; sharp teeth or restorations), chemical or thermal (tobacco usage) aggravate/exacerbate the development of erosive OLP and therefore patient discomfort. This may explain why erosive mucosal sites occur commonly in trauma prone sites such as within the buccal mucosa or lateral surfaces of the tongue.

Systemic drug therapy is described in the literature for the treatment of lichen planus. The problems with this approach are the chronic nature of OLP and therefore the need to maintain the drug therapy long term and potential side-effects from this form of therapy. Systemic therapy may have a role in the management of a patient in conjunction with topical therapy, for short periods.

A major controversy regarding oral lichen planus is its premalignant potential. In the next magazine edition, I will present the controversies associated with this long held view. ♦

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QUESTIONS FOR CDP POINTS

- Two common clinical presentations of oral lichen planus seen are: _____ and _____
- Three histopathological diagnostic features associated with oral lichen planus are: _____; _____; and _____
- The evidence described in the literature for an association between oral lichen planus and hepatitis C is: _____ and _____
- Define an oral lichenoid reaction? _____

- List four causes for an oral lichenoid reaction _____; _____; _____; and _____
- What is the Koebner effect? _____
- List two forms of therapy used for the treatment of oral lichen planus? _____ and _____

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