DECREASED CD44 EXPRESSION IS ASSOCIATED WITH INCREASED HYALURONIC ACID ABUNDANCE IN HUMAN LICHEN SCLEROSUS

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NIH-NIDDK
CAIRIBU 2020 Annual Meeting

Introduction & Objective

INTRODUCTION

- Lichen sclerosus (LS) is a poorly understood inflammatory condition of the genital skin affecting 1:300 adults
- Men with LS develop severe urethral stricture due to profound fibrosis which fails surgical management in >50% of cases
- Female cutaneous LS lesions display:
  - increased stromal hyaluronic acid (HA) deposition which is known to drive inflammation and fibrosis in other diseases
  - decreased epidermal CD44 expression which is the principal receptor responsible for HA degradation
- These changes have not been characterized in male patients nor urethral tissue
- Therefore, we propose that decreased CD44 expression may cause HA accumulation and drive inflammation and collagen deposition in LS related urethral stricture

OBJECTIVE

- To test the hypothesis that epithelial CD44 expression is decreased and stromal HA abundance increased in LS compared to non-LS tissues

Methods

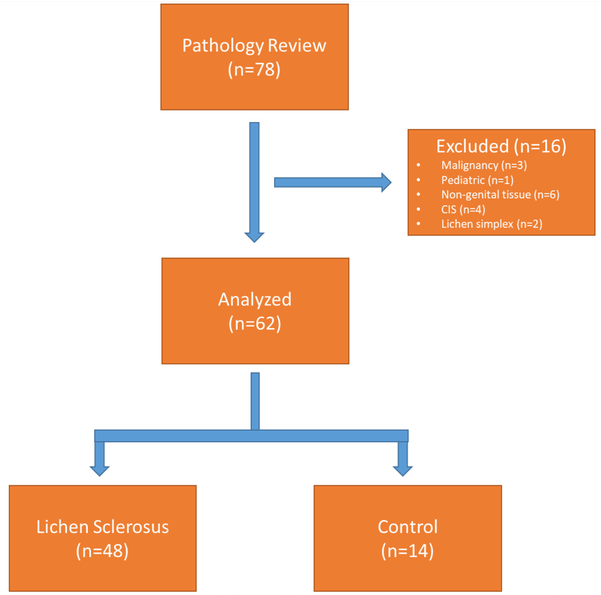

Figure 1. *Schematic of patients included in the study. Patients were identified through review of pathology records after circumcision, urethral biopsy, urethroplasty, buried penis repair, penile biopsy, or vulvar biopsy. Patients with concurrent malignancy or carcinoma in situ, lichen simplex, pediatric patients, and non-genital tissue were excluded. Review of pathology reports identified 46 patients with pathologic diagnosis of lichen sclerosus and 14 controls without lichen sclerosus.*

Immunohistochemistry

Quantify CD44 expression and HA abundance in three histologic compartments:

- *Epithelial (+ e cadherin)*
- *Inflammatory (+ CD45)*
- *Stromal (- e cadherin, - CD45)*

Image Analysis

- 6 ROIs per slide (2 ROIs per compartment)
- *CD44 expression and HA abundance quantified as mean optical density in each compartment*

Statistical Methods

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

Results

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

	Lichen Sclerosus (n=48)	Control (n=14)
Gender, no (%)		
Male	24 (50)	4 (29)
Female	24 (50)	10 (71)
Procedure Type, no (%)		
Circumcision	9 (19)	1 (7)
Urethral Biopsy	3 (6)	1 (7)
Urethroplasty	4 (8)	1 (7)
Buried Penis Repair	7 (15)	0
Penile Biopsy	1 (2)	1 (7)
Vulvar Biopsy	24 (50)	10 (71)
Tissue Type, no (%)		
Foreskin	9 (19)	1 (7)
Urethra	7 (15)	2 (14)
Penile shaft skin	8 (17)	1 (7)
Vulva	24 (50)	10 (71)

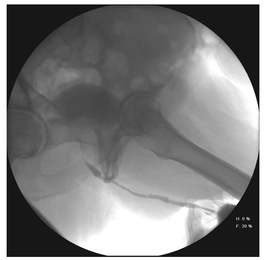

Figure 2. Representative clinical images of lichen sclerosus related urethral stricture disease. A retrograde urethrogram demonstrates the characteristic involvement of the entire male anterior urethra with sparing of the proximal bulbar urethra (A). Intraoperative photograph of the characteristic whitish discoloration of the periurethral glans penis with meatal stenosis (B).

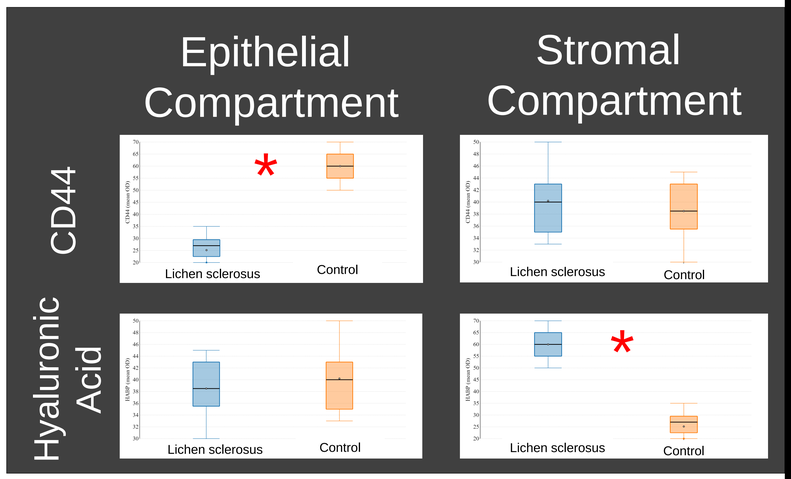

Figure 3. Expected results of comparison of optical density of CD44 (A and B) and hyaluronic acid staining (C and D) in the epithelial (A and C) and stromal compartments (B and D). Consistent with our hypothesis, we expect that mean epithelial CD44 expression will be lower in lichen sclerosus patients compared to control (A), and stromal HA abundance will be higher in lichen sclerosus compared to control (D). Red asterisk indicates $p<0.05$.

Discussion

We expect our quantitative approach to demonstrate downregulation of epidermal CD44 expression and increased stromal HA accumulation in human LS. These data will provide a foundation to support the overarching hypothesis that CD44 dysregulation drives HA accumulation and propagation of inflammation and fibrosis in LS and related urethral stricture disease.