Histopathological Spectrum of Lichen Sclerosus Et Atrophicus

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Abstract

Introduction: Lichen sclerosus (LS) et atrophicus is an inflammatory disorder of unknown etiology affecting skin and mucosa, especially the genital area. Clinically, its main features are whitish papules which converge to form plaques and atrophic patches. Histopathology of LS et atrophicus is characterized by the constellation of an atrophic epidermis with loss of rete ridges, some lymphocytes in the basal layer, a subepidermal band of sclerosis, and a lichenoid infiltrate of lymphocytes beneath that band is diagnostic of LS. Materials and Methods: Skin specimens from 25 patients with LS were collected from the hospital records for 5 years. The diagnosis of all cases was made on the basis of clinical morphology and histopathologic features. Sections were stained with hematoxylin and eosin, periodic acid-Schiff, and Elastic-Van Gieson. Criteria evaluated included hyperkeratosis, epidermal atrophy, follicular plugging, basal cell vacuolation, vascular ectasia, hyalinosis, inflammatory infiltrate, dermal edema, and deep dermal fibrosis. Results and Conclusion: Of a total of 25 patients, 18 patients had extragenital (EG) LS and 7 had genital manifestations. Mean age of patients with EG was 28 years, and genital was 38 years. To summarize, the main histopathological findings seen in LS are essentially the same as reported in literature, namely, hyperkeratosis, epidermal atrophy, follicular plugging, basal cell vacuolation, vascular ectasia, hyalinosis, inflammatory infiltrate, dermal edema, and fibrosis.

Keywords: Extrap genital, genital, histopathology, lichen sclerosus et atrophicus

Introduction

Lichen sclerosus (LS), et atrophicus, described originally by Hallopeau, in 1887 is an inflammatory disorder of unknown etiology affecting skin and mucosa, especially the genital area.[1,2] Although reported in all age groups, a bimodal incidence is observed as it affects prepubertal girls and especially menopausal women.[3,4] Clinically, its main features are whitish papules which converge to form plaques and atrophic patches. Histopathology of LS is characterized by alterations in the epidermis and dermis as well as inflammatory cell infiltration. The constellation of an atrophic epidermis with loss of rete ridges, some lymphocytes in the basal layer, a subepidermal band of sclerosis, and a lichenoid infiltrate of lymphocytes beneath that band is diagnostic of LS.[5,6]

Materials and Methods

The present study was retrospective wherein skin specimens from 25 patients with LS were collected from the hospital records over a period of 5 years. The diagnosis of all cases was made on the basis of clinical morphology and histopathologic features. Sections were stained with hematoxylin and eosin (H and E), periodic acid-Schiff (PAS), and Elastic-Van Gieson. Criteria evaluated included hyperkeratosis, epidermal atrophy, follicular plugging, basal cell vacuolation, vascular ectasia, hyalinosis, inflammatory infiltrate, dermal edema, and fibrosis.

Observations and Results

Of a total of 25 patients, 18 patients had extragenital (EG) (Group I) LS and 7 had genital (Group II) manifestations [Table 1]. None of the patients had both genital as well as EG involvement. Mean age in Group I was 28 years, and Group II was 38 years. In Group I, the youngest and the oldest patient were of 1 year and 56 years, respectively; whereas in Group II, it was 4 years and 70 years, respectively. None of the patients had any past significant history or autoimmune disease. Serological studies
| Cases | Duration (years) | Hyperkeratosis | Follicular plugging | Epidermal atrophy | Basal cell vacuolation | Vascular ectasia | Dermal hyalnosis | Dermal inflammation | Deep dermal fibrosis | Loss of fibers on VVG stain |
|-------|----------------|----------------|------------------|------------------|-----------------------|----------------|----------------|-------------------|----------------------|-----------------------------|
| EG    |                |                |                  |                  |                       |                |                |                   |                      |                             |
| 1     | 0.75           | -              | +                | +                | -                     | +              | -              | +                 | +                    | +                           |
| 2     | 3              | -              | +                | +                | -                     | +              | +              | -                 | +                    | +                           |
| 3     | 1              | +              | +                | +                | +                     | -              | +              | +                 | -                    | -                           |
| 4     | 3              | +              | -                | +                | +                     | -              | +              | +                 | +                    | -                           |
| 5     | 2              | -              | -                | +                | -                     | +              | +              | +                 | +                    | -                           |
| 6     | 1              | +              | +                | +                | -                     | +              | -              | +                 | -                    | +                           |
| 7     | 2              | -              | +                | +                | -                     | +              | -              | +                 | -                    | +                           |
| 8     | 1              | +              | -                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 9     | 7              | +              | -                | +                | +                     | -              | -              | -                 | -                    | -                           |
| 10    | 1              | +              | +                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 11    | 2              | +              | -                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 12    | 1              | +              | -                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 13    | 3              | +              | -                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 14    | 0.5            | -              | +                | -                | +                     | +              | -              | +                 | +                    | +                           |
| 15    | 0.25           | +              | -                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 16    | 4              | -              | +                | +                | +                     | -              | +              | +                 | +                    | -                           |
| 17    | 3              | -              | +                | +                | +                     | +              | +              | +                 | +                    | -                           |
| 18    | 3              | +              | -                | +                | -                     | +              | +              | +                 | +                    | +                           |
| Total (%) | 11 (61) | 7 (38.8) | 16 (89) | 12 (67) | 18 (100) | 13 (72) | 13 (72) | 14 (78) | 13 (72) |                             |
| Genital |                |                |                  |                  |                       |                |                |                   |                      |                             |
| 1     | 0.4            | -              | -                | -                | -                     | +              | -              | +                 | -                    | -                           |
| 2     | 5              | +              | +                | -                | +                     | +              | +              | +                 | +                    | +                           |
| 3     | 0.16           | +              | +                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 4     | 5              | +              | -                | +                | +                     | +              | +              | +                 | +                    | +                           |
| 5     | 15             | -              | +                | +                | -                     | +              | +              | +                 | -                    | +                           |
| 6     | 3              | +              | -                | -                | +                     | +              | +              | +                 | +                    | -                           |
| 7     | 6              | +              | +                | -                | +                     | +              | +              | +                 | +                    | +                           |
| Total (%) | 6 (86) | 4 (57) | 2 (28.5) | 4 (57) | 7 (100) | 6 (86) | 7 (100) | 3 (43) | 6 (86) |                             |

EG: Extranexual, VVG: Verhoeff-Van Gieson
for viral infections were negative. The most commonly affected sites were neck, back, and thigh in the EG region. One case each of the upper lip and breast were also present. Vulva and prepuce were the affected areas in genital region. The various histopathological features observed in all the cases have been tabulated in Tables 1 and 2. These findings were reported by the same set of observers to avoid any inter-observer variability.

The patients were followed up for 6 months to 2 years. The variable response was observed to treatment with high-potency steroids. None of the cases developed any hypertrophic or verrucous changes clinically thus, ruling out malignancy.

**DISCUSSION**

LS is a sclerosing inflammatory dermatosis, commonly affecting anogenital skin, with less common EG involvement varying from 15% to 20%.[5-8] However, the present study has more of EG cases. It is likely that a disease that is typically described in the genital area is not usually biopsied by the clinician who is fairly confident of this diagnosis.[5] In EG lesions, which have more clinical mimics, are frequently biopsied to confirm the diagnosis. The etiology of this disease is still unknown, and various factors such as hormonal, immunological alterations, genetic aberrations and *Borrelia burgdorferi*, hepatitis C virus and human papilloma virus (HPV) infection have been implicated.[7,8] However, in all our cases, there was no significant family history or history of any autoimmune disease.

Our study confirms previous data suggesting that LS more commonly affects women than men. The male to female ratio in our study was 1:2. The mean age group affected was 31 years, 28 for EG, and 38 for genital lesions. This was lower than the age group reported by Sang et al.[9] Although this disease mainly affects middle-aged and elderly women, the youngest patient in the present study was a male infant. The most common locations for EG disease are the buttocks, thighs, breasts, submammary area, neck, back and chest, shoulders, axillae, and wrists.[8] The common sites in the present study were neck and back [Figure 1]. Genital lesions were commonly seen on the vulva and prepuce [Figure 2].

Typically, EG lesions are polygonal, bluish white papules which coalesce to become atrophic plaques. These lesions are prone to koebnerization and may express themselves in areas of physical trauma, continuous pressure, and scarring.[5-8] In genital region, the main features are whitish papules which converge into plaques, often with erythema, ecchymosis, hyperkeratosis, fissures, excoriations, and telangiectasias. The mucosa is always spared so is the vagina and cervix in contrast to lichen planus. With progression, the skin atrophies and whitens, exhibiting a cigarette paper appearance. Symptoms include pruritus, burning, dyspareunia, dysuria, and painful defecation.[5,10]

The literature mentions vacuolar interface reaction in conjunction with dermal sclerosis as the minimum diagnostic criterion for LS. This study highlights other histopathological findings that could support a diagnosis of LS and help avoid diagnostic errors. Salient histologic findings observed in our cases were as mentioned in Tables 1, 2 and Figures 1, 2. In early lesions, these features may be quite subtle and may mimic those of psoriasis, lichen planus, or lichenoid dermatitis, thus making clinicopathologic correlation pivotal for the final diagnosis. In addition, these changes are often more prominent in adnexal structures than in interfollicular skin.[10] In the present study, hyperkeratosis was seen in 86% cases of genital and 61% cases of EG ones. Epidermal atrophy and thinning were more commonly seen in EG cases (93%), suggesting that EG lesions are more evolved.[11] Inflammation was observed in nearly all the genital lesions while dermal sclerosis was predominantly a feature of EG areas [Table 2 and Figures 1, 2].

In routine H and E sections, the basement membrane may appear thickened because of the area of subepidermal sclerosis. However, PAS stain did not reveal any thickening in our cases [Figure 3b]. This is in contrast to the observation of Fung and LeBoit who noted thickening in 44% cases.[12]

**Vascular ectasia was the most commonly seen histomorphological features in all the cases.** Our findings

| Table 2: Relative distribution of findings in all cases |
|-----------------------------------------------------|
| **Morphological findings** | **EG (%)** | **Genital (%)** |
|----------------------------|------------|----------------|
| Epidermal hyperkeratosis   | 11 (61)    | 6 (86)         |
| Keratotic plugging         | 7 (38.8)   | 4 (57)         |
| Atrophy                    | 16 (89)    | 2 (28.5)       |
| Basal cell vacuolation     | 12 (67)    | 4 (57)         |
| Vascular ectasia           | 18 (100)   | 7 (100)        |
| Dermal hyalinosis          | 13 (72)    | 6 (86)         |
| Inflammation               | 13 (72)    | 7 (100)        |
| Deep dermal sclerosis      | 14 (78)    | 3 (43)         |

EG: Extragénital

**Figure 1:** (a) Clinical picture of extragenital lichen sclerosus, (b) microphotograph showing epidermal atrophy and dermis hyalinosis (H and E, ×40), (c) microphotograph showing follicular plug in epidermis and vascular ectasia in dermis (H and E, ×100)
However, these ectatic blood vessels along with the epidermal atrophy can also be caused due to the use of topical steroids. Although these features cannot be reliably attributed to be caused by the disease process or treatment, the use of steroids will also be accompanied by other changes such as reduction in both epidermal and dermis thickness, loss of sebaceous glands, and subcutaneous fat loss, none of which were seen in our cases.\[13\] LS usually shows a spectrum of vascular changes ranging from lymphocytic vasculitis to granulomatous phlebitis and leukocytoclastic vasculitis. The lymphocytic vasculitis may occur in the form of concentric lymphohistiocytic infiltrate, dense perivascular lymphohistiocytic cuffing with fibrin deposition, or intramurally in muscular vessels. Recent studies have identified autoantibodies to glycoprotein extracellular matrix protein 1, which may explain the histopathologic evidence of vasculitis and thickening of the blood vessels wall in LS.\[2,5\]

These findings were not seen in any of our case.

The dermis in LS is characterized by loss of elastic fibers leading to homogenization of upper dermis along with a band like lymphohistiocytic infiltrate and an increase of these fibers and fibrosis in lower dermis [Figure 3a]. The loss of elastic fibers in the upper dermis has been attributed to the degradation of elastic fibers (elastolytic change) by elastase-type proteases secreted from dermal fibroblasts or activated macrophages. On the other hand, an increase of elastin in the lower dermis may reflect a repair process.\[14,15\] Morphea also shows deep dermal fibrosis but is not accompanied by the loss of elastic fibers in the papillary dermis as seen in LS [Table 3]. Although dermal hyalinosis/sclerosis is a diagnostic criterion for LS, it may be missing in early lesions.\[6\] Similarly, keratotic plugging may be more prevalent in the lesions of shorter duration.\[9\] However, no correlation existed between the duration of disease process and histological criteria as also reported by Marren et al.\[16\]

Inflammation primarily comprised lymphocytes and can be present in lichenoid or diffuse pattern beneath the zone of subepithelial edema. The inflammatory component can be a persistent or recurring phenomenon, thus has poor correlation with the duration or site of disease.\[6\] The CD3, CD8, and CD57 positive lymphocytic population is located just below the edematous dermis.\[17\] The infiltrate is initially dense, which along with the basal vacular degeneration raises the differential of lichen planus. The subsequent edema, loss of dermal elastin, paucity of cytoid bodies, and lack of wedge-shaped hypergranulosis are features specific to LS. Mycosis fungoides is another differential diagnosis sharing features such as epidermotropism and coarse collagen bundles in dermis [Table 3].\[2,18\]

Resolution of LS is usually difficult. However, in some cases, especially in prepubertal girls, it may remit spontaneously. Rarely, transformation into squamous cell carcinoma has been reported in 4%–6% of genital cases. Although the exact carcinogenic mechanism is still debatable, several HPV-independent hypotheses have been postulated.\[1,2,4,10\] Given the long-term malignant potential, 6 months follow-ups and histopathological examination are recommended for all patients with genital LS, especially the clinically suspicious ones. In the present study, none of our biopsies showed any features of dysplasia or koilocytosis due to frequent association with autoimmune diseases such as alopecia, vitiligo, thyroid, and pernicious anemia; screening tests comprising blood tests for iron, B12, glucose, thyroid function, and autoantibody levels should be done for all patients.\[4\]

The treatment modality of choice is topical corticosteroids though EG lesions are less responsive than genital ones. The next most frequent, of controversial efficacy, are tacrolimus, pimecrolimus, calcipotriol, testosterone, retinoids, antimalarial agents, photodynamictherapy, and surgery. CO2 laser and oral stanozolol have also been reported as possible treatment modalities.\[2,4,2\]
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**Table 3: Common mimics of lichen sclerosus et atrophicus and their differentiating points**

| Differentials       | Site affected                  | Clinical features                                                                 | Histopathological findings                                                                 | Special stains                       | Treatment                                      |
|---------------------|--------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|--------------------------------------|-----------------------------------------------|
| Lichen sclerosus    | Genitals, upper trunk, neck, arms | Flat ivory white papules with progressive atrophy and scarring                  | Atrophic epidermis with basal vacuolar change (flattened rete pegs)                         | PAS: BM thickening                   | Superpotent topical corticosteroids           |
|                     |                                |                                                                                  | Zone of subepidermal edema and homogenized collagen                                          | VVG: Loss of elastic fibres, lymphocytes usually |                                |
|                     |                                |                                                                                  | Lymphocytic infiltrate beneath edema                                                        |                                      |                                |
|                     |                                |                                                                                  | Ectatic blood vessels                                                                       |                                      |                                |
| Vitiligo            | Face, extremities, dorsal hands, and genitals; symmetrical fashion              | Well-demarcated depigmented patches with normal skin texture                         | Absent/decrease in melanin pigment                                                          | Masson-Fontana stain:               | Corticosteroids for localized disease, PUVA, or laser therapy for widespread disease |
|                     |                                |                                                                                  | Interface dermatitis                                                                       | Loss of melanin S100 (IHC): Loss of melanocytes                                             |                                |
| Morphea             | Scalp, trunk, and extremities                                             | Indurated plaques with ivory center and violaceous hue                               | Reticular dermal fibrosis extending into subcutis (increase in elastic fibers)            | VVG stain: Preservation of elastic fibers                                               | Topical corticosteroids, calcitriol, phototherapy |
| Lichen planus       | Oral mucosa, flexor surfaces of forearm, legs and glans penis                 | Flat-topped violaceous papules                                                      | Compact orthokeratosis and hypergranulosis                                                   |                                      |                                |
|                     |                                |                                                                                  | Basilar squamatization; Civatte bodies                                                     |                                      |                                |
|                     |                                |                                                                                  | Elongated rete pegs                                                                        |                                      |                                |
|                     |                                |                                                                                  | Interface dermatitis with dense lichenoid infiltrate                                        |                                      |                                |
| Tinea versicolor    | Upper trunk, arms                                                          | Well-demarcated macules and patches with variable depigmentation                   | Budding yeast and pseudohyphae in cornified layer                                           | PAS and GMS for fungus                 | Topical antifungals                          |
| Mycosis fungoides   | Lower part of trunk, thighs, entire body in late stages                     | Erythematous atrophic patches with or without hypopigmentation                     | Psoriasiform hyperplasia of epidermis with hyperkeratosis                                   |                                      |                                |
|                     |                                |                                                                                  | Lichenoid infiltrate with atypical epidermotropism                                        | Demonstration of monoclonality for CD4 by IHC, molecular study for clonal TCR rearrangement | Topical steroids, PUVA, retinoids, chemotherapy                                      |
| Radiation dermatitis| Upper back, sites of irradiation                                          | Morphea-like lesion, ulcer, vascular lesion, history of irradiation present           | Atrophic epidermis with basal vacuolar change                                                |                                      |                                |
|                     |                                |                                                                                  | Swollen collagen fibers in dermis showing irregular eosinophilic staining                  |                                      |                                |
|                     |                                |                                                                                  | Atypical radiation fibroblasts and telangiectatic blood vessels                           |                                      |                                |

PAS: Periodic acid–Schiff, BM: Basement membrane, VVG: Verhoeff-Van Giesen, IHC: Immunohistochemistry, GMS: Gomori’s methenamine silver, TCR: T-cell receptor, PUVA: Psoralen and Ultraviolet A therapy

**Conclusion**

The main histopathological findings seen in LS are essentially the same as reported in literature, namely, hyperkeratosis, epidermal atrophy, follicular plugging, basal cell vacuolation, vascular ectasia, hyalinosis, inflammatory infiltrate, dermal edema, and sclerosis. Apart from this, we noticed some interesting differences between the EG and genital forms of LS. However, since the figures are too small to comment on, studies comprising larger series of patients are required to bring out a statistical significance.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Lever, Walter F. 1909-, and David E. Elder. *Lever’s Histopathology of the Skin*, 10th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2009.
2. Patterson, James W. 1946-, and Gregory A. Hosler. *Weedon’s Skin*
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Pathology. Fourth edition.: Churchill Livingstone Elsevier, 2016.
3. Yu L, Li Z, Feng S. Lichen sclerosus of face: A case report and review of literature. Indian J Dermatol 2016;61:120.
4. Tasker GL, Wojnarowska F. Lichen sclerosus. Clin Exp Dermatol 2003;28:128-33.
5. Fistarol SK, Itin PH. Diagnosis and treatment of lichen sclerosus: An update. Am J Clin Dermatol 2013;14:27-47.
6. Weyers W. Hypertrophic lichen sclerosus sine sclerosis: Clues to histopathologic diagnosis when presenting as psoriasiform lichenoid dermatitis. J Cutan Pathol 2015;42:118-29.
7. Larre Borges A, Tiodorovic-Zivkovic D, Lallas A, Moscarella E, Gurgitano S, Capurro M, et al. Clinical, dermoscopic and histopathologic features of genital and extragenital lichen sclerosus. J Eur Acad Dermatol Venereol 2013;27:1433-9.
8. Coelbo WS, Dimiz LM, Souza Filhi JB. Lichen sclerosus et atrophicus: Report of two cases with atypical presentations. An Bras Dermatol 2006;81 S Suppl 3:S297-300.
9. Oh SH, Ryu DJ, Lee KH, Lee JH. Clinicopathologic comparison of genital and extragenital lichen sclerosus et atrophicus. Korean J Dermatol 2008;46:633-40.
10. Regauer S, Liegl B, Reich O. Early vulvar lichen sclerosus: A histopathological challenge. Histopathology 2005;47:340-7.
11. Lester EB, Swick BL. Eosinophils in biopsy specimens of lichen sclerosus: A not uncommon finding. J Cutan Pathol 2015;42:16-21.
12. Fung MA, LeBoit PE. Light microscopic criteria for the diagnosis of early vulvar lichen sclerosus: A comparison with lichen planus. Am J Surg Pathol 1998;22:473-8.
13. Abraham A, Roga G. Topical steroid-damaged skin. Indian J Dermatol 2014;59:456-9.
14. Shiba Y, Ono K, Akiyama M, Fujimoto N, Tajima S. Increase of elastic fibers in lichen sclerosus et atrophicus. J Cutan Pathol 2014;41:646-9.
15. Godoy CA, Teodoro WR, Velosa AP, Garippo AL, Parra ER, et al. Unusual remodeling of the hyalinization band in vulval lichen sclerosus by type V collagen and ECM 1 protein. Clinics (Sao Paulo) 2015;70:356-62.
16. Marren P, Millard PR, Wojnarowska F. Vulval lichen sclerosus: Lack of correlation between duration of clinical symptoms and histological appearances. J Eur Acad Dermatol Venereol 1997;8:212-6.
17. Carlson JA, Grabowski R, Chichester P, Paunovich E, Malfetano J. Comparative immunophenotypic study of lichen sclerosus: Epidermotropic CD57+lymphocytes are numerous − Implications for pathogenesis. Am J Dermatopathol 2000;22:7-16.
18. Busam KJ. Foundations in Diagnostic Pathology: Dermatopathology. New York: Saunders; 2015.