SIU/ICUD Consultation on Urethral Strictures: Anterior Urethra—Lichen Sclerosus

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We reviewed the current literature on lichen sclerosus as it related to urethral stricture disease using MEDLINE and PubMed (U.S. National Library of Medicine, National Institutes of Health) up to the current time. We identified 65 reports, 40 of which were considered relevant and form the basis of this review. Lichen sclerosus is now the accepted term, and balanitis xerotica obliterans is no longer acceptable. This common chronic inflammatory skin condition, mainly affecting the genitalia, remains an enigma, with uncertain etiology, varied presentation, and multiple treatments. In the early stages of the condition, a short course of steroids may be beneficial for some patients. If persistent, patients need long-term surveillance because of the potential development of squamous cell carcinoma. If diagnosed early, lichen sclerosus can be controlled, preventing progression. But once the disease has progressed, it is very difficult to treat. Surgical treatment by circumcision can be curative if the disease is treated early when still localized. Once progression to urethral involvement has occurred, treatment is much more difficult. Meatal stenosis alone is likely to require meatotomy or meatoplasty. Treatment of the involved urethra requires urethroplasty. Single-stage and multiple-stage procedures using oral mucosa have both been reported to give acceptable results, but the use of skin, genital or nongenital, is not recommended, because being skin, it remains prone to lichen sclerosus. With extensive disease, affecting the full length of the urethra, consideration should be given to perineal urethrostomy. A significant number of patients may prefer this simpler option. UROLOGY 83: S27–S30, 2014.

Lichen sclerosus (LS) is a chronic inflammatory, hypomelanotic, lymphocyte-mediated skin disorder, which in men involves the prepuce and glans, and frequently leads to phimosis, meatal stenosis, and urethral strictures.

LS was first described in 1875 by Weir.[1] In 1928, Stühmer coined the term balanitis xerotica obliterans and proposed a traumatic etiology.[2] The International Society for the Study of Vulvar Disease has formally adopted the term lichen sclerosus,[3] and this committee recommends that the term LS also be used in men instead of balanitis xerotica obliterans.

ETIOLOGY

The etiology of LS remains unknown, but an autoimmune mechanism seems most likely. Autoantibodies to extracellular matrix protein 1 (ECM-1) were detected in the serum of 67% of LS patients and in only 7% of the control group.[4] Oxidative damage of lipids, deoxyribonucleic acid, and protein in LS patients may explain the mechanism of sclerosis, autoimmunity, and carcinogenesis of LS.[5]

There is no significant genetic basis for LS, although 11% of patients with LS do have a family member also affected.[6]

Some reports have linked LS to *Borrelia burgdorferi*, but a recent case-control series found no association.[7]

EPIDEMIOLOGY

The estimated prevalence is 1 in 300 to 1 in 1000. Traditionally, the peak incidence was reported in men aged 30-50 years, but a contemporary male epidemiologic study reported a much earlier peak at 21-30 years.[8] Generally considered to be much more common in females and Caucasians,[9] a recent publication, however, showed the incidences in black and Hispanic male populations to be double the incidence among white males.[8]

CLINICAL FEATURES

LS in males affects the foreskin and glans in 57%-100% and the meatus in 4%-37%, with involvement of the urethra in approximately 20% of patients.[10,11] Extragenital presentation is rare. The whitish appearance of the skin is secondary to decreased melanin production and loss of melanocytes.[12] Disease progression may lead to phimosis and urethral stricture consequent upon high pressure voiding, with reflux of urine into the urethral glands of Littré producing inflammation and fibrosis.

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DIAGNOSIS

Diagnosis of LS remains primarily clinical and histologic. An assay for circulating autoantibodies to ECM-1 was recently shown to be a possible indicator of disease severity.[13]

HISTOLOGIC DIAGNOSIS

In the early stages of LS, hydropic (vacuolar) degeneration of the basal cell layer is seen, with edema of the papillary and reticular dermis along with inflammatory infiltrate (of lymphocytes) at the dermoepidermal junction. Hyperkeratosis and stratum malpighii atrophy are seen in the late stages.

The differential diagnosis includes lichen planus, vitiligo, psoriasis, and carcinoma in situ.

PROGNOSIS

A recent epidemiologic study in the United Kingdom suggests that early treatment may prevent the development of severe symptoms and possibly allow patients to avoid surgery.[11]

MALIGNANT POTENTIAL OF LS

The premalignant potential of LS of the vulva has been well recognized for some time.[14]

Several studies have looked at penile cancer series and found LS present in 28%-50% of patients. LS was associated with low grade and stage cancers.[15,16]

Amongst patients presenting with LS, penile cancer was occurred in 2.3%-8.4%. The mean time from LS diagnosis to penile cancer was 12 years, suggesting the need for long-term surveillance.[10,17]

MEDICAL MANAGEMENT OF LS

Traditional nonsurgical treatment for LS consists of topical steroids or emollients to alleviate the skin manifestations of the disease. In severe disease, a biopsy specimen may be necessary to confirm LS and the absence of squamous cell carcinoma. Steroid administration inhibits the chronic inflammatory response, and in a study of 40 boys, produced clinical improvement in 41%.[18]

Although the ideal topical agent has not yet been determined, clobetasol propionate (0.05%), twice daily for 2-3 months with gradual dose reduction, has been used successfully,[19] as have betamethasone (0.05%), mometasone (0.1%), and hydrocortisone (2.5%-10%).

The significant side effects of these medications must always be considered. Potent steroids should be avoided in children, and patients instructed to wash their hands after use to prevent contact with other sensitive areas (eg, the eyes) and to prevent partner exposure.

The macrolide-derived immunomodulator tacrolimus (FK506) has been used topically with success in LS involving the glans and penis.[20] Tacrolimus works by inhibiting the production of interleukin-2 and the subsequent T-cell activation. A great deal of data are available on its use in psoriasis, but minimal data exist on its use in LS.

Topical testosterone has also been reported to have a beneficial effect but has not been extensively studied in men with LS.[21] Studies have shown that clobetasol was still superior to testosterone propionate.[22]

Retinoid acitretin, the systemic aromatic, has also been studied in patients with severe LS resistant to topical steroid.[23] A dose of 35 mg daily for 20 weeks produced a 36% complete and 36% partial response compared with 6% and 13% in the control group. Side effects are common, however, including cheilitis (dry, cracking lips) in 75% of patients and skin peeling in 48%.

NONSURGICAL MANAGEMENT

Photodynamic Therapy

Photodynamic therapy using the Diomed 630 laser after giving the photosensitizing agent 5-aminolevulinic acid resulted in a 38% complete resolution in women with vulvar LS.[24]

The carbon dioxide (CO_2) laser has been used successfully to treat patients with LS that do not involve the meatus or the urethra. Re-epithelialization occurred by 6 days after treatment.[25]

SURGICAL MANAGEMENT

There is no surgical gold standard for the treatment of urethral strictures in patients with LS. All recommendations have been based on nonrandomized studies and expert opinion. Surgical management depends on the progression of disease and consists of circumcision, meatal dilation, meatotomy, and urethral reconstruction.

Circumcision

When confined to the prepuce, circumcision results in long-term cure in 92% of patients.[10] If LS recurs after circumcision, a repeat circumcision is not recommended, because it can lead to buried penis and severe phimosis, making further treatment more difficult.

Meatotomy

Meatal stenosis can lead to significant complications. Simple meatotomy is generally ineffective in patients with LS. However, an extended meatotomy in patients with refractory stenosis was successful in 87%.[26] Malone described a novel ventral/dorsal meatotomy with an inverted V relaxing incision. No recurrences or fistulas were reported. Satisfaction with the procedure from a cosmetic standpoint was also good, with 100% of patients pleased with their cosmesis, and only 15% complained of spraying.[27]

Urethral Reconstruction

When LS involves more than just the meatus, urethral reconstruction must be considered. Flap repairs using genital skin has been described. Although the initial success was encouraging, recurrence rates have been unacceptable

with longer follow-up, reaching 50%-100%.[28,29] Currently, the use of genital skin is not considered to be appropriate. Being skin, it remains prone to the same disease process.

Being nonskin, oral mucosa grafts has proven to be the tissue of choice as a 1- or 2-stage procedure. Oral mucosa has a pan-laminar plexus, which allows it to be thinned, while preserving beneficial physical characteristics without adversely affecting vascular characteristics. The use of the lingual mucosal graft as a dorsal graft in a single-staged procedure achieved an 83% success rate.[30]

One-stage urethral reconstruction with a dorsal graft can be performed if the urethral lumen is >6F. For strictures in the penile urethra, a circumferential incision is made, and the penis is degloved. If the stricture extends beyond the penoscrotal junction, a midline perineal incision is used. The urethra is dissected from the corpora cavernosa along the entire length of the stricture. A dorsal urethrotomy is performed, the oral mucosal graft is secured to the corpora cavernosa, and the urethra is secured to the graft. Dubey et al[31] showed good results using this technique: 22 of 25 patients (88%) had success at a mean follow-up of 32.5 months. Kulkarni et al[32] confirmed these good results with a 91% success rate with a mean follow-up of 38 months.

In a 2-stage reconstruction, a midline penile incision is made along the full length of the urethral stricture. Complete urethral plate excision is usually recommended, due to the involvement of LS in the remaining urethra. The first stage involves securing the oral mucosa graft to the tunica albuginea. The second stage, tubularization, is performed 6-12 months later. Success rates of the 2-stage approach vary from 72%-82%.[32,33]

It is not always appropriate to reconstruct the urethra, and a perineal urethrostomy should be considered in patients with the most severe disease. Perineal urethrostomy success rates vary from 72%-100%.[32,33]

CONCLUSION

Lichen sclerosus is now the accepted term, and balanitis xerotica obliterans is no longer acceptable. A short course of topical steroids may be beneficial for some patients. Patients with persistent LS need long-term surveillance because of the possible development of squamous cell carcinoma.

If diagnosed early, LS can be controlled, preventing progression, but once the disease has progressed, it is very difficult to treat. Surgical treatment can be curative if the disease is treated early. The use of genital skin is not recommended in patients with urethral involvement. Oral mucosa grafts have been shown to be successful in patients with LS, although long-term data are not yet available.

RECOMMENDATIONS

1. The accepted term for this condition is lichen sclerosus (LS) and the term balanitis xerotica obliterans should no longer be used (Level A).
2. The use of short-term topical steroids should be considered in patients with early LS (Level A).
3. Circumcision can be used for LS confined to the foreskin or glans (Level A).
4. Genital skin should not be used for urethral reconstruction in patients with LS (Level A).
5. Long-term follow-up in patients with persistent LS is required to evaluate the patient for malignant transformation (Level B).

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