Histopathological and clinical traps in *lichen sclerosus*: a case report

DACIANA ELENA BRĂNIŞTEANU1), DANIEL CONSTANTIN BRĂNIŞTEANU2), GABRIELA STOLERIU1), DAN FERARIU3), CĂTĂLINA MARIA VOICU1), LOREDANA ELENA STOICA6), CONSTANTIN CĂRUNTU5), DANIEL BODA6), FLORINA MIHAELA FILIP-CIUBOTARU7), ANDREEA DIMITRIU1), CEZAR-DORU RADU8)

1)Department of Dermatology, "Grigore T. Popa" University of Medicine and Pharmacy, Iassy, Romania
2)Department of Ophthalmology, "Grigore T. Popa" University of Medicine and Pharmacy, Iassy, Romania
3)Department of Pathology, Regional Institute of Oncology, Iassy, Romania
4)Department of Dermatology, University of Medicine and Pharmacy of Craiova, Romania
5)Department of Immunology, "Victor Babeş" National Institute for Research and Development in Pathology and Biomedical Sciences, Bucharest, Romania
6)Dermatology Research Laboratory, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
7)Department of Adult Family Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, Iassy, Romania
8)"Gheorghe Asachi" Technical University, Iassy, Romania

Abstract

*Lichen sclerosus et atrophicus* and limited systemic scleroderma (acrosclerosis) are inflammatory skin diseases that ultimately evolve into two distinct modes of atrophic scar formation, but which can easily be confused clinically. They are very rarely associated. The literature has reported cases in which *lichen sclerosus* was associated with various forms of scleroderma, but often with localized morphea. The characteristic histopathological picture of *lichen sclerosus* includes a thin epidermis, with orthohyperkeratosis and vascular degeneration in the basal layer, loss of elastic fibers, and band-like inflammatory infiltrate in the papillary dermis, while systemic sclerosis is characterized by excessive deposition of collagen in the dermis, accompanied by reduction in adnexal structures and their entrapment in collagen, and the presence of perivascular lymphocytic inflammatory infiltrate. We present the case of a 40-year-old female patient clinically diagnosed with systemic scleroderma and *lichen sclerosus* involving the genital mucosa. Physical examination in conjunction with laboratory findings (elevated antinuclear, anti-Scl-70, anti-SSA antibodies and immunogram) induced the supposition of the coexistence of *lichen sclerosus* and systemic scleroderma, fact confirmed by pathological examination. Systemic therapy with corticosteroids, immunosuppressive and phlebotropic drugs, peripheral vasodilators and other tropic adjuvants and topically potent topical corticosteroids was initiated. The course was favorable under therapy, the hardened skin slightly regaining elasticity, relief of itching and disappearance of *lichen sclerosus* lesions. Our case reaffirms the uncommon association of these two disorders. The importance of history, physical and laboratory examinations in making a diagnosis of certainty in emphasized.

Keywords: *lichen sclerosus et atrophicus*, systemic scleroderma, acrosclerosis.

Introduction

*Lichen sclerosus et atrophicus* and limited systemic scleroderma (acrosclerosis) are inflammatory skin disorders that ultimately evolve into two distinct types of scar formation.

*Lichen sclerosus et atrophicus* is a disease of unknown etiology, which most commonly involves the genital mucosa, the causative factors of which are genetic predisposition and infectious agents (human papilloma virus, spirochetes). This disease is a chronic inflammatory dermatosis that presents with severe itching, epidermal atrophy and dermal sclerosis affecting predominately the anogenital area of post-menopausal females [1]. It can affect both sexes, mainly females in the fifth and sixth decades of life [2]. The literature reports cases in which *lichen sclerosus* is associated with various forms of scleroderma, but most commonly with localized morphea [3]. There is an association with autoimmune diseases like vitiligo, thyroid disorders, type I diabetes, and alopecia areata [4]. Other pathogenic factors are low levels of androgens, genetic susceptibility, chronic infections, and trauma [4–6]. Characteristic histopathological features of *lichen sclerosus* involve epidermis and superficial dermis, with marked attenuation of the epidermis with hyperkeratosis, degeneration of the basal layer, follicular plugging, a band of homogenized collagen in the papillary dermis above a lymphocytic infiltrate [7]. Extensive vacuolar degeneration of the basal layer and edema may lead to fragility of the dermal–epidermal junction resulting in bulla formation in the case of a bullous *lichen sclerosus* [8].

Scleroderma is a connective tissue disease of unknown cause, produced by autoimmune mechanism, and characterized by marked fibrosis of the dermis and epidermal atrophy associated with visceral involvements. While *lichen sclerosus* does not cause significant damage to internal organs, limited systemic scleroderma is associated with extracutaneous involvements that occur in the late stages of disease, in order of frequency these being pulmonary, renal and/or gastrointestinal.
We are presenting the case of a rare association of *lichen sclerosus* and acrosclerosis.

**Case presentation**

We present the case of a 40-year-old female patient, living in a rural area, who presented to the Clinic of Dermatology, Iassy, Romania, for the investigation of Raynaud’s phenomenon simultaneously affecting the fingers and toes and for the treatment of some ulcers at the level of left medius, left thumb, and right medius.

Multiple skin and mucous membranes biopsies were performed in different stages of disease evolution. The biopsy specimens were sent to the Department of Pathology for diagnosis.

**Anamnestic history**

The onset of the Raynaud’s phenomenon was three years ago (with episodic vasospasm of the digital arteries triggered by cold, which caused pallor, followed by cyanosis and congestion), simultaneously affecting the fingers and toes. Some trophic changes affecting the fingers, forearms, dorsal sides of the hands and posterior thorax have been added in time, being more evident during the last year. The patient did not previously seek medical attention and care. The trophic changes in the fingers and toes culminated with the occurrence two months earlier of ulcers on the left thumb, left medius, and also right medius. She was not aware of either atrophic-cicatricial plaques on the posterior chest or genital mucosal changes, although latter were associated with constant itching.

The history revealed that she worked for 10 years in a toxic environment (zinc exposure) and has been smoking about 10 cigarettes/day for the past 20 years.

**General physical examination**

Presence of “Byzantine icon” facies was evidenced. When examining the musculoskeletal system, a tendency of fingers to be fixed in flexion position and bilateral swelling of the small joints of the hands was noticed.

**Local examination**

Objective physical examination upon admission revealed indurate skin over the forearms and dorsal aspect of the hands. Fingers also showed a degree of indurations, thinning and a tendency to be fixed in flexion position (Figure 1), and subcutaneous nodules and ulcers on the pulp of the left hand fingers II and III (Figure 2) and right hand finger III. Small, round, white, atrophic, asymptomatic plaques were present on the upper half of the posterior thorax (Figure 3). As to the face, a narrowing of the mouth orifice and the presence of radial furrowing around the mouth were seen (Figure 4). Genitally, there was erasing drawing large labia and the lining had a glossy, shiny appearance, being thinned and itchy (Figure 5). Perianal, she presented a 4 cm round, slightly hyperpigmented atrophic plaque extending to the vulva (Figure 6).

As following local examination, we were not sure whether the lesions at the level of posterior thorax were *lichen sclerosus* or drop-like morphea, a series of further investigation were initiated.

The reported case was supervised periodically regarding the early detection of potential eye touches given by the disease itself, as well in the monitoring of therapy with Hydroxychloroquine.

**Laboratory findings**

The significantly elevated levels of: antinuclear antibodies (298 IU), anti-Scl-70 antibodies (401.7 IU/mL), anti-SSA antibodies (409 IU), and immunogram (IgA 708 mg%, IgM 77%, IgG 4870%) supported the diagnosis of systemic scleroderma. Other findings were an increase in erythrocyte sedimentation rate (ESR) (50 mm/h) and IgE (>2000 IU) and the presence of a thrombocytopenia (90 000/mm³), which according to hematology consultation was not significant. Some possibly associated infections (*Borrelia burgdorferi*, hepatitis viruses B and C) were excluded.
Additional investigations were performed to identify the visceral involvements. Thus, chest X-ray revealed a right basal oval opacity, interpreted as encysted pleurisy, and samples ventilatory revealed the presence of a mixed respiratory dysfunction.

Abdominal ultrasound revealed two liver hemangiomas and the presence of some lymphadenopathies of 10–20 mm in the long hepatic, celiac, interaortocaval, perigastric, and left lumboaortic long axis that required further explorations. Abdominopelvic computed tomography (CT) revealed, in addition to the above-described lymphadenopathies, a diffuse duodenal wall thickening, the performed biopsy refuting the diagnosis of lymphoma. Digestive endoscopy made the diagnoses of Barrett’s esophagus and hiatal hernia.

During hospital stay two skin biopsies were performed, one from the most indurate area on the lateral aspect of the left forearm and the other from a round atrophic lesion on the posterior thorax. Pathological examination of the forearm lesion revealed a skin fragment covered by a loose crust of orthokeratotic keratin. The epidermis was atrophic with linear disposition (Figure 7). The papillary dermis was collagenized and reticular dermis showed thickened collagen fibers with loss of reticular pattern (Figures 8–10). A decrease in number of skin appendages (Figure 11) and their ascension in the dermal–epidermal junction with linear disposition were also noticed. The histopathological findings correspond to scleroderma.

Pathological examination of the lesion on the posterior thorax identified a skin fragment with uneven epidermal thickness, acanthotic areas, foci of orthokeratotic hyperkeratosis, areas in which the epidermis was acanthotic with associated hypergranulosis (Figure 12) and papillary dermis showed a moderate band-like chronic inflammatory infiltrate (Figure 13). Papillary dermis was slightly collagenized and the dermis presented slightly thickened collagen fibers, with preserved reticular pattern. The morphological diagnosis was lichenoid-type lesion with reactive changes in the epidermis, and associated scleroderma features (Figures 14 and 15). A special silver staining, Fontana–Masson, was also performed. It showed hypopigmentation in the lesion area, associating appearances of pigment incontinence (Figure 16) in contrast to the pigmentation of the neighboring basal layer (Figure 17).

Figure 7 – Atrophic epidermis with a tendency to linear disposition, absent skin appendages, marked collagenization of superficial and reticular dermis (Giemsa staining, ×40).

Figure 8 – Thick dermis with papillary layer reduction, [Hematoxylin–Eosin (HE) staining, ×50].

Figure 9 – The disappearance of elastic fibers architecture in the profound dermis – detail (HE staining, ×200).

Figure 10 – Thick dermis, papillary layer reduction and diffuse collagenization [Van Gieson (VG) staining, ×100].
Figure 11 – Low number of ascended, atrophic appendages (HE staining, ×40).

Figure 12 – Epidermis with irregular acanthosis, hypergranulosis, dense hyperkeratosis accompanied by focal parakeratosis (HE staining, ×40).

Figure 13 – Hydropic degeneration of the basal layer, isolated Civatte bodies, “sawtooth” appearance, rare appearances of interface dermatitis, with moderate lymphomonocytary inflammatory infiltrate and with reactive fibroblasts (HE staining, ×200).

Figure 14 – Lichenoid-type lesion (VG staining, ×40).

Figure 15 – Hypopigmentation in the lesional area with associated appearance of incontinentia pigmenti [Fontana–Masson (FM) silver staining, ×100].

Figure 16 – Depigmented lesion in the lichenoid-type lesion area (FM silver staining, ×100).


**Discussion**

The etiology of *lichen sclerosus* and localized scleroderma is unclear and probably multifactorial. The relationship between these lesions remains controversial and few data on the coexistence of these two entities have been published. These two diseases rarely occur in the same lesion and their pathogenesis is similar. Familial cases suggest the role of genetic factors. The coexistence of these lesions with other autoimmune diseases suggests that autoimmune mechanisms play a major role in their pathogenesis, also incriminated being the influence of environmental factors.

*Lichen sclerosus* and scleroderma are two clinical entities that can easily be confused. In the literature, there are case reports in which *lichen sclerosus* was associated with various forms of scleroderma. Some studies have shown that *lichen sclerosus* is present in 40% of the cases of localized morphea, and 2/3 of the cases of the generalized morphea, being most frequently overlooked by the patients because itching, the most common symptom, is associated to other causes.

Patients with localized scleroderma, especially those with morphea, should be carefully examined for concomitant *lichen sclerosus* (recommended by screening program) especially in the anogenital regions, as it is estimated that approximately 5% of patients with *lichen sclerosus* develop squamous cell carcinoma. Thus, the screening of these patients for *lichen sclerosus* and its treatment would have a major impact on cancer prevention, because only 20% of patients report genital itching and no patient reports clinical symptoms.

The presence of *lichen sclerosus* together with systemic scleroderma is sporadically noticed, most cases being associated with localized morphea.

Certainty diagnoses were made by the histopathological examination of skin biopsies, although data in the literature sometimes mention difficulty in differentiating from each other.

In our patient, the differential diagnosis was made based on clinical and histopathological criteria. In cutaneous *lichen sclerosus* with genital mucosa involvement, the differential diagnosis includes localized scleroderma (plaque morphea), in which the epidermis is atrophic in most case, with a tendency of linear disposition, marked collagenization of papillary and reticulate dermis, and ascension of skin appendages. In this lesion category, no aspects of hyperkeratosis with hypergranulosis or irregular basal epithelial hyperplasia with abundant accompanying inflammatory reaction in the dermal–epidermal interlining were seen. Also, chronic atrophic acrodermatitis, anetoderma, atrophoderma of Pasini and Pierini, Bowen’s disease, extramammary Paget’s disease, Queyrat’s erythroplasia, idiopathic guttate hypomelanosis, lichen planus, lichen nitidus, and vitiligo should be excluded.

Systemic scleroderma should not be confused with localized scleroderma (plaque morphea), scleredema, scleromyxedema, eosinophilic fasciitis, carcinoid syndrome, scleroderminform changes following exposure to polyvinyl chloride, Isoniazid, epoxy resins, silica.

*Lichen sclerosus* has a specific histological pattern. At the onset, superficial dermal edema is associated with a band-like lymphocytic infiltration in the lower part. In this early stage, homogenized collagen and wide ecstatic capillaries in the dermal papillae, just below the basal membrane, are also seen. Inflammatory infiltrate can be sparse or dense, lichenoid or interstitial, with epidermal lymphocyte exocytosis and lymphocytic/lymphohistiocytic vasculitis. In early lesions, the histological changes are often more prominent in adnexal structures than in the interfollicular areas. Adnexal structures show acanthosis, luminal hyperkeratosis, hypergranulosis with or without hair dystrophy and basement membrane thickening. In the formed lesions, the epidermis is thinned with ortho-hyperkeratosis and vacuolar degeneration of the basal layer. Hyperkeratosis is particularly marked at follicular ostium and may lead to follicular plugging. Vacuolar degeneration at the dermal–epidermal junction and the flattening of rete ridges predispose to the development of blisters that may become hemorrhagic. Loss of elastic fibers is typical for *lichen sclerosus*, feature that is not found in scleroderma. In older lesions, the mononuclear infiltrate is reduced and sparse, and small islands of mononuclear cells are scattered within the hyalinized dermis. Centrally, there is an area of dense hyperkeratosis accompanied by focal parakeratosis, area where the dermis presents slight acanthosis with associated hypergranulosis. In this area, there is focal hydropic degeneration of the basal layer, with interface dermatitis and isolated Civatte bodies. In the basal area of the epidermis, pigment loading is reduced and there is a “sawtooth” appearance to the superficial dermis. In the same area, at the level of the superficial dermal plane there is a moderate lymphomonocytary inflammatory infiltrate with reactive fibroblasts. On the lesional slopes or in depth the dermis shows marked collagenization with a smaller number of skin appendages or ascended in the superficial plane. Moreover, dermal melanophages may occur due to keratinocyte or melanocyte destruction. In early lesions, multiple serial sections and special stains [Periodic Acid–Schiff (PAS), Fontana, Virchoff, Toluidine Blue] are recommended.

The association of *lichen sclerosus* with systemic scleroderma suggests a common pathogenetic mechanism.

---

**Figure 17 – Pigmentation of neighboring basal layer (FM staining, ×200).**
Conflict of interests
The authors declare that they have no conflict of interests.

References
Histopathological and clinical traps in lichen sclerosus: a case report


Corresponding author
Daniel Constantin Brănișteanu, Lecturer, MD, PhD, Department of Ophthalmology, “Grigore T. Popa” University of Medicine and Pharmacy, 16 Universității Street, 700115 Iassy, Romania; Phone +40721–377 160, Fax +40232–210 608, e-mail: dbranisteanu@yahoo.com

Received: April 18, 2015

Accepted: October 19, 2016