Review Article

Genital lichen sclerosus et atrophicus in females: An update

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Abstract

Lichen sclerosus et atrophicus is an acquired chronic inflammatory dermatosis commonly affecting the vulvar and perianal regions. It is associated with an increased risk of vulvar cancer even though it is not a premalignant condition itself. The true precursor of cancer associated with lichen sclerosus (LS) is vulvar intraepithelial neoplasia (VIN), differentiated type. The diagnosis is usually clinical, but in some cases, a biopsy can be performed, especially to exclude VIN or cancer. All females with anogenital LS can be offered clobetasol propionate 0.05% ointment on a regimen for 3 months (once a day for a month, followed by alternative days for a month, and then, twice weekly for a month), combined with a soap substitute and a barrier preparation.

Key words: Clobetasol propionate 0.05% ointment, genital lichen sclerosus et atrophicus, pruritus, vulvar intraepithelial neoplasia malignancy

INTRODUCTION

Lichen sclerosus et atrophicus (LSA) is an acquired chronic inflammatory dermatosis commonly affecting the vulvar and perianal regions. The term "lichen plan atrophique" was first coined by Hallopeau in 1887 and was later termed as "lichen plan sclereux" by Darier. Various terminologies have been proposed over a period of time such as lichen sclerosus (LS), kraurosis vulvae, circumscribed scleroderma, leukoplakic vulvitis, lichen albus, hypoplastic dystrophy, white spot disease, Csillag's disease, and Weissflecken dermatoses, and the term Balanitis Xerotica Obliterans is used to describe the severe and late scarring LS (lichen simplex chronicus [LSc]) of penis in males. The International Society for the Study of Vulvovaginal Disease has proposed to use the term lichen sclerosus, and it is proven to be entirely distinct from lichen planus.

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EPIDEMIOLOGY

1. Prevalence – It is estimated to occur in 1 in 30 older women and 1 in 900 prepubertal girls
2. Age and sex – It is ten times more common in women than men and is known to affect females of any age with two peaks of incidence, in prepubertal girls and in postmenopausal women. The average age of diagnosis is 7.6 years in girls and 60 years in postmenopausal women
3. Ethnicity – It is more commonly reported in Caucasian women but has also been reported in native Africans, Orientals, and other dark-skinned patients
4. Associated diseases – In women, LS is often associated with at least one autoimmune disease as compared to men[1,2] [Table 1].

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Table 1: Diseases associated with lichen sclerosus et atrophicus

Systemic	Dermatological
Thyroid diseases - Most common (Hashimoto's thyroiditis)	Psoriasis
Type I diabetes mellitus	Vitiligo
Systemic lupus erythematosus	Alopecia areata
Systemic sclerosis	Morphea
CREST syndrome	Lichen planus
Others - Primary biliary cirrhosis	Mucous membrane pemphigoid
Polymyalgia rheumatica	Atrophoderma of Pasini and Pierini
Prolactinoma	
Pernicious anemia	

ETIOLOGY

- Autoimmunity – An autoimmune basis has been proposed for the etiopathogenesis of LSA. Two separate population-based studies of genital LSA noted an increased prevalence of psoriasis in patients with LSA, 17.0% and 7.5%, respectively, compared with a 1.5%–2.5% incidence in the general population[3]
- Recently, autoantibodies against extracellular matrix protein 1 have been proposed to play a role in the pathogenesis of LSA
- Genetics – A genetic basis has been proposed with positive family history in 12% of cases and is seen in identical and nonidentical twins.[4] An association with human leukocyte antigen Class II antigen DQ7 and interleukin-1 receptor antagonist gene polymorphisms has been identified in several studies[5]
- Infection – Infection with spirochetal microorganisms such as *Borrelia burgdorferi*[6] and atypical mycobacterial infections have been reported. Human papillomavirus (HPV) and hepatitis C virus have also been implicated as possible causative agents[7,8]
- Hormonal factors – Higher incidences of vulvar LS in postmenopausal women and prepubertal girls with a low estrogen level suggest a hormonal influence, but a protective effect from estrogen has not been shown. One theory of the etiology has been a reduction of the enzyme 5α-reductase in the vulva. Androgen-sensitive fibroblasts in the vulvar skin are responsible for sclerosis
- Koebner's phenomenon and role of local factors – LSA shows Koebner's phenomenon at sites of trauma, burns, radiotherapy, and vaccination. It can also occur post vulvectomy and in episiotomy scars
- Atopy
- Allergic contact dermatitis
- Obesity
- Anatomical abnormality.

PATHOGENESIS

- Hypoxia–ischemia theory – A recent study indirectly found that ischemic stress accompanied by poor oxygenation may be implicated in the pathogenesis of LS. Hypoxia or ischemia can stimulate mitochondrial dysfunction and endoplasmic reticulum stress. Hypoxia and ischemia also induce the activation of dermal fibroblasts and plays a major role in the progression of dermal sclerosis in systemic sclerosis, a disease that may coexist and share common clinical and pathological features with LS. Of the endogenous hypoxia markers, hypoxia-inducible factor (HIF)-1a and its target gene glucose transporter (GLUT)-1 are known to mediate essential homeostatic responses to reduced availability of oxygen. Under hypoxia, HIF-1a expression increases, followed by the upregulation of GLUT, which is seen in LSA
- Impairment in cell kinetics – Studies have shown active regeneration of collagen despite the degeneration of connective tissue in LSA. *In situ* hybridization with human sequence-specific complementary DNAs to type I procollagen demonstrated active fibroblasts in lesional skin of LSA patients, further confirming a high level of collagen synthesis in LSA
- Altered p53 expression and increased epidermal cell proliferation have been reported. CD1+ Langerhans cells are found to be present in all stages of the disease.

CLINICAL FEATURES

Sites of predilection

LS (LSc) in females has varied presentations and most commonly involves the vulvar and perianal regions. Involvement of the perianal region is more frequently seen in females than males and may be seen in up to 30% of the cases. The entire vulvar area (from the clitoris to the anus) may be involved. The most common areas where LS is found are on the labia majora and labia minora. Extragenital lesions (neck, shoulder, breast, etc.) occur less frequently than genital LSA.

SYMPTOMS

1. Intractable itching – Majority of the patients complain of severe pruritus with pruritus ani

2. Skin lesions – It consists of white, polygonal papules that coalesce into smooth, porcelain-white/ivory white plaque, or patches. These atrophic plaques may have a cigarette paper-like texture with wrinkled and fragile surface which is associated with telangiectasia, purpura, erosions, fissuring, or ulceration. Atrophy can lead to loss of labia minora and burying of the clitoris and may progress to gradual obliteration of the labia minora and stenosis of the introitus. Sometimes, hemorrhagic blisters and erosions are also seen, which might be confused with sexual abuse [Figure 1]
3. Anogenital LS – It is characterized by shiny porcelain-white atrophic plaques, which may become confluent extending around the vulvar and perianal skin and is known by various names such as figure-of-eight configuration, "keyhole," "hourglass," or "lotus flower" appearance [Figure 2]
4. Other symptoms – Irritation, soreness, urinary obstruction, dysuria, and dyspareunia are also seen. Prepubertal girls usually complain of itching and soreness as in adults, but they can also have dysuria, constipation, pain on defecation, soiling, fissuring, and bleeding.

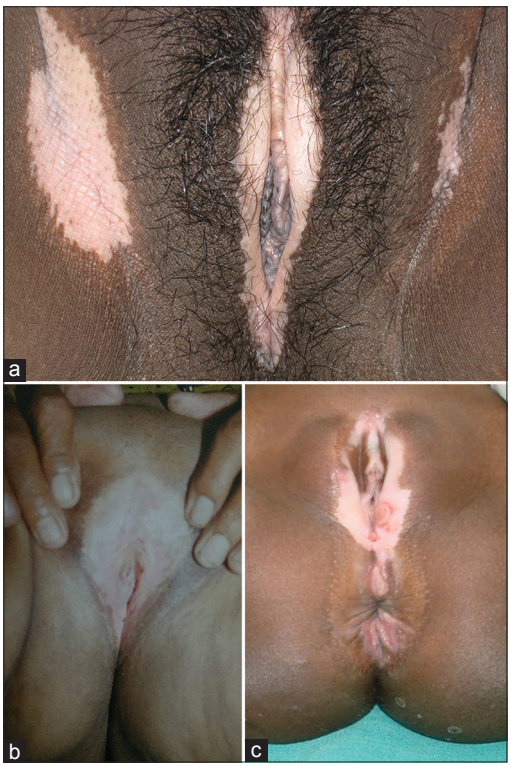

Figure 1: (a) 57 year old female with pruritic white atrophied patches involving labia majora and bilateral groinfolds. (b)- 10 year old girl with external genital mucosal atrophy leading toloss of labia minora ,burrying of clitoris and progressive stenosis of intoitus. (c) 12 year old girl with erosions on white artophied patches on vulva

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of anogenital LSA includes genital lichen planus, vitiligo, LSc, morphea, cicatricial pemphigoid, vulvar intraepithelial neoplasia (VIN), and extramammary Paget's disease.

DIAGNOSIS

- Clinical – In most cases, the diagnosis of vulvar LS is clinical. A thorough clinical history (including autoimmune disease and phenomena in the patient and family) and gynecological examination, complemented with evaluation of the mouth, extragenital skin, and appendages, usually helps in making diagnosis
- Günthert *et al*.[9] developed a physician-administered clinical scoring system to validate the diagnosis made clinically and to evaluate treatment response during subsequent follow-ups. This can be an important tool in an otherwise difficult-to-diagnose condition [Table 2].

Physician-administered clinical scoring system

- In a study conducted by Naswa *et al*., presence and severity of each of the six clinical features were assessed. The most common features were hyperkeratosis and atrophy found in 86.11% of cases with at least one-third of the cases having Grade 2 (severe changes). Erosions were seen in 75% of cases corresponding with intractable itching, which was found as the most common presenting symptom. The physician-administered clinical score ≥4 was found in 80.56% of cases, emphasizing that this clinical score indeed helps in validating the diagnosis of vulvar LS with clinical confidence. The remaining 20% of cases had typical

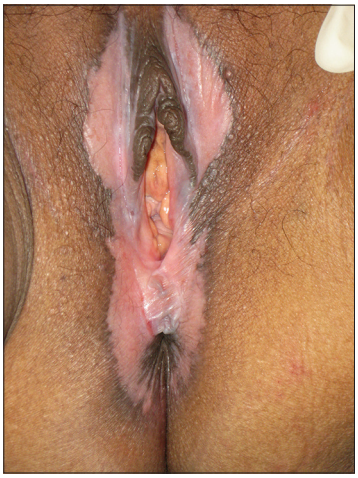

Figure 2: Figure of eight appearance in 59 year old female diagnosed with LSa

Table 2: Physician-administered clinical scoring system (0, 1, and 2)

Lesions	Grade 1 (moderate changes)	Grade 2 (severe changes)
Erosions	1-2 small erosions	>2 erosions or confluent lesions
Hyperkeratosis	Involving vulva and perineum up to 10%	Involving vulva and perineum >10%
Fissures	Rhagades affecting posterior introitus	Generalized vulvar rhagades
Agglutination (adherence of labia minora or majora)	Partial	Complete
Stenosis	Narrowing of introitus, still two fingers can be passed	Narrowing of introitus, can be passed by <2 fingers
Atrophy	Shrinkage of labia minora and clitoris	Labia minora and clitoris no longer visible

symptoms, who were followed up periodically (or confirmed with biopsy)[10]

- Dermatoscopy – In a study conducted at Pusan National University Hospital, Busan, Korea, to demonstrate the diagnostic usefulness of dermatoscopy in differentiating lichen sclerous et atrophicus from morphea, it was found that the significant dermatoscopic features of LSA were comedo-like openings and whitish patches, whereas that of morphea were fibrotic beams. The results showed a close correlation between dermatoscopic patterns and their underlying histologic features. The comedo-like openings represented follicular plugging, and the whitish patches indicated atrophy of the epidermis which are typical histopathologic features of LSA. The fibrotic beams observed in morphea indicate sclerotic dermis
- Histopathology – Most guidelines do not favor routine biopsy. It is, however, agreed that suspicious lesions (erosions/ulcerations, hyperkeratosis, pigmented areas or ecchymosis, and warty or papular lesions), particularly when resistant to adequate first-line therapy, should be biopsied. The main objective of a vulvar biopsy is to exclude VIN or cancer.[11,12]

MANAGEMENT

- British Association of Dermatologists guidelines for the management of LS 2018 are as follows:
  1. All people with LS should be managed by a health-care professional experienced (secondary care specialist or general practitioner with specific training) in treating the condition
  2. Commence treatment of LS following a firm clinical diagnosis or with histological confirmation, where necessary
  3. Undertake a full history for all people with LS, including dyspareunia and psychosexual issues. Document urinary symptoms. Perform a detailed examination documenting architectural change at baseline
  4. Advise all people with LS to avoid all irritant and fragranced products
  5. Provide all people with LS up-to-date patient information on the condition
  6. All people treated for LS should be followed up to assess response to treatment and to advise on long-term control
  7. Offer all females with anogenital LS clobetasol propionate (CP) 0.05% ointment on a regimen for 3 months (once a day for a month, alternative days for a month, twice weekly for a month), combined with a soap substitute and a barrier preparation
  8. Discuss the amount of topical treatment to be used, the site of application, and the safe use of an ultrapotent topical steroid with the patient
  9. Offer continued use of CP 0.05% for ongoing active LS disease
  10. Consider an individualized treatment regimen of topical steroid to maintain disease control and prevent scarring in females with ongoing active LS disease despite good compliance. Treatment should be titrated to maintain symptoms and resolution of skin thickening and ecchymosis although pallor may not completely resolve
  11. Consider referral to a specialist vulvar clinic in all females (including children and young people), with LS not responding to a topical steroid, or if surgical management is being considered
  12. Consider intralesional triamcinolone (1–2 mg) in females with LS with topical steroid-resistant, hyperkeratotic areas after intraepithelial neoplasia or malignancy has been excluded by biopsy
  13. Refer female children and young people with LS to specialized vulvar services (vulvar clinic, pediatric dermatologist, or urologist experienced in managing LS).[13]

Treatment failure

If treatment with topical corticosteroids appears to fail to bring LS under control, then it is important to consider the following:

- Is noncompliance an issue? Sometimes, patients may be alarmed at the contents of the information insert, warning against the use of topical corticosteroids in the anogenital area. Patients with poor eyesight and/or limited mobility or flexibility may not be able to apply the medication appropriately. It is also important to ensure that the medication is being applied in an adequate amount and to the correct site
- Has the correct diagnosis been made? If a biopsy was not done previously, it should be considered to exclude differential diagnoses including lichen planus, mucous membrane pemphigoid, or genital intraepithelial neoplasia. Another differential diagnosis is vitiligo, but this does not cause any architectural change and is asymptomatic; however, vitiligo may coexist with LS
- Is there an additional superimposed problem such as the development of a contact allergy to the medication (refer for patch testing), urinary incontinence (refer for urological advice), herpes simplex infection, or candidiasis (treat infection appropriately); some patients can have LS and psoriasis together which may be more difficult to control
- Those patients with hyperkeratotic LS often require further treatment and should be referred to a specialist clinic. Systemic retinoids may be considered in this group
- Has the patient developed vulvodynia? If the LS has been successfully treated, but the patient remains symptomatic, often with burning or soreness being a predominant symptom rather than itch, always consider vulvodynia.[13]

Evidence-based therapy

- Topical corticosteroids – In the study by Bracco *et al.*, 1993, the efficacy of topical CP was compared to placebo after 3 months' application. CP was found significantly better than placebo. The study found no events of adverse drug reactions (e.g., predisposition to infection, worsening of skin atrophy, and contact dermatitis) in either the CP or placebo group[14]
- Topical androgens – In a study by Bracco *et al.*, 1993, the authors found that, after 3 months' application, testosterone was significantly less effective than CP[14]
- Topical progesterone – In the study by Bracco *et al.*, 1993, topical application of progesterone (2% cream) for 3 months was not significantly better than placebo[14]
- Topical immunomodulators (tacrolimus, pimecrolimus, and cyclosporine) – Goldstein, 2011, tested the efficacy and safety of pimecrolimus (1% cream) against CP (0.05% cream) after 12 weeks' application and found that there were no significant differences between pimecrolimus and CP in relieving pruritus and burning/pain. However, pimecrolimus was less effective than CP; no adverse drug reactions occurred in either the pimecrolimus or CP group. However, the use of topical immunosuppressants should be for short term as safety of these drugs is still unknown, and this condition carries a risk of neoplastic change.[15]

Laser therapy in lichen sclerosus et atrophicus

Laser ablation is an acceptable treatment for patients who have symptoms due to LS of the vulva that are refractory to other measures. Such cases may be successfully treated with carbon dioxide laser with excellent surgical results and minimal risk[16,17] [Table 3].

COMPLICATIONS AND THEIR MANAGEMENT

Malignancy – Squamous cell carcinoma in females with genital lichen sclerosus

The risk of developing malignancy is approximately 3.5%–5%. However, histopathological examination of vulvar squamous cell carcinomas (SCCs) indicates that about 60% occur on a background of LS. LS may act as both an initiator and promoter of carcinogenesis by mechanisms that seem to be independent of HPV. However, HPV may be found in VIN associated with LS. SCC of the vulva should be managed by gynecological oncologists as surgery has to be individualized according to the tumor size

Table 3: Summary of treatment

Minimize irritants, avoidance of urinary contact
Use soap substitution
Moisturization with emollients
Treatment of infections
Ultrapotent or potent topical corticosteroids once daily at night for 4 weeks, and then on alternate nights for 4 weeks, and then twice weekly for a further 4 weeks. Continued suppressive therapy according to the ongoing inflammatory activity
In cases resistant to topical corticosteroids, intralesional triamcinolone acetonide can be considered
In corticosteroid-resistant cases, application of topical calcineurin inhibitors, topical retinoids in hyperkeratotic lesions, systemic retinoids, LASER therapy, or photodynamic therapy
Surgery for intraepithelial neoplasia or carcinoma
Long-term surveillance

and location, particularly in early invasive disease. Persistent ulcerated area unresponsive to therapy may be malignancy and can be missed if incomplete diagnosis without additional biopsies is done.[18,19]

At present, there is no diagnostic tool to differentiate between LS that will remain benign versus LS that will evolve into SCC. Two biomarkers, p53 and monoclonal antibody MIB1, have shown promise in retrospective tissue studies, but further testing is necessary. The standard of care for cancer screening in this population remains serial examination with directed biopsies for new, evolving, or suspicious lesions and teaching self-examination.

Other cancers reported with LS include verrucous carcinoma,[20] basal cell carcinomas, and melanomas.[21]

Scarring

a. Introital narrowing of anterior and/or posterior fusion of the labia can lead to a narrowing of the introitus. If narrowing of the introitus is significant and causes dyspareunia or difficulty with micturition, surgery may need to be considered, using part of the posterior vaginal wall in the reconstruction to prevent further adhesions and stenosis due to koebnerization. Topical steroids, together with the use of vaginal dilators, must be used postoperatively to prevent readhesion. The topical steroid can be started 48 h postoperatively once daily until the area is fully epithelialized and then reduced in frequency on an individual basis to maintain the control of symptoms and signs[13]
b. Pseudocyst of the clitoris-occasionally, clitoral hood adhesions seal over the clitoris and keratinous debris builds up underneath forming a painful pseudocyst. These patients should be reviewed with a gynecologist. Division of adhesions may be needed if symptomatic or recurrently infected.[13]
    1. Sensory abnormalities such as vulvodynia may occur after any inflammatory condition of the vulva or vestibule. Typically, the patient remains symptomatic despite objective clinical improvement or resolution of the skin lesions. Neuropathic pain does not respond to topical corticosteroids, and treatment must be directed to this entity
    2. Psychosexual problems – Psychosexual issues are common and may persist after successful treatment. Patients who have any chronic genital disorder will often lose their interest in sexual activity, leading to problems with sexual dysfunction. It is important to give patients the opportunity to express their concerns about their sexual function and to offer a referral to someone with the necessary expertise to address these problems.

Table 4: Summary

LS is a chronic inflammatory condition with malignant potential and significant impact on quality of life with bimodal peak in postmenopausal women and prepubertal girls with a low estrogen level, suggesting a hormonal influence
It is often associated with autoimmune conditions
This condition is characterized by intense pruritus and white, polygonal papules that coalesce into smooth, porcelain-white/ivory white plaque, or patches
In most cases, the diagnosis of vulvar LS is clinical. Suspicious lesions (erosions/ulcerations, hyperkeratosis, pigmented areas or ecchymosis, and warty or papular lesions), particularly when resistant to adequate first-line therapy, should be biopsied to rule out malignancy
Physician-administered clinical scoring system of vulva is a handy tool to diagnose and later evaluate the progression of the disease
Early diagnosis is the key to prevent undesirable sequelae having impact on quality of life
Ultrapotent or potent topical corticosteroids once daily at night for 4 weeks, then on alternate nights for 4 weeks, and then twice weekly for a further 4 weeks. Continued suppressive therapy according to the ongoing inflammatory activity
In resistant cases, intralesional triamcinolone acetonide, application of topical calcineurin inhibitors, topical retinoids in hyperkeratotic lesions, systemic retinoids, LASER therapy, or photodynamic therapy can be considered

LS=Lichen sclerosus

Impact on quality of life

LS has a significant impact on the quality of life, particularly on sexual functioning. Many affected people feel embarrassed; some have persistent itching and pain (despite successful control of the inflammation), and many are concerned about how the disorder may progress, particularly because of the potential of this condition for neoplastic change [Table 4].

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Meyrick Thomas RH, Ridley CM, McGibbon DH, Black MM. Lichen sclerosus et atrophicus and autoimmunity – A study of 350 women. Br J Dermatol 1988;118:41-6.
2. Cooper SM, Ali I, Baldo M, Wojnarowska F. The association of lichen sclerosus and erosive lichen planus of the vulva with autoimmune disease: A case-control study. Arch Dermatol 2008;144:1432-5.

3. Eberz B, Berghold A, Regauer S. High prevalence of concomitant anogenital lichen sclerosus and extragenital psoriasis in adult women. Obstet Gynecol 2008;111:1143-7.
4. Powell J, Wojnarowska F. Childhood vulvar lichen sclerosus: An increasingly common problem. J Am Acad Dermatol 2001;44:803-6.
5. Gao XH, Barnardo MC, Winsey S, Ahmad T, Cook J, Agudelo JD, *et al.* The association between HLA DR, DQ antigens, and vulval lichen sclerosus in the UK: HLA DRB112 and its associated DRB112/DQB10301/04/09/010 haplotype confers susceptibility to vulval lichen sclerosus, and HLA DRB10301/04 and its associated DRB10301/04/DQB10201/02/03 haplotype protects from vulval lichen sclerosus. J Invest Dermatol 2005;125:895-9.
6. Eisendle K, Grabner T, Kutzner H, Zelger B. Possible role of *Borrelia burgdorferi* sensu lato infection in lichen sclerosus. Arch Dermatol 2008;144:591-8.
7. Powell J, Strauss S, Gray J, Wojnarowska F. Genital carriage of human papilloma virus (HPV) DNA in prepubertal girls with and without vulval disease. Pediatr Dermatol 2003;20:191-4.
8. Bunker C, Shim T. Male genital lichen sclerosus. Indian J Dermatol 2015;60:111-7.
9. Günthert AR, Duclos K, Jahns BG, Krause E, Amann E, Limacher A, *et al.* Clinical scoring system for vulvar lichen sclerosus. J Sex Med 2012;9:2342-50.
10. Naswa S, Marfatia YS. Physician-administered clinical score of vulvar lichen sclerosus: A study of 36 cases. Indian J Sex Transm Dis AIDS 2015;36:174-7.
11. Pugliese JM, Morey AF, Peterson AC. Lichen sclerosus: Review of the literature and current recommendations for management. J Urol 2007;178:2268-76.
12. Neill SM, Lewis FM, Tatnall FM, Cox NH, British Association of Dermatologists. British association of dermatologists' guidelines for the management of lichen sclerosus 2010. Br J Dermatol 2010;163:672-82.
13. Lewis FM, Tatnall FM, Velangi SS, Bunker CB, Kumar A, Brackenbury F, *et al*. British association of dermatologists guidelines for the management of lichen sclerosus, 2018. Br J Dermatol 2018;178:839-53.
14. Bracco GL, Carli P, Sonni L, Maestrini G, De Marco A, Taddei GL, *et al*. Clinical and histologic effects of topical treatments of vulval lichen sclerosus. A critical evaluation. J Reprod Med 1993;38:37-40.
15. Goldstein AT, Creasey A, Pfau R, Phillips D, Burrows LJ. A double-blind, randomized controlled trial of clobetasol versus pimecrolimus in patients with vulvar lichen sclerosus. J Am Acad Dermatol 2011;64:e99-104.
16. Kartamaa M, Reitamo S. Treatment of lichen sclerosus with carbon dioxide laser vaporization. Br J Dermatol 1997;136:356-9.
17. Peterson CM, Lane JE, Ratz JL. Successful carbon dioxide laser therapy for refractory anogenital lichen sclerosus. Dermatol Surg 2004;30:1148-51.
18. Shah R, Ghiya R, Iyer A, Marfatia YS. Lichen sclerosus: A case report with review of literature. Indian J Sex Transm Dis 2007;28:40-2.
19. Guo H, Peng X, Jin C, Wang L, Chen F, Sa Y, *et al*. Lichen sclerosus accompanied by urethral squamous cell carcinoma: A retrospective study from a urethral referral center. Am J Mens Health 2018;12:1692-9.
20. Brisigotti M, Moreno A, Murcia C, Matias-Guiu X, Prat J. Verrucous carcinoma of the vulva. A clinicopathologic and immunohistochemical study of 5 cases. Int J Gynecol Pathol 1989;8:1-7.
21. Thomas RH, McGibbon DH, Munro DD. Basal cell carcinoma of the vulva in association with vulval lichen sclerosus et atrophicus. J R Soc Med 1985;78 Suppl 11:16-8.