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PLENARY ABSTRACT

Lichen Planus and Lichen sclerosus: new insights

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Lichen planus is a common inflammatory interface dermatosis, that has multiple mucosal and skin manifestations and so may present to many different specialities: oral medicine or surgery and dentistry, dermatology, gynaecology and genitourinary medicine. This has hampered management and research into the condition.

Involvement of the skin is one of the most common manifestations and is usually accompanied by itch, typically presenting as purple plaques with the white streaks of Wickham's striae, sometimes the plaques may be thickened to form hypertrophic lichen planus, and rarely areas may erode and ulcerate. Variants include lichen plano-pilaris with involvement and destruction of hair follicles and the micropapular form lichen nitidus. Scalp involvement results in destructive scarring. Similarly nail involvement may cause scarring with fusion of the cuticle to the nail plate and loss of the nail.

Oral involvement may present with a lacy white pattern on the buccal mucosa and elsewhere. Desquamative gingivitis and oral erosive disease are less common but very troublesome manifestations and can be difficult to distinguish from mucous membrane pemphigoid. Oesphageal involvement occurs and leads to strictures and dysphagia.

Vulval lichen planus may be clinically similar to the skin involvement, however vulval erosive lichen planus is more common and similar to erosive oral disease, with whitening, painful erosions and also scarring. The scarring can be severe and result in complete loss of vulval architecture with difficulties with intercourse and micturition. It can be impossible to distinguish it clinically from vulval lichen sclerosus. A minority of erosive lichen planus patients also have skin involvement (Kirtschig *et al*., 2005). In addition some have vaginal involvement with desquamative vaginitis and vaginal stenosis, the oral vulval vaginal syndrome.

Rare sites involved include the ears and lacrimal ducts.

Lichen planus can be seen in association with the subepidermal bullous dermatoses. When bullous pemphigoid arises in the setting of lichen planus this is called lichen planus pemphigoides and oral lichen planus has been described arising in long standing subepidermal blistering diseases. Interestingly in both these situations the target antigen for the circulation basement membrane antibodies is BP180/BPAg2/collagen XVII.

Erosive Lichen planus and lichen sclerosus of the vulva are both diseases of postmenopausal women and may be difficult to differentiate clinically and histologically and may appear to convert from one to the other over time. They are both associated with autoimmune disease (see table 1) (Cooper *et al*., 2008).

Lichen planus and lichen sclerosus are interface dermatoses with involvement of the basement membrane zone, a lymphocytic infiltrate and altered expression of basement membrane zone components (Marren *et al*., 1997; Cooper *et al*, 2005). T lymphocytes play an important role in the induction and regulation of specific immune responses including the production of autoantibodies against naturally occurring antigens as well as T cells in cell-mediated autoimmune diseases. Studies have demonstrated the presence of a predominantly T cell infiltrates (CD4 + and CD8 +) in the dermal band of inflammatory cells in patients with vulval lichen planus and lichen sclerosus but little is known of their antigen specificity. There is evidence from our recent work that the NC16A epitope of BP180 is a target for T cell responses in both these diseases. (Baldo *et al*., 2009). In addition circulating basement membrane zone antibodies, chiefly targeting BP180 have been described in both these condition, and provide evidence for a B cell response to basement membrane zone components (Howard *et al*., 2004; Cooper et al, 2005; Baldo *et al*, 2010a). Thus there is evidence from our recent work that the NC16A epitope of BP180 elicits B and T cell responses in both these diseases which suggests that autoimmunity to basement membrane components by T cells and B cells contributes to the pathogenesis of lichen sclerosus and lichen planus.

Table 1 The Association of Erosive Lichen Planus and Lichen Sclerosus of the Vulva with Autoimmune Disease: a Case-Control Study

	Lichen Planus	*Lichen sclerosus*	*Controls*	P *value LP vs Controls*
Autoimmune disease	29%		9%	p < .001
Thyroid disease	15%	16%	8%	p < .001
Pernicious anaemia	1%	4%	0.1%	
Alopecia areata	4%	3%	0.1%	p < .001
Thyroid antibodies	19%		9%	p < .001
ANA	25%		9%	p < .001
Family history autoimmune disease	30%	30%	Not known	

Adapted from Cooper *et al*, 2008

Table 2 LP patients with positive NC16A–specific T cell response and circulating BMZ autoantibodies showing target antigens identified

Patients	*T Cell Response*	*Autoantibodies IIF*	*IB ELISA (molecular weight)*	
Lichen planus with positive T cells				
LP	+	+	+ **BP180 BP 230**	–
LP	+	+	–	–
Lichen planus with negative T cells				
LP (N = 3)	–	–	–	–

Key: Positive T cell responses in bold
IIF Indirect immunofluorescence; IB Immunoblotting;
N Number negative for Tcell responses
Adapted from Baldo *et al*., 2009

The auto-reactive T cells targeting the NC16A domain may play a significant role in the pathogenesis of vulval lichen planus and lichen sclerosus, although this finding needs further larger studies to determine if T cells are specifically associated with lichen sclerosus and lichen planus, or secondary to basement membrane zone damage, as both are interface dermatoses characterised by basement membrane zone inflammation and damage.

Interestingly both vulval lichen planus and lichen sclerosus are associated with the development of vulval cancer and it may be that oxidative stress which has been demonstrated in both these conditions could be contributing to carcinogenesis and also to the susceptibility to autoimmune disease and auto-reactivity to the basement membrane zone (Sander *et al*., 2004; Sander *et al*., 2005).

It is therefore possible to construct a speculative hypothesis for the pathogenesis of lichen planus of the vulva and possibly elsewhere. An antigen in the epithelium (for example hepatitis C in Latin countries) stimulates an immune reaction which by epitope spreading leads to an autoimmune B and T cell reaction to basement membrane components, chiefly BP180. This would accord with the band of lymphocytes at the BMZ and the BMZ destruction so characteristic of lichen planus. In some cases a B cell reaction may become prominent resulting in lichen planus pemphigoides, and in longstanding immunobullous disease the reverse occurs with T cell auto-reactivity to BP180 arising and being manifest clinically as oral LP.

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