Clinical Recommendation: Pediatric Lichen Sclerosus

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Abstract

Lichen sclerosus is a chronic inflammatory condition affecting the anogenital region that may present in the prepubertal or adolescent patient. Clinical presentations include significant pruritus, labial adhesions, and loss of pigmentation. Treatment includes topical anti-inflammatory agents and long-term follow-up as there is a high risk of recurrence and an increased risk of vulvar cancer in adult women with history of lichen sclerosus. These recommendations are intended for pediatricians, gynecologists, nurse practitioners and others who care for pediatric/adolescent girls in order to facilitate diagnosis and treatment.

Key Words: Vulvar Lichen Sclerosus, Pediatric, Adolescent

Background

Lichen sclerosus (LS) is an inflammatory dermatologic condition usually affecting the anogenital area in both sexes with less than 10% occurrence reported elsewhere on the skin.1,2 It was first described by Hallopeau in 1887.3 The disease was known by multiple names including lichen sclerosus et atrophicus and kraurosis vulvae until the International Society for the Study of Vulvovaginal Disease in 1976 adopted the term lichen sclerosus.

Epidemiology

Lichen sclerosus has been reported in all age groups and both sexes but most often occurs in postmenopausal females. Approximately 7%-15% of all cases are found in prepubertal females.4 The true prevalence is difficult to determine since many patients are asymptomatic but has been reported to be 1 in 900-1,100.5,6 A recent study of 44 Finish girls diagnosed under the age of 19 with lichen sclerosus from 1982-2010 found a mean age of onset of symptoms of 7 years and 86% were prepubertal at the time of presentation.6

Pathogenesis

The exact pathogenesis of lichen sclerosus remains unclear and complex. It is generally accepted that lichen sclerosus is an autoimmune disorder. The condition has been associated clinically and immunologically with autoimmune thyroiditis, pernicious anemia, vitiligo, morphea, and alopecia areata.2,6 Fourteen percent of girls with lichen sclerosus had concurrent autoimmune disease.2,6 The genetic contribution to the development of lichen sclerosus remains unclear. Familial cases have been described in both identical and non-identical twins and siblings with no clear inheritance pattern.4,7 In the Lagerstedt study, 2 of 44 girls (4.5%) had Turner syndrome versus a prevalence of 0.05% of Turner syndrome in the general population.8 Other areas under investigation in the pathogenesis of lichen sclerosus include immunocytologic alterations, sex hormone factors, infections, trauma, and connective tissue alterations.2,8

Lichen sclerosus is believed to occasionally be a result of a Koebner phenomenon, the occurrence of a lesion as result of skin injury.8 The skin injury may be related to a severe sunburn, radiation, infection, or trauma.

Clinical Presentation

Symptoms

Children presenting with lichen sclerosus may have a wide variety of complaints. Typical complaints include vulvar irritation and pain, vulvar pruritus, dysuria, bleeding due to skin fissures, painful defecation, and constipation.5,9,10 The extent of the anogenital lesion does not correlate with the intensity of symptoms; thus, small lesions may result in significant complaints.8 Compulsive scratching of genitalia and grabbing at clothing due to itching may be disturbing to parents and teachers and confused with masturbation. The vulvar irritation and pain may be more significant at night.2,6 Children may present with behavioral changes due to a combination of symptoms and a desire for attention from a concerned parent.2,6 Older adolescents may present with dyspareunia and lacerations at the base of the posterior fourchette from trauma during intercourse. The anogenital lesions may also be detected incidentally by a parent or physician when the patient is asymptomatic.5

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Delay in Diagnosis

The symptoms of lichen sclerosus can mimic other conditions, so lichen sclerosus is often misdiagnosed, which can lead to a delay in the correct diagnosis.\textsuperscript{11,12} The average delay from onset of symptoms to diagnosis is 1 to 2 years.\textsuperscript{6} Most patients have been treated for vulvovaginal candidiasis and urinary tract infections by the time of diagnosis. This delay can often lead to frustration for both the patient and her parents. One recent study showed 67% of girls with lichen sclerosus had reduced quality of life when asked directly by survey.\textsuperscript{6} Patients diagnosed with lichen sclerosus report that most healthcare providers are not well informed about the disease.\textsuperscript{13} Lichen sclerosus shares many similar physical findings as found in sexual abuse which has lead to mistaken diagnoses of abuse.\textsuperscript{14} In 1 pediatric vulvar dermatology clinic the possibility of child abuse had been raised in 77% of the children diagnosed with lichen sclerosus.\textsuperscript{5} Sexual abuse and lichen sclerosus are not mutually exclusive; both diagnoses should be considered. If there is any concern for sexual abuse, the child should be evaluated jointly with a healthcare provider who is appropriately trained in child abuse evaluation and management.

Diagnosis

In most cases, the diagnosis of lichen sclerosus is made based on history and physical exam findings. The characteristic clinical appearance of lichen sclerosus is of ivory white or rose colored plaques. The border is often distinct, and the affected lesion can spread to the perineal skin and perianal region causing a classic “figure of eight” shape. The plaques can be atrophic with a shiny or crinkled “cigarette paper” appearance or can be thickened due to hyperkeratosis as a result of repeated excoriations. The repeated excoriations can lead to ecchymoses, hemorrhage, and superficial erosions (Fig. 1). The superficial erosions can be painful and are at risk for secondary superimposed infection.

With skin changes described above, genital scarring may occur which can result in labial and clitoral hood adhesions, a buried clitoris, and narrowing of the vaginal introitus.\textsuperscript{8,15,16} Rarely the inflammatory reaction can cause pigmentary disturbances and melanocytic proliferations leading to nevi.\textsuperscript{17,18} The differential diagnosis for lichen sclerosus includes lichen planus, vitiligo, psoriasis, eczema, and contact dermatitis (Table 1). Vitiligo is most often confused with lichen sclerosus due to the hypopigmentation; however, patients with vitiligo are typically asymptomatic and do not have evidence of vulvar structure atrophy. Lichen planus, a similar immune-mediated inflammatory disorder affecting the vulva, is rare in children and more typically presents in the peri- and post-menopausal years.\textsuperscript{19} Lichen sclerosus is not associated with vaginal mucosal involvement and rarely affects the oral mucosa whereas lichen planus typically involves the oral and vaginal mucosa.\textsuperscript{20,21} In most children the lesion can be diagnosed on clinical exam, and the patient treated with a trial of therapy first. If the treatment fails or the diagnosis is in doubt a vulvar biopsy for tissue diagnosis can be performed. The threshold for vulvar biopsy in children is higher than in post-menopausal women due to the increased difficulty in performing biopsies in children and the decreased risk of malignancy in this younger age group. When biopsy is performed due to uncertainty regarding the diagnosis, the characteristic histologic findings include thinning of the epidermis, loss of rete pegs, and hydropic degeneration of basal cells, hyperkeratosis, and dermal fibrosis with perivascular inflammation.\textsuperscript{22}

Treatment

The goals of therapy are relief of the symptoms and resolution of the signs of atrophic changes and scarring.

Table 1

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Distinguishing Features</th>
</tr>
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<tbody>
<tr>
<td>Lichen simplex chronicus</td>
<td>Can be primary diagnosis or in association with lichen sclerosus that has been long-standing, usually in adult patients</td>
</tr>
<tr>
<td></td>
<td>Chronic hypertrophic plaques</td>
</tr>
<tr>
<td></td>
<td>Histology shows widening and deepening of rete ridges</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>Occurs usually in peri- and post-menopausal years</td>
</tr>
<tr>
<td></td>
<td>Usually involves vaginal and oral mucosa</td>
</tr>
<tr>
<td>Eczema</td>
<td>History of allergen exposure and skin sensitivity in other areas</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>Similar to eczema in appearance</td>
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<tr>
<td></td>
<td>Often involves knees and elbows</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Intense erythema with discrete borders and silvery scale</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Satellite lesions present</td>
</tr>
<tr>
<td>Trauma/abuse</td>
<td>Asymmetric lesions</td>
</tr>
<tr>
<td>Seborrhea</td>
<td>Lacerations</td>
</tr>
<tr>
<td></td>
<td>Often involves scalp and nasolabial folds</td>
</tr>
<tr>
<td></td>
<td>Oily-appearing, erythematous, symmetric lesions, fine scale over erythematous base</td>
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</table>

Fig. 1. Typical appearance of lichen sclerosus in a 9-year-old with 1-year history of vulvar pruritus.
The mainstays of therapy include topical high potency corticosteroids and topical immune modulators. Unfortunately randomized controlled trials for lichen sclerosus therapy in children and adolescents do not exist. Although topical testosterone, dihydrotestosterone, and progesterone have been used in the treatment of lichen sclerosus in the past, a 2011 Cochrane review by Chi et al did not find that topical androgens are effective in the treatment of adult women with lichen sclerosus. Thus these agents should not be used in the treatment of lichen sclerosus in adults or children. In general, 1 month after initiating treatment, the patient should be seen to evaluate the compliance with and response to treatment along with possible side effects.

In addition to treating the lichen sclerosus, specific symptoms may need to be treated. Vulvar pruritus may be treated with anti-histamines such as diphenhydramine and hydroxyzine. Persistent vulvodynia may be treated with antidepressants such as tricyclic antidepressants or serotonin reuptake inhibitors and antiepileptic drugs such as gabapentin. Vulvar irritation may be treated with a hypoallergenic topical emollients such as A&D ointment. Topical anesthetics can also be used but may be associated with contact dermatitis (Table 2).

### Use of High Potency Corticosteroids

The very high potency steroids clobetasol propionate and betamethasone valerate are the most commonly used topical corticosteroid medications for treatment of lichen sclerosus. Prolonged use of topical steroids can be associated with thinning of the dermis, secondary superimposed infections, and rarely hypothalamic-pituitary-adrenal axis suppression. Although there has been concern about use of high-potency steroids in the pre-pubertal population due to the relatively atrophic hypoestrogenic skin and theoretical risk of increased absorption, studies have found use of topical steroids safe in this population. Ointments are generally recommended as they have increased penetration and decreased contact dermatitis. Rarely if a female develops a contact dermatitis due to sensitivity to the vehicle in which the steroid is suspended, the physician may consider a referral to a compounding pharmacy to create the steroid with a hypoallergenic vehicle. Corticosteroid treatment regimens reviewed ranged from weekly administration to twice-daily application with corticosteroid tapering varying from decreased frequency of use to decreased potency steroid or both. A case series of 15 premenarchal girls treated with clobetasol ointment twice daily for 2 weeks then daily for 2 weeks then tapered to triamcinolone then hydrocortisone found a 93% improvement of symptoms and vulvar abnormalities. Flares after treatment occurred in 82% of the 11 girls followed, occurred on average 2.19 times per year, and were successfully treated with repeated courses of clobetasol therapy. Side effects were minimal and included yeast superimposed infection in 1 patient and transient erythema in another. A subsequent study that evaluated the response to 36 girls with lichen sclerosus confirmed good response (72% complete, 25% partial) to topical clobetasol.

In 2011 a Cochrane Review by Chi, Kirtschig et al addressed the most common treatments and their efficacy in adults, but did not have enough patient numbers to make specific recommendations for children. The reviewers found clobetasol more effective than placebo in the studies.
reviewed. Ventolini et al compared weekly topical high potency steroid use to high potency steroid use plus intradermal triamcinolone use and found the use of triamcinolone injections decreased the time for relief of symptoms; however, the use of topical high potency steroid in this study was less frequent than standard practice.27

Immune Modulators

Topical calcineurin inhibitors pimecrolimus and tacrolimus have also been used for treatment of lichen sclerosis. Theoretical advantages are decreased systemic immunosuppression and decreased risk for atrophic changes in the local skin. Data regarding use of immune modulators is limited but there have been multiple case reports of success with use of topical calcineurin inhibitors. Bohm et al published a case series of 3 prepubertal females treated once daily with tacrolimus 1% with long lasting remission of up to 1 year.29 Goldstein et al published a case report of a 10 year-old girl treated with pimecrolimus 1% twice daily for 3 months then every other day with remission achieved in 6 weeks and without recurrence at the time of publication.29 Similarly, Boms et al reported clinical remission within 4 months in 4 prepubertal girls with twice daily application of pimecrolimus 1%.30 A randomized controlled trial comparing pimecrolimus to clobetasol use in 38 adult women found significant symptom improvement in both groups (no statistically significant difference between groups), but histologic improvement was superior in the clobetasol group. No adverse events were reported in either group.31 In a case series of 29 adult women with lichen sclerosus who had previously had an inadequate response to corticosteroid treatment, 76% had clinical remission after 1 year.32 Both pimecrolimus and tacrolimus have a FDA black box warning concerning a possible causal relationship between long term use of topical calcineurin inhibitors and skin cancer and lymphoma. Due the black box warning and the known effectiveness of very high potency steroids it may be best to consider both pimecrolimus and tacrolimus as second line agents. Neither pimecrolimus or tacrolimus are recommended to be used in children under the age of 2.

Surgical Treatments

Surgery for lichen sclerosus is usually reserved for complications due to adhesions and scarring. Atrophy of the labia minora, scarring of the clitoral hood and labial/clitoral hood adhesions have been described.33 These complications can lead to urinary tract outflow obstruction, retention pseudocysts, and dyspareunia. Surgical procedures are typically performed to relieve adhesions and scarring through use of sharp dissection or laser.15 The patient should be maximized on medical management prior to surgery with plans to continue therapy during the recovery phase.15 One case series of surgical treatment of adolescents with significant pain due to labial and clitoral adhesions included placement of Surgicel (an oxidized cellulose polymer) at the surgical site with no recurrence of adhesions for 1 year.25

Recurrence

Lichen sclerosus should be thought of as a chronic condition with possible recurrence of symptoms after appropriate treatment.11,12,34 Recurrence rates of prepubertal lichen sclerosus after medical therapy have been reported to range from 44%-82%.6,11,25,35 It was previously thought that the condition resolved with puberty, but recent studies have shown that the symptoms and signs of the disease persist after puberty in a majority (75%) of patients.11,34 Focseneanu et al recently published a study of long-term follow-up of 36 girls diagnosed with prepubertal lichen sclerosus conducted through phone interviews the study evaluated patients’ perceptions of symptoms and need for further treatment over a period with a mean duration of 5 years after diagnosis.35 Remission was achieved in 83% most often following treatment with high potency topical steroid but relapse occurred in 44%. Intermittent maintenance was required for 3.1 years on average with mean average length of remission of 3.6 years. Architectural changes can be found even in the absence of symptoms; thus, continued regular follow-up is warranted.35

Risk of Malignancy

Squamous cell carcinoma is believed to develop via 2 independent pathogenic pathways. The more known pathway is associated with the HPV virus and termed HPV-associated usual VIN. The HPV independent pathway, also known as HPV-independent differentiated VIN (vulvar intraepithelial neoplasia), has been proposed to have lichen sclerosus as a precursor.36 Post-menopausal women with lichen sclerosus are known to have an increase risk of squamous cell cancer of the vulva, but the carcinogenic process is not understood.37 It is also unknown at this time if the same risk is present for children and adolescents diagnosed with lichen sclerosus. There is 1 case report of a 32-year-old female who was diagnosed with and ultimately died of advanced vulvar squamous cell cancer with concurrent lichen sclerosus since childhood.34 Although the biology of increased malignancy risk in the setting of chronic inflammation would suggest that well-controlled LS would have a lower risk of malignancy, there are no long-term studies validating such an assumption. Until more long term studies are complete, and the risk is better quantified it may be best to advise parents of the possible risk for vulvar cancer associated with lichen sclerosus and to stress the importance of long-term follow up to the patients’ parents with visits recommended every 6-12 months. Although HPV is not believed to be a part of the

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Itching</td>
<td>Antihistamine such as diphenhydramine or hydroxyzine</td>
</tr>
<tr>
<td>Irritation</td>
<td>Hypoallergenic topical emollients such as A+D ointment</td>
</tr>
<tr>
<td>Persistent pain</td>
<td>Tricyclic antidepressants such as amitryptiline and desipramine</td>
</tr>
<tr>
<td></td>
<td>Serotonin reuptake inhibitors such as fluoxetine, Gabapentin</td>
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Table 2: Treatment of Symptoms
pathogenesis of lichen sclerosus associated squamous cell carcinoma of the vulva, all adolescent patients should be encouraged to complete the HPV vaccination series for the prevention of both cervical cancer and HPV related squamous cell carcinoma of the vulva.

**Recommendations**

**Level A**
- No long-term studies or randomized controlled trials in this population exist to permit Level A recommendations.

**Level B**

**Level II- 2 B**
- Initial therapy for lichen sclerosus should be with high potency topical steroids.

**Level II-3 B**
- Limited evidence suggests a future role for immune modulators in non-responders and those patients unable to tolerate steroid therapy.

**Level C**
- Lichen sclerosus should be suspected in patients presenting with any kind of urogenital complaint including dysuria, dyschezia, and constipation.
- Patients with lichen sclerosus should be monitored for symptoms and signs of other autoimmune disorders.
- Lichen sclerosus can be diagnosed in the pediatric/adolescent population without biopsy in patients presenting with the typical symptoms and appearance of LS lesions. A trial of therapy is recommended with biopsy reserved for patients with atypical lesions and those not responding to therapy as anticipated.
- Patients should be followed at 6–12-month intervals to monitor for symptoms, architectural change, and possible risk of malignancy.

**Conclusion**

Lichen sclerosus is a chronic condition commonly affecting pre-pubertal female that can be asymptomatic or associated with vulvar complaints. It can result in decrease quality of life along with vulvar atrophy and scaring. Treatment is usually a course of a high potency corticosteroid. Long-term follow up is recommended.

**Summary of Recommendations**

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I: Evidence obtained from at least 1 properly designed randomized controlled trial.
II-1: Evidence obtained from well-designed controlled trials without randomization.
II-2: Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than 1 center or research group.
II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

**Level A:** Recommendations are based on good and consistent scientific evidence.
**Level B:** Recommendations are based on limited or inconsistent scientific evidence.
**Level C:** Recommendations are based primarily on consensus and expert opinion.

**Acknowledgment**

NASPAG thanks the Education Committee and co-authors for their contribution to this document. This Clinical Recommendation reflects the currently available best evidence for practice at the time of publication. This recommendation is designed to aid practitioners in making decisions about appropriate patient care, but should not be construed as dictating an exclusive course of management. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

**References**