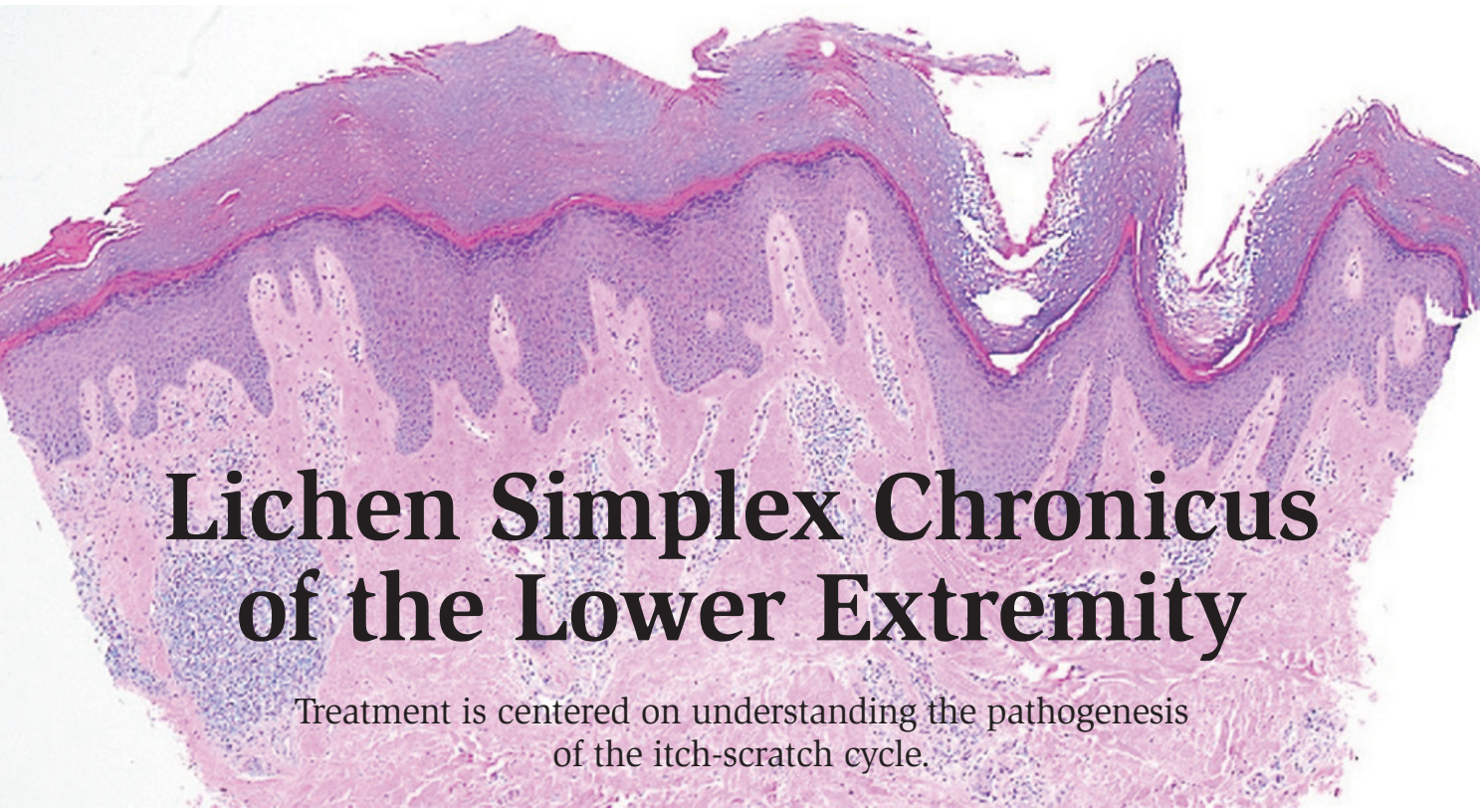

Lichen Simplex Chronicus of the Lower Extremity

Treatment is centered on understanding the pathogenesis of the itch-scratch cycle.

BY TREVOR S. PAGE, DPM AND G. DOCK DOCKERY, DPM

Introduction

Podiatric physicians and surgeons encounter lower extremity pruritic dermatologic conditions routinely, with varying levels of certainty and confidence in diagnosing and treating these clinical skin problems. It is imperative to be able to recognize common pruritic conditions for timely treatment and referral as needed, as it may be an important clue to the presence of underlying systemic disease.[1] Chronic pruritis can be burdensome, even debilitating, leading to change in affect and loss of sleep.[2] Lichen simplex chronicus (LSC), one of the more common chronic pruritic conditions affecting more than 12% of the general population, has been described as the most common dermatological condition resulting in consultation.[3,4] Defined as a form of chronic localized or circumscribed neurodermatitis, LSC presents with localized thick, scaly plaques resulting from habitual scratching or rubbing of the area.[5] Though a historical lack of research made LSC a difficult problem to adequately treat, advancements in the understanding of its pathogenesis and etiology promoted a substantial increase in treatment options. This article aims to review LSC from a podiatric perspective and offer insight into its diagnosis and treatment, while highlighting recent advancements.

Etiology and Epidemiology

LSC is a secondary neurodermatitis disorder linked to emotional factors. Psychosocial stress and emotional factors are commonly associated with LSC, with patients demonstrating a significantly higher prevalence of psychosomatic and psychiatric co-morbidities, including depression and anxiety. It also often presents in those with highly stressful or competitive lifestyles.[3,6] These emotional factors result in repeated and cyclic itching as a means to suppress the emotional disturbance. Localized plaques form because of the constant rubbing and scratching of the intractable itch in specific areas that are self-accessible, such as the ankles, shins, elbows, dorsal hands, neck, and anogenital regions.[3,5] These lichenified plaques of red papules then coalesce to form a red, scaly, elevated lesion with accentuated skin lines that are often accompanied by overlying excoriations and can range in erythematous shades (Figure 1a-1d).

Interestingly, it has been shown that the dermatology quality of life index (DQLI) was lower in patients with LSC than in those with other dermatological conditions such as psoriasis.[7] Though LSC is a largely pruritic disorder, it can result from disorders of the skin barrier and can also be secondary to other dermatoses.[8]

LSC is a prevalent condition, estimated to affect 12% of the population, primarily middle-aged patients between 30 and 50 years old. The prevalence of LSC in middle to late adulthood is hypothesized to be due to the increase in stress at this point in one's life.[7] Females are affected more than males at an established 2:1 ratio.[3] Additionally, the majority of those affected by LSC report a family history of atopic dermatitis, allergic rhinitis, and/or asthma.[9]

Histopathology

Histopathology of LSC shows a hyperkeratotic plaque with foci of para-

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keratosis, prominent granular cell layer, irregularly thickened and prominent granular layer, thickened and elongated epidermal rete ridges, acanthosis, pseudoepitheliomatous hyperplasia, papillary dermal fibrosis, and mild spongiosis. Examination of the superficial dermis may reveal perivascular and interstitial inflammation with histiocytes, lymphocytes, and occasional eosinophils, with thickened collagen bundles (Figure 2).[3,5,8] All of these features are consistent with the diagnosis of LSC.

Pathophysiology

Unfortunately, the exact pathophysiology of LSC remains unknown; however, LSC is universally regarded as a chronic pruritic process, evoked from psychological stress or secondary to other dermatoses leading to a chronic itch-scratch cycle. Pruritis is classified as either acute histaminergic or chronic non-histaminergic—each having their own neuronal pathways. Though the specific pruritogenic molecules and their specific receptors on C-nerve fibers for LSC have also not yet been identified, because LSC is chronic in nature, it is believed to follow the non-histaminergic pruritis pathway. This involves the binding of currently unknown pruritogens to G-protein coupled receptors (GPCR) and/or the transient receptor potential ion channels (TRP).

Two specific TRPs, vanilloid 1 (TRPV1) and ankyrin-1 (TRPA1), are identified to play a significant role between pruritogenic molecules and nociceptive stimuli, including itch.[10] Qui and colleagues demonstrated a significantly down-regulated expression of TRPA1in biopsy results of patients with LSC compared to controls.[11] This suggests that TRPA1 may play a role in the pathogenesis of LSC. Additionally, TRPV1 is known to play a significant role in pathogenesis of other pruritic skin conditions and is hypothesized to play a role in LSC, though it has not yet been proven.[12]

Moreover, current literature is investigating the neuroimmune interactions in LSC. Under chronic inflammation and during times of stress, immune cells increase their production of neurotrophins and neuropeptides, resulting in increased cutaneous inflammation and pruritis.[13] This neuroimmune interaction supports the finding that LSC is commonly found in patients with highly stressful lives. Additionally, intraepidermal nerve fiber density has been found to be significantly reduced compared to contralateral control tissue and was associated with reduced thermosensitivity. It is hypothesized that these injured nerve fibers develop spontaneous activity perceived as itch.[14]

Though scratching temporarily relieves the pruritic sensation by activating pain-sensory fibers that inhibit itch at the level of the spinal cord, this same scratching can lead to a pathologic process known as the itch-scratch cycle.[15] Epithelial damage from scratching leads to the release of cytokines, proteases, and antimicrobial peptide, ultimately activating immune cells and

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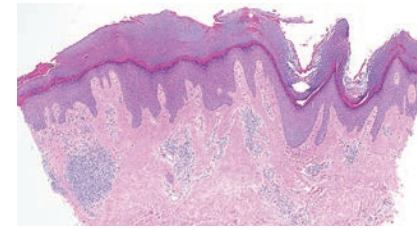

Figure 2: Histopathologic examination of a punch biopsy specimen from the ankle region demonstrates hyperkeratosis, patchy parakeratosis, hypergranulosis, acanthosis, and vertically oriented collagen bundles in the papillary dermis (papillary dermal fibrosis) consistent with a diagnosis of lichen simplex chronicus. *(Courtesy of Emily DeSantis, MD, Dermatopathologist, Sagis Pathology, Houston, Texas.)*

Reducing inflammation remains a cornerstone of treatment, and high-potency topical corticosteroids should be considered for first-line treatment.

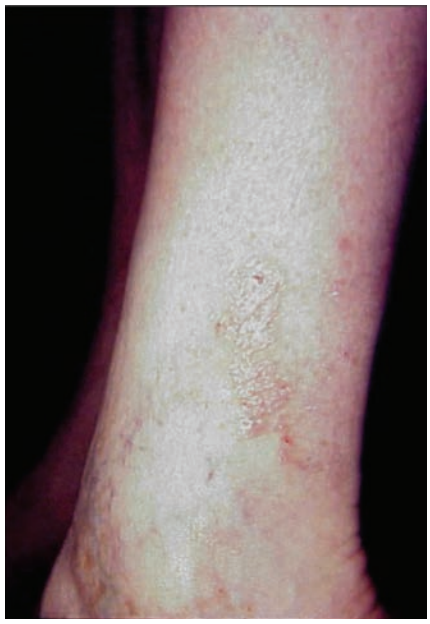

Figure 1a: Chronic LSC caused by repeated compulsive scratching with a single finger.

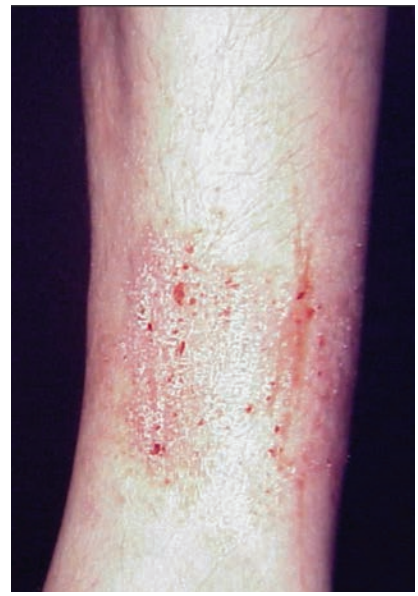

Figure 1b: Chronic LSC caused by compulsive linear scratching with all four fingers of the same hand at one time.

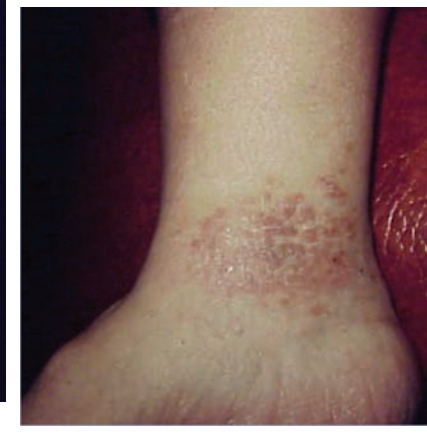

Figure 1c: Chronic LSC secondary to repetitive circular scratching of the medial ankle.

TABLE 1

Recommended Treatments for Lichen Simplex Chronicus Based on Disease Severity

Mild Disease	Moderate Disease	Severe Disease
Emollients	Gabapentinoids (gabapentin)	Nemolizumab
Topical calcineurin inhibitors	Antidepressants (SSRI, TCAs i.e. imipramine)	Dupilumab
High-potency topical steroids	For night-time itch: Mirtazapine, sedating antihistamines	Janus kinase inhibitors (i.e. tofacitinib)
Combination of topical steroids and salicylates	Topical acetaminophen	Transcutaneous electrical nerve stimulation
Menthol	Cyclosporine	Focused ultrasound
Pramoxine	Methotrexate	
Topical doxepin	Narrow-band ultraviolet B	
Topical aspirin with dichloromethane		
Topical ketamine/amitriptyline/lidocaine		

SSRI: selective serotonin uptake inhibitors; TCA: tricyclic antidepressants.

Modified from Ju T, et al. Lichen simplex chronicus itch: An update. Acta Derm Venereol 2022:102:4367.

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itch sensory neurons and channels, as described above. This results in the itch-scratch cycle. Once the area becomes lichenified from chronic rubbing or scratching, there may be pleasure derived from additional rubbing and scratching of the pruritic area. This effect probably explains the high rate of recurrence of this chronic lesion. Of note, this itch-scratch cycle can result in disruptions in the skin and subsequently lead to infectious processes.[3,8,16,17] Also reported in the literature, though extremely rare, is that the long-lasting effects of LSC lesions may lead to alterations in keratinocyte proliferation and differentiation and may eventually give rise to malignant transformation.[3,5,8]

Diagnosis

The diagnosis of LSC is clinical and, as is the case with all dermatologic pathologies, includes obtaining a thorough medical history and physical examination. A thorough work-up can direct the clinician to determining the root cause of the itch, whether psychological, environmental, or secondary to other dermatoses, such as eczema or psoriasis, which can be very useful in developing the most effective treatment. When presented with skin lesions of unknown etiology, podiatric physicians should conduct a full dermatologic examination. Moreover, allergic patch testing can aid in ruling out reactions due to contact dermatitis. Potassium hydroxide, fungal cultures, and polymerase chain reaction (PCR) can help exclude fungal etiologies. Skin punch biopsies can be performed to confirm the diagnosis and to distinguish the lesion from other conditions such as lichen planus, squamous cell carcinoma, mycosis fungoides, psoriasis, and contact dermatitis. Blood tests, specifically immunoglobulin E, can be ordered to support atopic etiologies.[3,8]

Differential Diagnosis

Several entities may resemble the clinical presentation of LSC due to their eczematous appearance and to their pattern(s) of distribution. The most common list of differential diagnosis of LSC includes lichen planus, atopic dermatitis, eczema, psoriasis, contact dermatitis, in situ squamous cell carcinoma, and mycosis fungoides.

Treatment

Scientific literature outlines a plethora of treatment approaches for LSC, as these lesions have been historically challenging to treat (Table 1). There is a notable paucity of high-level studies critically evaluating therapeutic options for LSC. Overall, existing studies center around first removing any triggering factors, thus aiding to restore function to the barrier layer, and then second, reducing inflammation.[3] As LSC is the result of habitual scratching, the authors of this paper employ anecdotal and evidence-supported successful approaches to prevent the patient's ability to scratch. This, in time, helps to eliminate the emotional and psychological itch, including application of occlusive dressings, such as an Unna boot, for 10-14 days and/or having the patient wear cotton gloves, especially during the night.[18] Moreover, reducing inflammation remains a cornerstone of treatment, and high-potency topical corticosteroids should be considered for first-line treatment.[3]

For more severe lesions, intralesional steroid injections, such as triamcinolone acetonide, may also be considered. Many other topical medications have been evaluated for treatment of LSC with mixed results. Of note, capsaicin, though a popular anti-pruritic, has not been found efficacious for the treatment of LSC pruritic.[19]

If topical treatments fail, systemic treatments should be considered. Pharmaceuticals—including gabapentin, selective serotonin reuptake in-

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hibitors, sedating antihistamines, and tricyclics—have all been documented in the literature to provide potential benefit, especially for nocturnal itch.[20,21] Non-traditional treatments have also been reported, including targeted narrowband ultraviolet phototherapy, transcutaneous electrical nerve stimulation (TENS), focused ultrasound therapy, and local injections of botulinum toxin, all with promising results, but are in need of further investigation.[22-25] For patients who fail conservative interventions, surgical measures include cryosurgery, and for persistent cases, surgical excision of localized lesions may be justified.[8,26,27] However, lesion excision has a higher risk of recurrence of the lesion within the scar tissue, thereby complicating treatment. Overall, treatment of LSC revolves around eliminating triggers, preventing the patient's ability to scratch and reducing inflammation, but despite emerging evidence there remains a paucity of high-quality trials supporting treatments for LSC and larger controlled studies are needed.[28]

TABLE 2

Treatment Pathway for Lichen Simplex Chronicus

Clinical Examination
- Obtain complete H & P
- Identify location and lesion characteristics

Make Clinical Diagnosis
- Create Differential Diagnosis

Obtain Lesion Punch Biopsy
- To confirm diagnosis and rule-out other conditions

Patient Education/Behavioral Modification
- Explain condition and cause and effect of rubbing and scratching
- Have patient trim fingernails short

Treat Underlying Cause (If Known)

Prescribe Topical Steroid
- High-potency topical corticosteroid ointment (i.e. clobetasol propionate)

Recommend 100% Cotton Disposable Gloves
- To be worn at nighttime to reduce effects of rubbing and scratching while sleeping

Oral Antihistamines
- Oral H1-blocking antihistamines at bedtime

Application of Unna Boot Dressing
- Apply initially or if patient is unable to control rubbing and scratching

Inject Lesions with Steroid
- Small or persistent lesions may be locally injected (i.e. triamcinolone acetonide 5 to 10 mg/mL)

Referral to Medical Specialist
- Refer to Dermatologist or psychologist if condition persists.

Conclusion

LSC, often referred to as neurodermatitis, is a chronic, localized, pruritic dermatitis resulting from habitual rubbing and scratching with associated neurologic and psychiatric components to the disease process. Accordingly, these lesions affect self-accessible areas, commonly found in the lower leg, ankles, and feet. Podiatric physicians and surgeons should be familiar with the etiology and pathophysiology of the disease in order to properly diagnose and effectively triage or treat LSC lesions of the lower extremity. Though our full understanding of LSC is incomplete, current treatment is centered in our understanding of itch and the pathogenesis of the itch-scratch cycle. Current treatments and research are the cornerstone to the care of this condition, aimed at eliminating itch triggers and repairing the skin barrier by preventing the ability to scratch and thereby reducing inflammation. For a current treatment pathway for LSC, see Table 2. **PM**

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