Male and female genital lichen sclerosus. Clinical and functional classification criteria

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Abstract

Introduction: Lichen sclerosus (LS) is a chronic inflammatory disease affecting mainly the genital mucous membranes in both sexes. In the past, different terms were used to describe the disease, rendering a unique and specific clinical classification impossible.

Aim: New therapeutic approaches are being defined, which may contribute to a proper clinical management, however, a stage classification is essential to better define appropriate treatment for every stage of the disease.

Material and methods: One hundred and fifteen patients (50 women and 65 men) with a diagnosis of LS were enrolled between January 2014 and September 2016. All patients underwent cutaneous biopsy to confirm the clinical diagnosis of LS. Clinical and symptomatological parameters were used in order to put the patients into the correct stage of LS. The Dermatology Life Quality Index (DLQI) was used to classify patients based on subjective symptoms. Different cutaneous alterations and structural modifications of the genital mucosa were also taken into consideration in order to assign every patient to a specific stage.

Conclusions: Lichen sclerosus is clinically described differently in females and in males and every form of LS is put into one of two stages according to the degree of severity: early and late stages. Within the clinical practice, it is useful to screen patients for groups of early or late forms of the disease in order to obtain a uniform subdivision of patients: those who may benefit from localized treatments, require a systemic drug and must undergo physical treatments (surgical, stem cells infiltrations).

Key words: clinical staging, classification, diagnosis, lichen sclerosus, prognosis, treatment criteria.

Introduction

Lichen sclerosus (LS) is a chronic inflammatory disease with an uncertain etiology, affecting mainly the genital mucous membranes in both sexes. It is more frequently observed among women, with a male to female ratio (M : F) which varies between 1 : 3 and 1 : 5 [1]. The first descriptions of LS date back to the late 1800s and since then many terms have been used to define the disease (Table 1) [2–10].

Throughout the twentieth century, the international literature described LS using several definitions related to the clinical presentation of the disease in different studies (i.e. scleroderma circumscribed, leukoplakic vulvitis, primary atrophic vulvitis or balanitis, bullous lichen planus and atrophic chronic acrodermatitis, atrophic bullous scleroderma). For many decades, these descriptions have limited the development of standardized criteria for a useful and accurate management of LS.

Towards the end of the 1970s, the International Society for the study of Vulvar Disease [9, 10] finally coined the term lichen sclerosus to describe this pathology.

Lichen sclerosus mainly affects the genital mucosa and may be located or extended to the oral mucosa, even if the simultaneous involvement of both sites is not frequently observed [11, 12]. The disease leads to progressive alteration of the four main functions of the mucous tissue: hydration, elasticity, ability to resist mechanical stimulation and proprioceptive transmission. These changes explain most of the symptoms of the disease, which worsen over time and are associated with the destruction of the anatomic structures of the genital region in an advanced stage in both sexes.
In clinical practice, the spectrum of symptoms of LS seems closely related to different phases of the disease [13]. Lichen sclerosus has different clinical pictures in the two sexes for the anatomical differences that exist in the male and female and also subjective symptoms are differently reported by different patients, often regardless of the severity of the disease.

For this reason it is often necessary to manage the initial stages of LS as if they were the most advanced stages of the disease, especially when the subjective symptoms do not correlate with the clinical picture. Furthermore, prognostic studies have shown that if LS is detected early and advanced therapy is started, it responds better to conventional therapies [14, 15] with consequent minor anatomic-functional sequelae and a lower risk of stem cells from adipose tissue [22–24] and in our preliminary experience, we observed that patients treated with stem cells in the earlier stages of the disease had a better response than those treated later (work in progress).

Material and methods

A description of clinical presentations of LS in the different phases has been drafted. The study was carried out at the outpatient department of the Dermatological and Plastic and Reconstructive Surgery Unit of San Gallicano Dermatological Institute IRCCS – IFO of Rome.

The study includes data of 115 patients affected by genital lichen sclerosus, between January 2014 and September 2016.

Fifty patients were female, with a median age of 60 years (range: 0–86 years, and one nine-month-old patient) and sixty-five patients were male, with a median age of 48 years (range: 17–82 years).

To better understand the phase of LS we adopted in our Center the following procedures for every patient. During the first visit, all patients underwent a physical examination and a thorough medical history was taken in order to evaluate different levels of damage to the ano-genital area caused by LS (alterations of skin pigmentation, presence of skin fissures, changes of skin elasticity, anatomic alterations). A biopsy was performed for all suspected cases of LS (except for the nine-month-old patient). The clinical appearance and the symptoms were evaluated in order to divide the patients into different stages of genital lichen sclerosus and refer every patient to a specific treatment or specific follow-up.

All patients answered the questions of the Dermatology Life Quality Index (DLQI) [21]. The patients were asked about the impact of their disease and its treatment on their lives. Four main stages were developed based on the answers of the patients.

Clinical description of LS groups

In early stages, female (Figures 1 A, B) patients complain of a mild discomfort, such as alterations of local sensitivity most often described as itching or burning, a feeling of tension or excessive sensitivity to touch, also caused by intimate apparel. Upon direct observation, a circumscribed blanching can be observed on one or more restricted areas of the mucosa (vaginal introitus, labia minora, fornix). At this initial stage, a clinical diagnosis is difficult to reach, and a histological punch biopsy is considered useful and proposed to the patient.

In males, the first manifestations of LS, which is often the reason for a specialist visit, are color alterations, with hypochromic spots causing a mottled appearance, usually spreading to the foreskin, frenulum or near the top of the glans. The initial subjective symptoms may be limited to mild itching or alteration of local sensitivity, as in women. Pain occurs only rarely. These symptoms some-

### Table 1. Definitions of lichen sclerosus in the scientific literature from 1800 to 1900

| Definition                          | Author          | Year   | Ref. |
|------------------------------------|-----------------|--------|------|
| Vulvar and oral ichthyosis         | Weir            | 1875   | [1]  |
| Craurosis of vulva                  | Breisky         | 1885   | [2]  |
| Lichen planus atrophicus           | Hallopeau       | 1887   | [3]  |
| Lichen planus sclerosus            | Darier          | 1892   | [4]  |
| Playing card scleroderma           | Unna            | 1894   | [5]  |
| Disease white spot                 | Westberg        | 1901   | [6]  |
| Lichen albus                       | Von Zumbusch    | 1906   | [7]  |
| Lichen planus sclerosus and atrophic | Montgomery & Ormsby | 1907 | [8]  |
| Dermatitis lichenoides atrophic     | Csillag         | 1909   | [9]  |
| Balanite xerotica obliterans        | Stuhmer         | 1928   | [10] |
times tend to worsen after sexual activity. At this stage, a clinical diagnosis is very difficult. A common feature of male patients with LS is the short, non-elastic frenulum, which always tends to restrict or distort erection. Often a short frenulum is the only, early manifestation of an initial phase of LS (early stage) (Figures 2 A, B).

In male genitalia the white spots may merge affecting the foreskin as well, which tends to form a non-elastic ring, which may lead to a slight phimosis [20]. In this phase, men complain of a burning sensation and there is an increased risk of infections. At that time, the patients tend to limit sexual activity in order not to aggravate the symptoms but often this is not reported to the specialists. These clinical and symptomatological aspects make the picture of LS more complex. Subsequently in both sexes fragility of the mucosa to mechanical stimulation appears, especially during sexual activity. Especially in women, the onset of mild dyspareunia and development of fissures resulting from decreased elasticity of the affected areas is described. These cases always need a psychologist’s intervention.

In the following more advanced stages, stable fissures appear in addition to the symptoms described above. In women these are frequently located on the posterior fork. Progression of atrophy and fusion of the minor labia takes place as well as atrophy of the major

Figure 1. A – Initial atrophy starting from the posterior fork, B – extension of hypotrophy in the minor labia

Figure 2. A – Hypochromic spot, B – extension of hypochromic spots with the appearance of mild ring fibrotic
labia (Figure 3 A). In this phase, the subjective symptoms are associated with neurosensory disorders, such as itching, burning and pain to the touch (allodynia) regardless of sexual activity. These symptoms are also present while walking, standing or sitting. Injuries also affect the clitoral hood that is progressively incorporated by sclerotic tissue, until it is completely covered. An initial vulvar ostium stenosis is present with possible alterations to the urinary meatus, such as urethral stenosis. During this advanced stage, patients also complain of alteration to the flow of urine. In men the extension of sclerotic areas may accentuate the phimosis and the initial appearance...

Figure 3. A – Atrophy and fusion of the labia minor, atrophy of the labia major, the clitoral hood is incorporated by sclerotic tissue, and vulvar ostium stenosis, B – disappearance of the clitoris, vaginal ostium stenosis progression, complete disappearance of the labia minora and severe atrophy of the labia majora

Figure 4. A – Accentuation of the phimosis. Merger of the foreskin at the level of balanopreputial sulcus and initial urethral stricture, B – tight phimosis
of urethral stenosis can cause the patient's urinary issues (Figures 4 A, B).

In more advanced stages, we have found a complete incorporation with hooding of the clitoris as well as vaginal ostium stenosis progression, complete disappearance of the labia minora and severe atrophy of the labia majora (Figure 3 B). In this phase, the entire vulvar region is transformed into extremely fragile sclerotic tissue, which has a tendency for easy fissure throughout the entire genital area. This leads the patient to interrupt sexual activity (apareunia), with urinary difficulties and frequent urinary tract infections. Therefore, their personal life is extremely compromised.

In males, worsening of the sclerosis in the internal tissues of the penile urethra can cause a distal urethral stricture that tends to extend proximally. In more severe cases, urodynamic alterations may worsen. Urethral stenosis is more common in men than in women [19]. In these advanced stages it is possible in both sexes to be diagnosed with a squamous cell carcinoma that arises on areas of LS.

A proposed classification in two stages based on clinical and subjective symptoms is presented in Table 2.

Table 2. Proposed classification in two stages

| LS stage | Clinical characteristics | Male | Female |
|----------|--------------------------|------|--------|
| Early    | Subjective symptoms      | Mild itching or alterations of local sensitivity | Alterations of local sensitivity (e.g. Stinging, burning, tension, allodynia) |
|          |                          | Burning sensation | Burning, itching |
|          |                          | Dyspareunia | Dyspareunia |
|          |                          | Pain is rare | |
|          | Clinical examination     | Color alterations (hypochromic spots with mottled appearance) | Circumscribed blanching (vaginal introitus, labia minora, fork) |
|          |                          | Short frenulum is highly characteristic | Mucosal fragility to mechanical stimulation |
|          |                          | Merging of hypochromic spots with formation of an inelastic ring responsible of phimosis | Decreased elasticity can lead to painful fissures |
|          |                          | Decreased elasticity can lead to painful fissures | |
|          | Disease duration         | Difficult to establish; does not always correlate with disease severity, some cases tend to have a more rapid clinical progression | Difficult to establish; does not always correlate with disease severity, some cases tend to have a more rapid clinical progression |
| Late     | Subjective symptoms      | Burning sensation | Burning, itching |
|          |                          | Dyspareunia | Allodynia becomes more severe even without mechanical stimulation (e.g. standing, walking or sitting) |
|          |                          | Urinary symptoms | Apareunia |
|          |                          | Symptoms at rest | Urinary difficulties |
|          |                          | Apareunia | Frequent UTIs |
|          |                          | Urodynamic alterations | |
|          | Clinical examination     | Stable fissures | Stable fissures, especially on the posterior fork |
|          |                          | Extension of the sclerotic areas with accentuation of phimosis | Diffuse atrophy and fusion/complete disappearance of the minor labia |
|          |                          | Paraphimosis is a possible complication | Atrophy of the major labia |
|          |                          | Mild urethral stenosis | Clitorial hood is progressively covered by sclerotic tissue |
|          |                          | Extension of the sclerotic areas can lead to distal urethral stricture that tends to extend proximally | Vulvar ostium stenosis, possible alterations to the urinary meatus (e.g. urethral stenosis) |
|          |                          | Urethral stenosis | Complete incorporation with hooding of the clitoris |
|          |                          | Vulvar ostium stenosis | Vulvar ostium stenosis |
|          | Complications            | Squamous cell carcinoma can arise in areas of LS | Squamous cell carcinoma can arise in areas of LS |
|          | Disease duration         | Does not always correlate with disease severity, some cases tend to have a more rapid clinical progression than others leading to different clinical pictures | Does not always correlate with disease severity, some cases tend to have a more rapid clinical progression than others leading to different clinical pictures |
The clinical aspects and the symptoms were evaluated in order to assign each patient to a more or less earlier or later stage of the disease.

At the onset of the disease, the symptoms are usually difficult to recognize, and vary from patient to patient. Initial symptoms reported by patients (surface tension, itching, burning and, less often, pain or presence of slight alterations of genitalia as hypochromic mucosal areas) were all taken into consideration. In fact, non-specific symptoms may persist for a long time and patients generally do not refer to a specialist in the initial stages. On the other hand, the overlapping of symptoms may be misleading resulting in a delayed diagnosis.

It is worthy considering that the female population from our series has the diagnosis of LS established later and already presenting more severe clinical forms. In our experience, women have the diagnosis of LS established later in life than men especially in the form of early LS (34% of women vs. 70% of men).

Subjective symptoms are differently reported by different patients often regardless of the severity of the disease. The disease is often misunderstood, given it is not always diagnosed in its early stages. Indeed, LS remains the prerogative of various clinical specialists (urologists, gynecologists, dermatologists, pediatricians, plastic surgeons), which is often misleading for patients and delays diagnosis.

In the advanced stages of the disease, subjective symptoms are associated with structural modifications of the genital mucosa. When clinical symptoms are less important (increase in the mucosal and cutaneous dryness, loss of elasticity of the skin) patients not always seek a specialist’s help early. Otherwise when the sclerotic aspect predominates subjective symptoms it can lead to extreme surface fragility and tendency to fissure the skin. In these phases, the architecture of the genitalia can be completely transformed with a negative impact on social relationships, sexual intercourse and quality of life [13]. In these advanced stages of LS, people visit the specialist early.

The clinical classification of LS in mainly two stages, early and late, was performed on the basis of the clinical picture and histological aspect confirming diagnosis in very early phases of the disease.

All patients in this study were subjected to punch biopsies of the genital lesions in every clinical stage. In early phases of poor clinical symptoms but where patients complained of more important subjective symptoms (itching, burning, feeling excessive sensitivity to touch), in our experience, the typical histopathologic aspects were already observed even if lightly present. Microscopic examination of H + E sections always reveals thickening of epithelium and atrophy of the malpighian stratum variously represented. In the dermis, loss of the elastic fibers is present with edematous hyalinized connective tissue. The perivascular band of lymphocytic infiltrate is present to a variable degree below the edematous stratus. In the more advanced forms of LS, the most important histological aspects include the atrophy of the epidermis, the massive homogenization of the collagen that can be variously associated with a different grade of lymphocytic infiltrate (data not shown). These histopathological features cannot be all represented in all phases of the disease.

In this study we also tried to measure how much LS could affect patients’ quality of life. All patients answered the questions of the Dermatology Life Quality Index (DLQI) [20]. The patients were asked about the impact of their disease and its treatment on their lives. Two main groups of severity of LS (early and late disease) were developed based also on the answers of the patients.

Among females with a very early LS diagnosis, 10/17 women (58%) patients represented the earlier stages with clinical pictures and subjective symptoms associated to a DLQI score between 0 and 11 (from no effects to small/moderate effects on patients’ life of the disease). Most female patients (60%) with a late LS (20/33 women with late LS) presented progression of atrophy and alteration of vulvar anatomy; these pictures are generally associated to very large effects on women’s life, especially as to difficulties with sexual partners and had a higher DLQI score (between 11 and 20). 40% of female patients (13/33 women) with a very late LS clinical form showed serious clinical pictures. In these cases LS had an extremely large effect on the patient’s life (DLQI score between 21 and 30 points) and we had to manage these LS variants with psychological support too.

As regards the males, 24.6% (16/65 men) were diagnosed in our Centre with early LS variants. They all (100%) complained of very large effects on their life and had a higher DLQI score (from 11 to 20 points).

Besides, about 61% (30/49 men) of male patients with a late LS complained of an impaired quality of life. They presented higher DLQI score (score from 11 to 20 points), while about 40% of males with a late LS H (19/49) showed the highest DLQI scores (21–30 points) according to the clinical aspect of important sclerosis, alteration of all penile anatomic structures and urethral stricture until phimosis.

Conclusions

Classification of the stages of the disease is necessary in order to achieve a uniform subdivision of patients, and to establish who may benefit from localized...
therapy, require systemic drugs or must undergo physical treatment (stem cell infiltrations) [22–24]. Within the clinical practice, staging of LS can be useful to obtain consistent data, control the disease itself and allow for a correct follow-up.

The two-stage classification (early and late disease) for LS is based on clinical and subjective symptoms and anatomical alterations of the genital region. All patients diagnosed with LS and confirmed by a histological examination underwent clinical evaluation, and filled out a questionnaire to measure the extent to which LS limits their quality of life [21].

Patients with severe clinical symptoms (local itching or burning, limit to daily life) and anatomical transformation of the local region (vulvar stenosis, atrophy of labia minor) were classified into more advanced stages. The severity of symptoms, usually, goes hand in hand with structural alterations.

In our experience, most of the patients with the advanced stage of LS are patients older than fifty years of age (in both sexes). The presence of advanced disease reduces the therapeutic options and the treatment response. Therefore, our study emphasizes the importance of early diagnosis of genital lichen sclerosus and the need for further studies in this field.

Conflict of interest
The authors declare no conflict of interest.

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