

Protein expression profiles among lichen sclerosus urethral strictures: Can urethroplasty success be predicted?

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INTRODUCTION: Urethroplasty is a well-supported and efficacious treatment option for male urethral stricture disease (USD). Lichen sclerosus (LS) is a chronic scarring condition that damages the urethra in many men with the disease. Strictures due to LS are often refractory and will recur at rates of 25- 71% after surgical reconstruction, compared to 8-18% of strictures due to other causes. We sought to determine predictors of urethroplasty failure in men with LS USD by evaluating protein expression profiles.

METHODS: Urethral tissue samples from non-consecutive patients with pathologically diagnosed LS undergoing urethroplasty for USD at a single institution were collected. A tissue microarray was created with cores from each sample and immunohistochemistry was performed for markers of inflammation, infection, cell cycle disruption, hormone receptor expression, and angiogenesis/oxidative stress. Patient demographics, stricture characteristics, type of urethroplasty, and clinical follow up data were collected. Stricture recurrence was defined by need for a subsequent procedure. Data were compared using R with significance of $\alpha=0.05$.

RESULTS

Fifty-eight men with LS urethral strictures who underwent urethroplasty were included in analysis. Thirty-four patients had successful reconstruction while 24 experienced stricture recurrence after urethroplasty. Median time to stricture recurrence was 25 months. Baseline demographics and comorbidities were not significantly different between groups. Median length of recurrent strictures was 8.0cm compared to 7.5cm in those that did not recur ($p=0.089$). Recurrent strictures were less likely to express IL-1b (4% vs. 27%, $p=0.0336$) and also less likely to express IgM than non-recurrent strictures (26% vs. 50%, $p=0.1$). Recurrent strictures expressed lower levels of Ki-67, but this did not reach significance. Recurrent strictures expressed significantly higher levels of VEGF ($p<0.001$).

CONCLUSIONS.

LS urethral strictures that recur after urethroplasty have different protein expression profiles compared to those from successful reconstructions. Further research is needed to clarify the role of these proteins in the pathophysiology of the disease. Better understanding of LS USD may help identify the patients preoperatively who are more likely to fail reconstruction and give insight into alternative or adjunct treatment.