Title
Editorial Comment.

Journal
Investigative Urology, 201(6)

ISSN
0021-0005

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Publication Date
2019-06-01

DOI
10.1097/01.ju.0000554665.15506.cb

Peer reviewed

The Koebner phenomenon describes the susceptibility to scarring of previously traumatized tissues. One potential trauma is infection, which has been suggested as a potential instigator in the development of LS.[13–15] Untreated gonorrhea is known to lead to strictures and prior studies have implicated *Borrelia burgdorferi* in LS.[3] Although our data do not reveal a direct link between infection and LS USD, we found that significantly more LS USD samples stained positive for latent Epstein-Barr virus RNA. Although they are rare, we identified block-like p16 staining and VZV only in LS USD. We believe that our exploratory findings warrant further investigation of other potential infectious agents which may have a role in the development of LS USD.

Our study has several notable weaknesses. This was an exploratory study designed to generate hypotheses for further investigation. Samples were collected from a single institution which is a tertiary referral center for urethral stricture disease, which may represent a more severe phenotype than those typically encountered in practice. Although considerable efforts were made to select tissue samples which were representative of active disease, TMA uses small cores of tissue, which limited our results. Our study is also limited in that it was observational and, therefore, did not address disease progression with time.

CONCLUSIONS

To our knowledge this is the first study investigating the histopathology of LS USD. LS urethral strictures demonstrate increased local inflammatory cells and cytokines compared to nonLS USD. Markers of oxidative stress, cell cycle dysregulation and loss of androgen receptor expression do not appear to be uniquely associated with LS USD. Positive staining for several viruses in LS USD samples suggests a possible infectious etiology. Further study and larger cohorts are needed to validate the findings of this exploratory analysis and further elucidate the pathophysiology of USD and to direct investigation of future treatment.

ACKNOWLEDGEMENTS

Drs. Jason Badrinarain and Jorge Yao, Pathline Emerge, Ramsey, New Jersey, were study collaborators. TMAs were created at the Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland. HPV analysis of block-like p16 staining samples was done at ProPath®, Dallas, Texas.

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EDITORIAL COMMENTS

Levy et al explored protein expression in LS induced USD tissue. LS USD is a terrible disease and different from other USDs. The tissues are more fibrotic and surgical results are poor with time.[1] In the patient with LS the systemic milieu seems to drive the disease (reference 2 in article). Using

tissue microarray the authors examined a variety of possible LS USD causative pathways.

Basic science is critically needed in reconstruction, where we lag behind others in urology. There is tremendous potential for new knowledge creation, better disease understanding and therapeutic breakthroughs. Case series and population based studies will only take us so far. Reconstruction needs more basic and translational research to move the field forward. It is encouraging that the AUA (American Urological Association) created the Physician Scientist Residency Training Award. We need to grow more physician-scientists. They will be best equipped to help us understand disease pathophysiology and develop the transformative therapies of the future. If we fail to do better, we will be stuck offering the same treatments for a disease with a clearly different cause and course.

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Lichen sclerosus associated urethral stricture disease is common in all parts of the world. In the Asian subcontinent we see more patients with LS urethral stricture. However, the true incidence of LS and associated urethral stricture is unknown.[1] LS can cause scarring, urethral stricture, sexual problems and decreased quality of life for patients.

This stricture disease can be in the meatus, the penile urethra, the bulbar urethra or panurethral. There are many theories about stricture in those with LS and the authors tried to find a correlation between various factors and LS. The most accepted theory so far is autoimmune. However, we are aware of the latest studies, which have tried to point at infective etiologies.

Not all patients with LS have stricture. Patients with LS who undergo endoscopic procedures like ureteroscopy and transurethral prostate resection remain at higher risk for a urethral stricture.

Stricture due to LS in any part of the urethra should be treated differently from other etiologies. This is a genital skin disease and the use of local skin as a graft or a flap is contraindicated. There is a contrasting opinion to excise all urethral tissue in penile urethral stricture cases and perform 2-stage buccal mucosa graft urethroplasty. In our multicenter experience urethral surgeries in patients with LS should be 1-stage buccal graft augmentation urethroplasty instead of staged procedures.[2,3]

The recurrence rate of stricture in LS cases is higher than for other etiologies. The recurrence rate of LS urethral stricture may be minimized once we have an answer to the exact etiology, leading to preventive medicine.

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