Extragenital bullous lichen sclerosus

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Lichen sclerosus is an inflammatory skin condition characterized by inflammation of the papillary dermis that leads to white scarlike plaques. It occurs classically in the genitals but also has extragenital manifestations with a variety of clinical presentations including a bullous variant. The purpose of this review is to characterize extragenital bullous lichen sclerosus, suggest that it may be more common than dermatologists realize, and discuss treatment of both routine and recalcitrant cases. (J Am Acad Dermatol 2014;71:981-4.)

Key words: bullous; cyclosporine; extragenital; lichen sclerosus; methotrexate; treatment.

Lichen sclerosus (LS) is an inflammatory skin condition characterized by white scarlike plaques. LS occurs classically in the genitals but also has extragenital manifestations. Scattered throughout the literature are "atypical" cases of bullous genital and extragenital LS.

Extragenital bullous LS is traditionally thought of as a rare variant of LS; however, no good epidemiologic studies have been done to support this idea. Given the number of case reports of extragenital bullous LS, the assumption that it is a rare variant may not be accurate. The purpose of this review is to characterize extragenital bullous LS and discuss a therapeutic ladder for this often difficult-to-treat disease.

Abbreviations used:

BMZ: basement membrane zone
LS: lichen sclerosus
UV: ultraviolet

EPIDEMIOLOGY

Classic genital LS is an uncommon disease with a prevalence difficult to estimate because of: (1) underreporting; (2) multiple names, including blurring of LS with morphea before 1940; (3) management by both dermatology and gynecology; and (4) asymptomatic presentations. A prevalence of 0.1% to 0.3% of patients was calculated by Wallace[1] in 1971. Studies have reported contradicting female:male ratios ranging from 10:1 to 1:1. In women, there is a bimodal distribution occurring prepubescently and postmenopausally. In men, the disease typically manifests in the fourth decade.[2]

Extragenital involvement of LS has been estimated between 15% to 20% of all patients with LS.[3] However, to our knowledge, there have been no reports on the epidemiology of extragenital bullous LS. A literature search was performed using PubMed, yielding 26 reports with a total of 31 patients dating from 1936 to present.[4-29] A 32nd patient is reported in this review (see "Treatment" section). The female:male ratio was 7:2 with an average age of 62 years, similar to classic genital LS. More than half (18) of the reported cases were within the last 22 years from 1992 to present; the remaining 13 cases were reported in the preceding 56-year period (1936-1992). The low number of cases found in the literature, especially prior to 1992, is likely a result of the aforementioned difficulties in identifying the prevalence of LS. Although this literature review does not show any trend, the number of cases reported (31), especially during the last 22 years, might suggest that extragenital bullous LS is more common than dermatologists may realize.

PATHOGENESIS

The origin of genital LS is unknown. Theories include: genetic predisposition, autoimmunity, trauma,

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infection, and hormonal abnormalities. Currently, autoimmunity in predisposed individuals is favored.

Several circulating antibodies have been found in a greater proportion of patients with LS than in control subjects. IgG antibodies against extracellular matrix 1 protein were shown in 74% of LS group serum versus 7% in control group serum.[30] Extracellular matrix 1 protein helps to regulate the basement membrane zone (BMZ). In addition, several studies have demonstrated bullous pemphigoid antigen 180 and 230 (BP180 and BP230, respectively) antibodies against the BMZ in patients with LS; yet, the most recent study showed no statistical difference versus control subjects.[31] Of relevance to bullous LS, all of the aforementioned antibodies target proteins within or regulating the BMZ. Similar to bullous pemphigoid, theoretically an autoimmune attack of these proteins could result in bullae formation.

CAPSULE SUMMARY

- Extragenital bullous lichen sclerosus (LS) presents as flaccid bullae favoring the trunk and proximal limbs.
- Extragenital bullous LS can be treated similarly to classic LS. Methotrexate can be used in resistant or extensive cases.
- Extragenital bullous LS may be more common than dermatologists realize and can present a therapeutic challenge.

CLINICAL FEATURES

Classic LS is characterized by ivory-white sclerotic atrophic plaques, most commonly in the anogenital region. Extragenital LS can occur anywhere on the body but favors the trunk (abdomen, chest, and back) and proximal extremities. Presenting symptoms are dryness and pruritus, but often extragenital LS can go unnoticed. Bullous LS may be both genital and extragenital, with flaccid bullae that may be hemorrhagic. The flaccid bullae lead to ulcerations and erosions that initially heal with significant postinflammatory erythema, and eventually obtain the characteristic ivory-white sclerotic plaques. A multitude of morphologic variants of LS have been reported including bullous LS (Table I).

PATHOLOGY

Early in the disease course, LS shows a lymphocytic vacuolar interface dermatitis with epidermal atrophy and orthohyperkeratosis. The most characteristic changes are edematous homogenization of the collagen and a loss of elastic fibers in the papillary dermis eventually leading to hyalinization and sclerosus of the papillary dermis.

Histologically, bullae formation (Fig 1) has been explained through 2 mechanisms. Firstly, the vacuolar dermatitis can lead to liquefaction degeneration of the basal layer disrupting the stability of the BMZ.[32] Secondly, edema of the papillary dermis disrupts the collagen fibers supporting the superficial capillaries and flattens the rete ridges. This weakened state coupled with epidermal atrophy may allow for blister formation with minimal trauma or sheering forces from regular movement.[4]

TREATMENT

The treatment of extragenital bullous LS is similar to that of genital LS (Table II).

First-line therapies

Recommended first-line therapies include super-potent topical corticosteroids with or without maintenance topical calcineurin inhibitors, intralesional corticosteroids, or oral corticosteroids. Based on the reported cases of extragenital bullous LS, the most common treatment is the application of topical corticosteroids,[4-6,8,11-13,16,17,20] a relatively safe and inexpensive modality.

The majority of cases used topical clobetasol propionate 0.05%, a class-1 super-potent steroid, once or twice daily with or without occlusion. Symptomatic response can be achieved within days to weeks; however, extragenital LS often does not respond as well as classic LS.[33] In 1 case, topical clobetasol was used initially for 2 weeks to achieve control followed by long-term daily use of pimecrolimus cream to ensure remission.[4] In limited disease, intralesional corticosteroids at anti-inflammatory doses (triamcinolone acetonide <10 mg/mL) may be used.[25]

Systemic steroids have been used with similar effects to topicals.[7,10] Because of the side effects of systemic corticosteroids, their use should be limited to widespread disease where topical application would be challenging, or cases refractory to topical treatment.

Three reported cases used systemic antibiotics because of presumed secondary infections or the belief that extragenital bullous LS is a reaction to *Borrelia burgdorferi*.[8,10,16] As extragenital bullous LS likely does not have an infectious cause, the use of antibiotics is recommended only if a secondary infection is present but not for primary disease management.

Second-line therapies

For patients who do not achieve adequate clinical control with corticosteroids, methotrexate or phototherapy may be used.