Lichen Sclerosus: a Review of the Condition and Its Management

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Lichen sclerosus is a chronic vulvar condition that is the most prevalent in pre-pubertal girls and post-menopausal women. It manifests as vulvar pruritus or distortion of the normal vulval architecture in later stages of the disease. It is mainly a clinical diagnosis, sometimes requiring histological confirmation by vulval biopsies. Superpotent topical steroid is the mainstay of treatment, aiming to relieve symptoms and prevent anatomical destruction and progression to premalignant or malignant conditions. Other treatment modalities include immunomodulating drugs for steroid-resistant disease, and surgical management in cases of intractable symptoms, failed medical treatment, or when restoration of anatomy and function is required.
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Introduction

Lichen sclerosus is a chronic dermatological disorder with features of marked inflammation and epithelial thinning[1]. The original term 'lichen sclerosus et atrophicus' described a hard, thickened, and atrophic rash. It is a benign but progressive condition characterised by symptoms of pruritus and pain. This review article aimed to discuss the clinical background, manifestations, diagnosis, and management of this disorder.

Epidemiology

Lichen sclerosus is often underdiagnosed and undertreated with the exact incidence and prevalence unknown. It is 10 times more common in women than in men[2]. The prevalence is estimated to range from one in 30 menopausal women[3] and one in four patients who attend specialist vulval clinics[4]. Bimodal peaks have been identified for the onset of the disease that mostly occurs in pre-pubertal girls and peri- or post-menopausal women.

Aetiology

The aetiology of lichen sclerosus is still unknown although associations have been identified with immunological, hormonal, genetic, and local factors.

Immunological Factor

Up to 20% of women with vulvar lichen sclerosus have co-existing autoimmune diseases, especially thyroid disease, type 1 diabetes mellitus, vitiligo, and alopecia areata. Immunoglobulin auto-antibodies have been identified in 44% to 74% of affected women[3,5,6].

Hormonal Factor

The role of hormones has been postulated in the pathogenesis of the disease as lichen sclerosus is mostly found in those with low oestrogen status before menarche and after menopause[3,4].

Genetic Factor

In an observational study in the United Kingdom, up to 12% of patients had a positive family history. A possible genetic link was suggested although the responsible gene has yet to be identified[6].

Local Factor

Koebner phenomenon, the development of isomorphic pathological lesions in traumatised uninvolved skin of a patient with a cutaneous disease, is observed in lichen sclerosus. Trauma, burn injury, irradiation, and sexual abuse have been suggested as triggering factors for development of the disease[7].

Clinical Manifestations

Vulvar pruritus is the hallmark of lichen sclerosus. It is usually the chief complaint and the most distressing symptom to affect a patient's daily life. If the disease involves the perianal area, it may manifest as anal discomfort, pain on defaecation, anal fissures, or even per-

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rectal bleeding. If there is fusion of the labia minora with consequent obstruction of the urethral opening, it can result in dysuria. Dyspareunia and sexual dysfunction are late symptoms of the disease when anatomical destruction has already set in leading to stenosis of the introitus and fusion of the labia[5,6].

The classical manifestation of lichen sclerosus is the presence of porcelain white plaques and atrophic depigmented areas over the vulvae known as leukoplakia. Some individuals may have ecchymosis changes such as purpura. In later stages of the disease, fissuring or even erosion may be seen. Hyperkeratosis characterised by waxy skin can result from the chronic insult to the affected skin. Chronic scratching due to the intense pruritus can lead to excoriation and lichenification which is thickening of the epidermis with exaggeration of normal skin lines[6,8].

The most commonly affected areas of the vulva include the medial labia majora, interlabial creases, labia minora, clitoral hood, and clitoris. Lesions may extend to the perianal region causing a 'figure-of-eight' pattern. Mucosal regions like the vagina, however, are seldom involved. In cases of extragenital involvement, the thighs, breasts, wrists, shoulders, neck, and back can be affected.

As the disease progresses, the normal vulvar architecture is lost. It begins with a loss of distinction between the labia majora and minora, followed by shrinkage of the introitus, possibly burying the clitoris. In the final stage, only a posterior pinhole orifice remains as a result of midline fusion of the vulvae[9] (Figure).

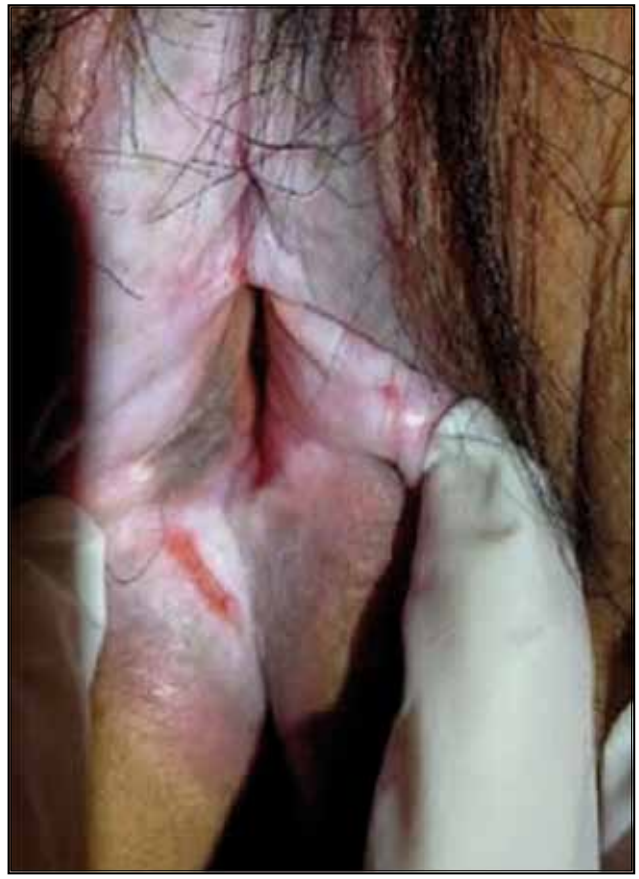

Figure. Leukoplakia with fusion of vulvae

Diagnosis

The diagnosis of lichen sclerosus can be made clinically in cases with typical manifestations and dermatological changes. Histological confirmation by vulval biopsy is indicated if a diagnosis cannot be made clinically or when there is a need to exclude a premalignant or malignant condition[10]. When initial treatment of lichen sclerosus fails, vulval biopsy should be performed to re-evaluate the diagnosis. As vulval leukoplakia has a wide range of differential diagnoses including underlying malignancy, some advocate biopsy in all cases of adult-onset vulvar lichen sclerosus. It is suggested that biopsy be performed before starting treatment as the characteristic histological features may be less evident after application of topical steroids[6].

Histopathology

A 4-mm punch or incisional biopsy, which provides sufficient tissue for evaluation, can be performed under local anaesthesia and should be taken from the most abnormal-looking area. Under the microscope, thinned epidermis and sub-epidermal hyalinisation with deeper inflammatory lymphocytic infiltrates can be identified[11].

Investigations

If there is a clinical suspicion of secondary infection over the areas with lichen sclerosus, wound swabs should be taken for culture to exclude any co-existant bacterial or fungal infections[6]. As lichen sclerosus is associated with autoimmune diseases, symptoms and signs of thyroid disease, type 1 diabetes mellitus, and pernicious anaemia should be sought and investigations performed when indicated[6,12].

Premalignant and Malignant Conditions

Patients with lichen sclerosus are at a higher risk of developing future malignancy or a premalignant condition of the vulva[13-15].

Vulvar Intraepithelial Neoplasia

Vulvar intraepithelial neoplasia (VIN) is a premalignant condition that may progress to invasive squamous cell carcinoma (SCC). Lichen sclerosus is associated with the differentiated type of VIN, while the usual-type VIN is more often related to human papillomavirus.

Vulvar Squamous Cell Carcinoma

In patients with lichen sclerosus, the lifetime risk of developing vulvar SCC has been quoted to be less than 5%, based on some retrospective case series[16]. The relationship between lichen sclerosus and melanoma, basal cell carcinoma, and verrucous carcinoma has not been identified[12]. It is suggested that early detection, use of potent topical steroids, more liberal biopsy, and excision of abnormally thickened skin resistant to treatment may reduce the risk of developing SCC[12,17].

Management

Treatment of lichen sclerosus aims to relieve symptoms to reduce the dysfunction and disfigurement caused by the disease. It should be initiated soon after diagnosis and within 2 years to prevent long-standing disease and progression causing irreversible distortion to normal vulvar architecture. Multidisciplinary input from the gynaecologist, dermatologist, urologist, or paediatrician may be necessary to provide optimal care[12].

Counselling and Patient Education

In chronic diseases, counselling and patient education play an important role in management. Information about the nature of the disease and the mainstay of treatment should be given, including the regimen and instructions about application of topical medication. Patients are advised against scratching the vulvar skin and to avoid any skin irritants, with emphasis placed on the importance of maintaining good perineal hygiene. Education should include the technique of regular self-examination using a mirror to detect any abnormal thickening or non-resolving ulcers that may indicate neoplastic changes[6].

Symptomatic Relief

Emollients and lubricants can be applied to the affected areas to reduce symptoms and dysfunction, but they cannot alter the course of the disease[17].

First-line Treatment: Topical Corticosteroids

Topical corticosteroids are the mainstay of treatment. Steroids of super-high potency are effective treatments for lichen sclerosus of which clobetasol propionate is the most commonly prescribed. Its use is well supported by multiple randomised controlled trials[18-20]. Mometasone furoate is less potent than clobetasol but is said to have a greater anti-inflammatory activity and a longer duration of action, although more evidence is needed to support its use as an effective alternative to clobetasol[21,22]. The optimal treatment regimen is unknown. A fingertip unit per application of clobetasol propionate 0.05% ointment is approximately 0.5 g. A thin film is applied over the affected area.

Treatment is divided into three phases. During the initial phase, topical steroid is applied daily or at night for 6 to 12 weeks, then treatment response is evaluated in terms of resolution of pruritus, pain, and skin changes including hyperkeratosis, fissuring, and ecchymoses. It is followed by tapering therapy with application of topical steroid at night for 4 weeks, reducing to alternate-day application for another 4 weeks, followed by twice weekly application for 4 weeks. If there is recurrence of symptoms during the tapering phase, frequency of treatment should be adjusted in order to achieve good control. Maintenance therapy aims to prevent recurrence of symptoms and to maintain normal anatomy. There is a suggestion that continuation of maintenance therapy is associated with a reduced incidence of differentiated VIN and vulvar SCC[23]. Common side-effects of topical steroids include cutaneous atrophy, telangiectasia, and striae. These can occur as early as 2 to 3 weeks following daily application and may be irreversible in some cases[24].

Second-line Treatment: Calcineurin Inhibitors

Topical calcineurin inhibitors, namely tacrolimus and pimecrolimus, have been shown by two small-scale randomised controlled trials to be effective in treating lichen sclerosus[18,25]. They are immunosuppressants that act by suppressing the T-lymphocyte response and reducing inflammation. It has been suggested that daily use of tacrolimus was less effective than daily use of clobetasol propionate, whereas twice daily use had similar clinical efficacy but lesser histological efficacy than super-high potency topical steroids[3]. Discrete case reports have demonstrated improvement when calcineurin inhibitors were used in patients with steroid-refractory vulvar lichen sclerosus[26-29], but more evidence of their efficacy is required. Calcineurin inhibitors do not cause cutaneous atrophy and are generally better tolerated than topical steroid, although some patients may experience a burning sensation during application. Concerns have been raised about their long-term safety, especially the risk of potential malignant transformation, so use for longer than 2 years is not advised[18,30].

Controversial Treatments

Other treatments have been suggested but their use is controversial. As well as oral acitretin and retinoids, topical progesterone and topical testosterone, non-pharmacological treatments such as ultraviolet A1 phototherapy and photodynamic therapy have also been used[31-34]. However, data for their efficacy are limited or conflicting. Moreover, some of these treatments are not easily accessible and some have poorly tolerated side-effects.

Surgical Management

In the majority of cases, surgery will not be considered unless there are complications as a result of anatomical distortion or intractable vulval symptoms that fail medical treatment. Vulvoperineoplasty can be considered if there is loss of normal vulvar architecture leading to malfunctioning and disfigurement including severe introital fissuring, stenosis, and clitoral adhesion. During the procedure, scarring and adhesions are freed, and repair is performed using tissue taken from the posterior vaginal wall. Postoperatively, manual dilation will help restore anatomy and function[35,36]. Simple vulvectomy is the last resort. If the disease is extensive and primary re-approximation of the vulva is not feasible, a skin flap or graft from the buttock or lateral thigh may be required. Great care should be taken to monitor for any infection or haematoma formation after surgery[37].

Follow-up and Recommendations

Follow-up is important to evaluate treatment response. When treatment fails to control symptoms or achieve disease regression, efforts should be made to ensure proper use of medication at the correct area, with the appropriate amount and frequency. Superimposed infection should be excluded and treated with antibiotics or antifungal agents if confirmed. Use of intralesional steroid can be considered for thick hyperkeratotic plaques[38]. Other causes or exacerbating factors such as menopausal changes and neuropathic vulvodynia should be identified and treated accordingly. A biopsy should be taken or repeated if malignancy is suspected.

It is suggested that women with lichen sclerosus are reviewed 3 months following treatment for active disease and annually by a general practitioner in cases of stable disease. Referral for specialist care should be made if treatment response is inadequate or disease has progressed[39]. Some have suggested specialist care because patients with lichen sclerosus are regarded as a high-risk group with a 2% to 4% lifetime risk of invasive vulval cancer[40].

Conclusion

Lichen sclerosus of the vulva is a chronic disease that presents with vulval leukoplakia and pruritus. The majority of cases can be diagnosed clinically by characteristic features. In severe cases, there is malfunctioning, anatomical destruction, and a potential risk of developing malignancy. Ultra-high potency topical steroid remains the gold standard and the first-line management. Second-line or surgical treatment can be considered if topical steroid fails.

Declaration

The authors have disclosed no conflicts of interest.

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