Lichen sclerosus as a clinical problem

Renata Przybylska[1], Katarzyna Plagens-Rotman[2], Krystyna Jaracz[1], Zygmunt Adamski[3], Magdalena Czarnecka-Operacz[3]

[1]Department of Neurological Nursing, Poznan University of Medial Sciences, Poznan, Poland
[2]Chair of Mother's and Child's Health, Poznan University of Medial Sciences, Poznan, Poland
[3]Department of Dermatology, Poznan University of Medial Sciences, Poznan, Poland

Adv Dermatol Allergol 2018; XXXV (6): 644–648
DOI: https://doi.org/10.5114/ada.2018.77618

Lichen sclerosus (LS) is a chronic skin disease, mainly diagnosed among women during the postmenopausal period, localized within the genital area [1–3].

The etiopathogenesis of LS is not fully understood, however it seems that the genetic and autoimmune background may have the strongest influence on its development. The relationship with injuries, hormonal disorders, and chronic irritation of the genitals is also suggested [4–9].

For skin lesions located in the area of the vulva, the most common symptoms experienced by patients are itching, skin burns and pain. From the therapeutic point of view, this usually involves antihistaminic and sedative therapy, as well as topical treatment with corticosteroids.

The clinical picture of LS is characterized by swelling of the vulva, which in the course of the disease becomes indurated and inflamed. Further on, it leads to reduction of skin flexibility, the labia are reduced, and the vaginal opening is narrowed. In addition, fissures may appear within the area of the posterior commissure [10].

Treatment of LS is based on the topical use of the corticosteroids twice a day for up to 4 weeks, followed by 1–2 times per week, as well as topical calcineurin inhibitors, retinoids and topical hormonal medications (ointments containing estrogens and progesterone). Furthermore, phototherapy and photodynamic therapy are also suggested [11–13].

The aim of this study is to present three case reports of women diagnosed with lichen sclerosus and a brief review of contemporary therapeutic approaches.

Case 1: A 70-year-old woman was treated in the Department of Dermatology, Poznan University of Medical Sciences, due to the exacerbation in the course of the limited systemic sclerosis and lichen sclerosus previously confirmed by the skin biopsy. The course of the disease was relatively long as it started 20 years before. The patient was hospitalized several times – last time in February 2014. Initially lesions with porcelain-white spots of inflammation were recorded within the thorax, axilla, groin and vulva (Figures 1 A–C). Within about a month, further lesions developed on the anterior abdominal area with clinical characteristics of hemorrhagic morphological-type blisters. A scattered porcelain-white sclerosis was observed on hospital admission. The patient reported intense itching sensation in skin lesions, general weakness, and constant hands tremor. Procaine penicillin (10 injections of 2.4 million IU i.m.) was administered as the basic treatment.

Diagnosis: Lichen sclerosus et atrophicus bullosus was confirmed by histopathological examination in May 2016. Concomitant diseases: type 2 diabetes, fatty liver disease, obesity, osteoarthritis, cataract and cholecystectomy in anamnesis. Laboratory findings: peripheral blood smear (LIM % – 47.1), serum glucose level (148 mg/dl), alanine aminotransferase (ALT; 38 U/l), aspartate aminotransferase (AspAT; 35 U/l) and glycated hemoglobin (HbA_{1c}; 8.3%).

Additional examinations: abdominal ultrasonography: Liver: fragmentally visible hyperechogenic liver steatosis, not enlarged, without focal changes, biliary tract not dilated, post-cholecystectomy condition. Pancreas: visible in the range of pancreas head and tail with normal echogenicity, the pancreatic duct not dilated, kidney with normal structure and shape without blockage and concretion. Spleen: homogenous, not enlarged, aorta not dilated, atherosclerotic lesions, empty bladder.

Chest X-ray: In the left middle pulmonary, 5 mm shading, probably accumulation of vascular shadows, pulmonary area without density and lesions.

Skin immunopathological examination: no deposits of IgA, IgM, IgG, IgG1, IgG4 and C3 were detected. In addition, antibodies against desmosome proteins of the spinous layer, or antibodies against the basement membrane (BMZ) in IgG class and IgG4 subclass on the substrate of the esophagus of the ape were not detected in the serum.

Treatment: Due to cyclosporine A (CsA) systemic treatment: 150 mg CsA twice a day and cream containing

Address for correspondence: Katarzyna Plagens-Rotman PhD, Chair of Mother's and Child's Health, Poznan University of Medical Sciences, 41 Jackowskiego St, 60-512 Poznan, Poland, phone: +48 607 165 279, e-mail: plagens.rotman@gmail.com
Received: 16.03.2017, **accepted:** 11.09.2017.

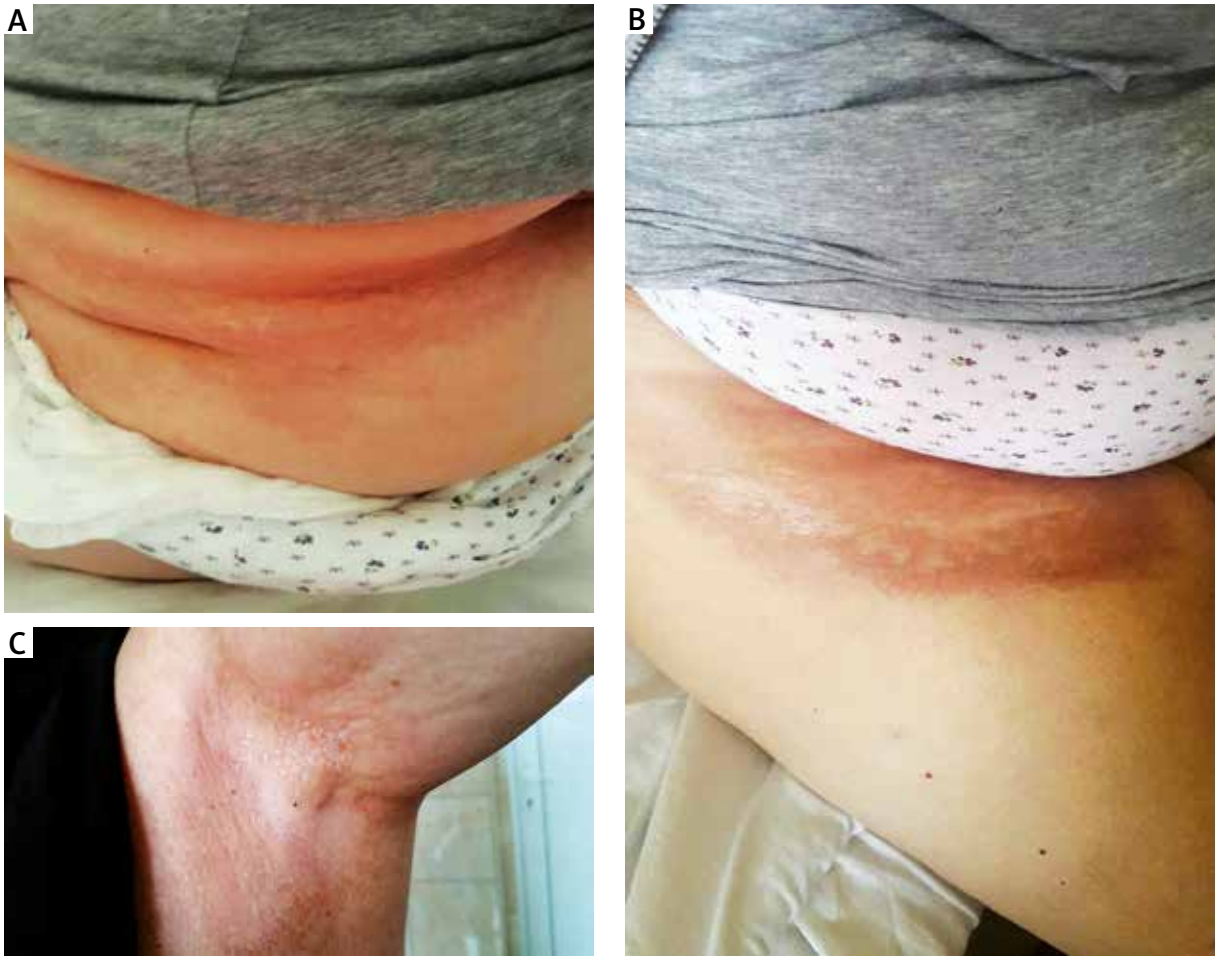

Figure 1. A, B, C – Patient with skin changes in the course of LS

vitamin A topically. Lesions of integument: Mometasone furoas in ointment twice a day. The vulva: cream with clotrimazolum;

Case 2: A 66-year-old woman diagnosed with lichen sclerosus of the vulva in the Department of Dermatology, Poznan University of Medical Sciences. The medical history since 2011: initially erythematous, follicular lesions around the wrist and the sacrum; since 2013 lesions in the oral cavity, atrophy of the vulva, leukoplakia – with pain, itching and burning sensation. Photodynamic therapy was applied for 10 weeks in 2013 and topical steroid treatment as well as cream containing vitamin A + E, but brought no significant improvement.

Diagnosis: Lichen planus confirmed by histopathological examination (April 2016). Concomitant diseases: spontaneous primary (essential) hypertension and thyroidectomy in anamnesis. Diagnostic findings: Direct IMF of the oral mucosa (direct immunofluorescence of the mucous membrane): no deposits of IgA, IgM, IgG, IgGl, IgG4, and C3.

Examination of basal membrane zone (BMZ) antibodies: negative for anti-BP180/anti-BP 230 IgG. Blood glucose: 106 mg/dl. High level of total cholesterol 283 mg/dl, low-density lipoprotein (LDL; 190.9 mg/dl), high-density lipoprotein (HDL; 58 mg/dl), triglycerides (171 mg/dl).

Gynecological examination: corpus uteri – body of uterus and uterine appendages examined by palpation with no lesions, no inflammation signs, lesions on the labia (lichen of the mucous membrane).

Laryngological examination: diffuse lesions in the oral mucosa (erosions), curvature of the nasal septum surgical examination.

Rectal examination: inconsiderable redness around the anus, internal and external anal sphincter with the correct contraction, no stenosis, no pain during examination.

Abdominal ultrasonography: Liver: hyperechogenic – moderate steatosis, not enlarged. A few cysts visible in the liver with a diameter of about 8 mm. Biliary tract: not dilated, a post-cholecystectomy condition. Pancreas: not enlarged, with normal echogenicity; the pancreatic duct not dilated; kidney with normal structure and shape without blockage and concretion, hypertrophied column of Bertin in both kidneys, left kidney with an inconsiderable scarring on the Bowman's capsule, empty bladder.

Treatment: Systemic treatment: Clindamacin i.v. (intravenous injection as the preventive treatment – biopsy of the oral mucosa). Topical – cream with vitamin A, Nystatin with hydrocortisone, and a zinc paste. The dermatological condition improvement was observed.

Case 3: A 78-year-old woman diagnosed with lichen sclerosus, and limited systemic sclerosis in the Department of Dermatology, Poznan University of Medical Sciences. Medical history of ca. 15–20 years, confirmed by skin biopsy in 2014.

Laboratory findings: Anti-nuclear antibodies (ANA) 1/5120, Ro – 52+, RNP (+), SS – A (+) in April 2016.

Direct immunofluorescence (DIF): lumpy deposits of IgA (+/–) i C3 (+/–) along the BZM, individual deposits of IgM below epidermis.

Concomitant diseases: type 2 diabetes, hypertension, urinary incontinence, depression, and hypothyroidism.

Treatment: By the time of the survey the patient had been treated with procaine penicillin UVB311 and UVA 1 with a relatively good result, however she was disqualified from further phototherapy due to the implanted pacemaker. The treatment with procaine penicillin and methotrexate is considered in the future. The patient was treated with topical ointment containing vitamin A + E on the infected callus, and 0.1% tacrolimus ointment on the ectropion lesions.

Adverse events during treatment (during the present hospitalization): An increased level of blood glucose (119 mg/dl), high level of erythrocyte sedimentation rate (30 mm/h), lymphopenia (0.94 × 10^3/µl).

Recommendations: At the early stage of LSA therapy, the patient must be informed clearly that the treatment may be long and therapeutic effects may require time.

- In order to avoid delays in diagnosis, patients with symptoms or with suspected LS require rapid intervention by a specialist and prompt treatment; biopsy should be done in case of:
  - doubt in making a diagnosis,
  - ineffective first-line treatment,
  - suspected cancer (cancer arising in extragenital presentations is described only rarely and may be coincident with other factors, but SCC can exist in genital LS) [14].
- Topical treatment – the basic LS treatment in women is topical corticosteroids [15, 16]:
  - It is recommended to use Clobetasol propionate 0.05% ointment twice a day for 4 weeks and the reduction of the dose to once a day afterwards (level of evidence: 1–2, grade of recommendation: A).
  - Lefevre *et al.* [17] had also demonstrated the effective use of weaker corticosteroids (clobetasone butyrate 0.05% or mometasone furoate 0.1%). Use of mometasone furoate 0.1%, once a day for 4 weeks and then twice a day for 2 months significantly improves the clinical picture of LS. After 12 weeks of the treatment almost all subjects showed full reversal of dermatological changes without side effects.
- Local sex hormones [18]:
  - The topical use of estrogens in LS treatment in not recommended.
  - The benefits of local use of testosterone and dihydrotestosterone in LS treatment were not indicated when compared to the topical treatment with Clobetasol propionate 0.05% (level of evidence: 1+, grade of recommendation: A).
  - The efficacy of 2% progesterone cream in LS treatment was not demonstrated when compared to the topical treatment with clobetasol propionate 0.05% (level of evidence: 1+, grade of recommendation: A).
- Topical ciclosporin is not recommended (level of evidence: 3, grade of recommendation: D).
- Calcineurin inhibitors:
  - Calcineurin inhibitors (CNIs), tacrolimus and pimecrolimus are a group of immunosuppressive drugs. Research conducted by Kim *et al.* [19] demonstrated high effectiveness and safety of topical application of tacrolimus twice a day when it comes to treatment of LS. It was also confirmed by the research conducted by Kauppila *et al.* [20], where in 20 of 29 women, improvement or clinical remission was observed. What is more, the authors found that calcineurin inhibitors are the effective method of treatment in patients not responding to corticosteroid treatment. Research conducted by Nissi *et al.* [21] showed that application of pimecrolimus 1% cream twice a day for 6 consecutive months brought relief in itching and lack of pain in 35% of women, and after 2 months in 42% of female patients. Furthermore, no systemic side effects were observed. Mild burning and itching in the first 3–14 days were reported by 50% of women.
  - However, it must be strongly emphasized that the use of calcineurin inhibitors in the area of external genitalia requires thorough examination of the patient who are at risk of human papilloma virus (HPV) infection.
  - Topical use of tacrolimus seems to be an effective and probably safe alternative in LS treatment in some patients (level of evidence: 2+, grade of recommendation: C).
  - Pimecrolimus and Clobetasol propionate 0.05% are effective in alleviating the itching and burning sensation of the skin. However, pimecrolimus showed lower effectiveness and Clobetasol propionate 0.05% should be used as the first-line treatment (level of evidence: 1+, grade of recommendation: B).
- Topical use of retinoids brings positive effects in the treatment of LS. They can be used when topical steroids do not improve the dermatological condition (level of evidence: 3, grade of recommendation: D).
- The treatment with vitamin E has no beneficial effect over emollients [22] (level of evidence: 2+, grade of recommendation: D).

- UVA1 phototherapy [22] is a potential first-line treatment method in cases of extragenital LS. UVA1 phototherapy can be taken under consideration when the use of topical corticosteroids do not show the improvement of the dermatological condition. However, well-documented development of cancers after PUVA and UVB exposition rises concerns, especially in the area of genitalia (level of evidence: 1+, grade of recommendation: B).
- The use of cyclosporine by oral route may be considered, but studies on the use of cyclosporine in men and children were not available (level of evidence: 3, grade of recommendation: D).
- Methotrexate of 10–15 mg a week together with systemic steroids for 6 months improves the treatment of LS (level of evidence: 3, grade of recommendation: D).
- LS treatment with Cycloferon is not recommended (level of evidence: 3 (lack of information concerning the control group), grade of recommendation: D).
- Penicillins and cephalosporins (Ceftriaxone 1 g in intramuscular injection every 2 weeks in 3 doses and then once a month (p.r.n; pro re nata, as the occasion arises; when necessary) or penicillin G, benzathine suspension (long duration) of 2.4 million units every 2 weeks in intramuscular injection at 3 doses. Then, once a month (p.r.n. basis), (level of evidence: 3, grade of recommendation: D).
- Emollients, e.g. ointments without fragrances, such as paraffin and Vaseline in equal parts, in the form of creams several times a day (level of evidence: 2+ to 3, grade of recommendation: D) [15, 23].

Psychological aspects with elements of care in lichen sclerosus [10, 18, 24]:

- Learning about the proper use of topical corticosteroids, with particular regard to thorough hand washing after their use, avoiding contact with sensitive areas, e.g. eyes.
- Reduction or elimination of certain sport activities, e.g. horse riding and cycling due to over-loading of the genital area.
- Awareness of an increased risk of cancer; all patients should be provided with a patient information leaflet along with evidence of this fact in their medical records.
- In case of development of a tumor, pain, changes in the appearance of the skin, medical advice should be sought as soon as possible.
- Awareness of an increased risk of autoimmune diseases.
- Taking oral contraceptives with anti-androgenic properties may be associated with an increased risk of LS.
- Pain during sexual initiation can have a significant impact on the sexual life of patients, leading to reduction or complete cessation of initiation.
- Patients suffer from embarrassment due to persistent itching.
- Reduction of social activity.
- For the need of washing external genitalia, water with a small amount of cream or ointment should be used; washcloths and sponges should be eliminated.
- Baths should be replaced with showers.
- Infected areas must be dried with a soft towel.
- Use of loose underwear made of silk is recommended.
- Fabric softeners and enzymatic washing powders should not be used.
- Soap, shower gels, peelings, deodorants and moistened wipes should be eliminated.
- Elimination of antiseptics.
- In the case of scratching tendencies, nail painting is not recommended.
- Use of emollients as moisturizing agents is highly suggested.
- Use of moisturizing agents to alleviate the ailments is recommended.

The selection of appropriate LS treatment still remains a challenge in dermatology and gynecology. Topical corticosteroids as a first-line treatment have been highly effective, however, side effects of their prolonged use and a relative risk of carcinogenesis must be considered, especially in case of genital LS. Emollients are recommended as a maintenance therapy.

Conflict of interest

The authors declare no conflict of interest.

References

1. Lavorato FG, Nery NS, Bomm L, et al. What is your diagnosis? Case for diagnosis. An Bras Dermatol 2013; 2: 29-8.
2. Thibaudeau S, Luc M. Clitoroplasty: a blunt technique for patients with lichen sclerosis. J Plast Reconstr Aesthet Surg 2013; 66: e298-9.
3. Higgins CA, Cruickshank ME. A population-based case-control study of aetiological factors associated with vulval lichen sclerosus. J Obstet Gynaecol 2012; 32: 271-5.
4. Bhargava K, Lewis FM. Lichen sclerosus occurring on vaginal mucosa secondary to uterine prolapse. J Obstet Gynaecol 2013; 33: 319-20.
5. Hadas E, Żerdzińska AA, Norek N, et al. Multifocal lichen sclerosus. Case report. Przegl Dermatol 2015; 102: 28-32.
6. Edmonds EV, Hunt S, Hawkins D, et al. Clinical parameters in male genital lichen sclerosus: a case series of 329 patients. J Eur Acad Dermatol Venereol 2012; 26: 730-7.
7. Bjekić M, Šipetić S, Marinković J. Risk factors for genital lichen sclerosus in men. Br J Dermatol 2011; 164: 325-9.
8. Kreuter A, Wischnewski J, Terras S, et al. Coexistence of lichen sclerosus and morphea: a retrospective analysis of 472 patients with localized scleroderma from a German tertiary referral center. J Am Acad Dermatol 2012; 67: 1157-62.
9. Kreuter A, Kryvosheyeva Y, Terras S, et al. Association of autoimmune diseases with lichen sclerosus in 532 male and female patients. Acta Derm Venereol 2013; 93: 238-41.
10. Olek-Hrab K, Jenerowicz D, Osmola-Mańkowska A, et al. Selected vulvar dermatoses. Ginekol Pol 2013; 84: 959-65.

11. Fistarol SK, Itin PH. Diagnosis and treatment of lichen sclerosus. Am J Clin Dermatol 2013; 14: 27-47.
12. Goldstein A, Creasey A, Pfau R, et al. A double-bind, randomized controlled trial of clobetasol versus pimecrolimus in patients with vulvar lichen sclerosus. J Am Acad 2011; 64: e99-104.
13. Przytocka-Sadowska A, Dańczak-Pazdrowska A, Szewczyk A, et al. Treatment of genital lichen sclerosus in women – review. Ginekol Pol 2012; 83: 458-61.
14. Neill SM, Lewis FM, Tatnall FM, Cox NH. British Association of Dermatologists' guidelines for the management of lichen sclerosus 2010. Br J Dermatol 2010; 163: 672-82.
15. Virgili A, Minghetti S, Borghi A, Corazza M. Proactive maintenance therapy with a topical corticosteroid for vulvar lichen sclerosus: preliminary results of a randomized study. Br J Dermatol 2013; 168: 1316-24.
16. Virgili A, Borghi A, Minghetti S, Corazza M. Mometasone fuoroate 0.1% ointment in the treatment of vulvar lichen sclerosus: a study of efficacy and safety on a large cohort of patients. J Eur Acad Dermatol Venereol 2013; 23: 189-94.
17. Lefevre C, Hoffstetter S, Meyer S, et al. Management of lichen sclerosus with triamcinolone ointment: effectiveness in reduction of patient symptom scores. J Low Genit Tract Dis 2011; 15: 205-9.
18. Kirtschig G, Becker K, Günthert A, et al. Evidence-based (S3) guideline on (anogenital) lichen sclerosus. J Eur Acad Dermatol Venereol 2015; 10: e1-43.
19. Kim G, Park H, Kim H, et al. Topical tacrolimus ointment for the treatment of lichen sclerosus, comparing genital and extragenital involvement. J Dermatol 2012; 39: 145-50.
20. Kauppila S, Kotila V, Knuuti E, et al. The effect of topical pimecrolimus on inflammatory infiltrate in vulvar lichen sclerosus. Am J Obstet Gynecol 2010; 202: 181e1-4.
21. Nissi R, Eriksen H, Risteli J, et al. Pimecrolimus cream 1% in the treatment of lichen sclerosus. Gynecol Obstet Invest 2007; 63: 151-4.
22. Kirtschig G. Lichen sclerosus – presentation, diagnosis and management. Dtsch Arztebl Int 2016; 113: 337-43.
23. Virgili A, Minghetti S, Borghi A, Corazza M. Long-term maintenance therapy for vulvar lichen sclerosus: the results of a randomized study comparing topical vitamin E with an emollient. Eur J Dermatol 2013; 23: 189-94.
24. Haefner HK, Aldrich NZ, Dalton VK, et al. The impact of vulvar lichen sclerosus on sexual dysfunction. J Womens Health 2014; 23: 765-70.