CD44 EXPRESSION IS DECREASED IN LICHEN SCLEROSUS

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Introduction & Objective

INTRODUCTION

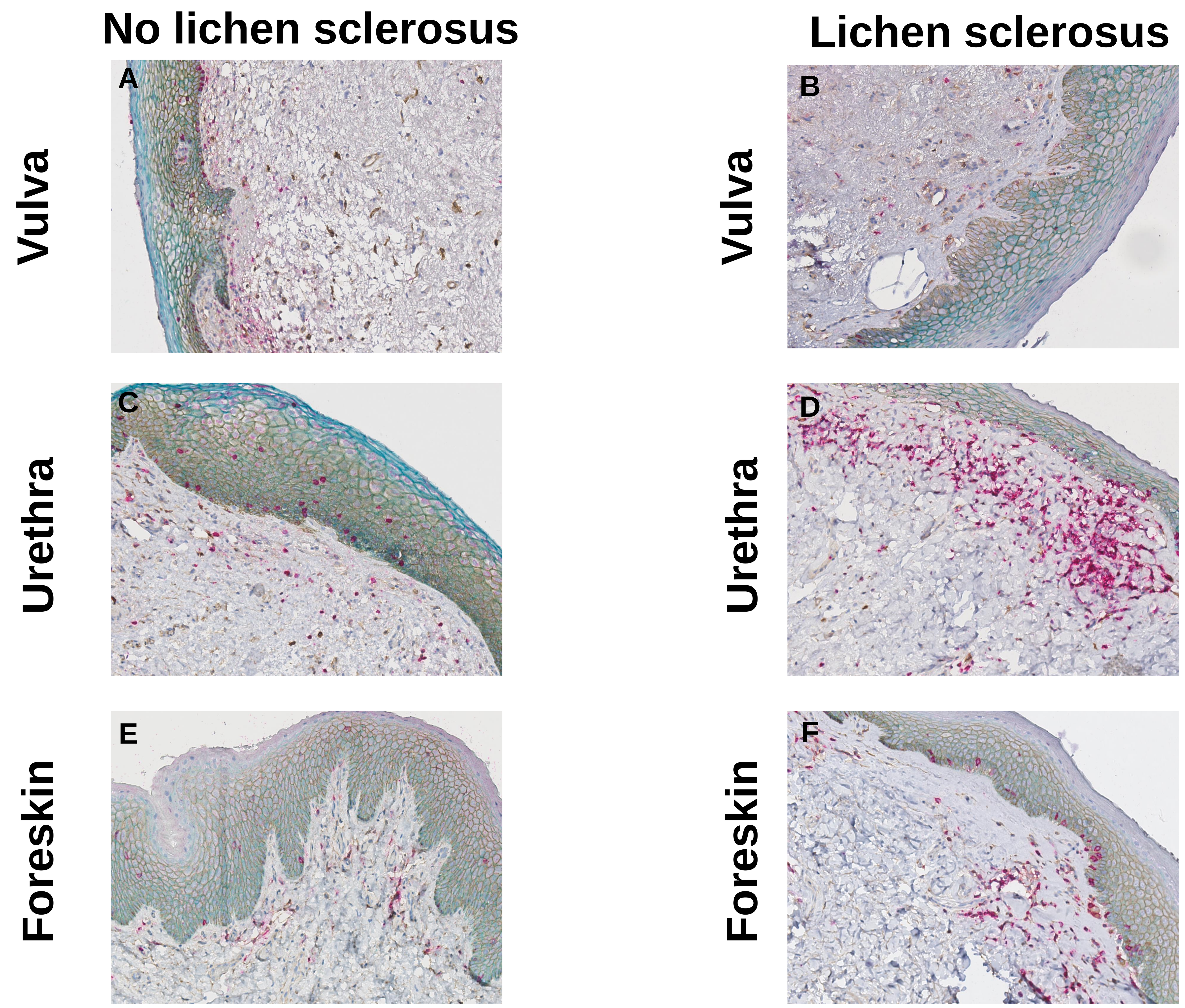
- Lichen sclerosus (LS) is an idiopathic chronic inflammatory disease which causes severe urethral stricture disease in affected men
- Decreased CD44 expression has been observed in female LS but is uncharacterized in men
- Reduced CD44 expression results in impaired epithelial barrier function through altered tight junctions which may drive chronic inflammation and fibrosis in LS

Decreased CD44 expression
↓
Impaired epithelial barrier
↓
Increased exposure to immunogenic and chemical irritants (urine)
↓
Chronic inflammation/fibrosis
↓
Lichen sclerosus

OBJECTIVE

To test the hypothesis that epithelial CD44 expression is decreased in human LS compared to non-LS tissues

Results



CD44 Optical Density by Tissue Type

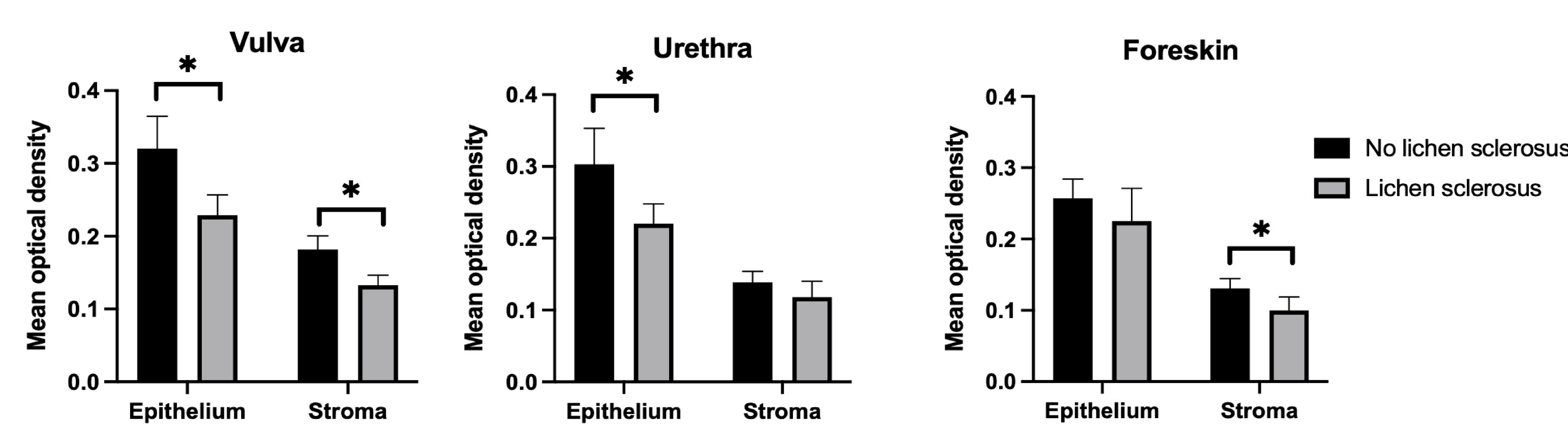


Figure 1. Results of multiplexed immunohistochemical staining to quantify CD44 staining. (A-F) Representative photomicrographs (20x) of vulvar (A), urethral (C), and foreskin (E) tissues without LS compared to the same tissue types with LS (B, D, F). LS tissues display typical pathologic findings including epidermal atrophy, loss of dermal rete pegs, dermal collagen deposition, and inflammatory infiltrate (B, D, F). There is also visible reduction in CD44 staining (brown) in the LS compared to non-LS samples. (G) Quantative comparison of mean optical density of CD44 staining in epithelial and stromal tissue compartments. Vulvar samples with LS demonstrate reduced CD44 staining in both epithelial and stromal compartments. Urethral samples with LS have reduced epithelial CD44 expression but similar stromal expression. LS foreskin has reduced stromal CD44 expression with similar epithelial expression. when all tissue types are pooled, there is a significant reduction in both epithelial and stromal CD44 expression (not shown). Asterisks indicates statistical significance at $p<0.05$. LS = lichen sclerosus

Methods

Subject identification

- Patients undergoing vulvar biopsy, circumcision, urethral biopsy, or urethroplasty with available surgical pathology
- Excluded active malignancy
- Re-reviewed with GU pathologist to confirm LS diagnosis

	LS (n=29)	Control (n=23)
Gender		
Male	20	14
Female	9	9
Tissue Type		
Vulva	9	9
Urethra	7	7
Foreskin	13	7

Table 1. Demographic and clinical information of included lichen sclerosus and control patients

Immunohistochemistry

- *Quantify CD44 expression in epithelial and stroma*

Image Analysis

- 3 ROIs per slide, segmented into stroma and epithelium, CD44 expression quantified as mean optical density

Statistical Methods

- *Mean OD reflecting CD44 expression were compared in each histologic compartment between LS and non-LS patients*

Discussion

- CD44 expression is decreased in LS tissues
- Diminished CD44 expression is associated with altered tight junctions resulting in impairment of epithelial barrier function in other diseases
- This suggests that increased epithelial permeability may drive chronic inflammation in LS through increased exposure to chemical and immunogenic irritants
- Future directions will characterize alterations in tight junction protein expression in LS and any modulating effect of corticosteroid administration