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Original Article

A case series of lichen sclerosus bullosa

硬化性苔蘚鬆解症的案例系列

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Lichen sclerosus (LS) is a chronic inflammatory dermatosis. It is most commonly found in the anogenital region of Caucasian females. Lichen sclerosus can be very distressing and lesions may result in psychological and functional impairment. Anogenital LS in women also carries a risk of malignant transformation. In both men and women, extragenital LS is an important differential diagnosis to consider in patients presenting with unusual sclerodermoid lesions. Early recognition and treatment of these lesions can lead to both resolution of symptoms and anguish for significantly affected patients. We present a case series of two patients with extragential bullous lichen sclerosus and briefly review LS in this clinical context.

硬化性苔蘚是一種慢性的炎症性皮膚病，最常見於白人女性的肛門生殖器部位。硬化性苔蘚可以對患者造成極大困擾，由此皮膚問題引申至心理及功能性的障礙；而女性患者肛門生殖器處的硬化性苔蘚更存在著癌變的風險。不論男女，如果在外生殖器有著硬皮病樣皮損，硬化性苔蘚是一個必要考慮的重要鑑別診斷，因及早察覺及治療能有效消除症狀以及患者的苦惱。我們以病例系列形式報告兩名有非生殖器大皰硬化性苔蘚患者的情況，並簡要地回顧此病。

Keywords: Anxiety, bullous lichen sclerosus et atrophicus, lichen sclerosus, morphoea

關鍵詞：焦慮、大皰硬化萎縮性苔癬、硬化性苔蘚、硬斑病

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Introduction

Lichen sclerosus (LS) is a chronic inflammatory dermatosis most commonly found in the anogenital region of Caucasian females. However, in both genders, extragenital lesions also occur. Bullous lichen sclerosus is an uncommon variant of LS. We report a case of localised extragenital bullous LS in a 69-year-old gentleman and a case of typical genital LS with bullous extragenital involvement in a 69-year-old lady.

Case 1

A 69-year-old man was referred by his general practitioner with a one-year history of chronic ulceration and blistering on his feet. Initially the patient noticed a creamy white discolouration on the medial aspect of his right heel which subsequently blistered and became ulcerated. A similar lesion developed over the lateral aspect of the left foot within several weeks. The patient described burning and itching in the affected areas. The lesions were originally thought to be related to chronic irritation from ill-fitting footwear but they progressed despite the application of emollients and review by a podiatrist. Vascular studies were normal. He was referred to a teaching hospital for specialist dermatological assessment.

At presentation, the patient was clearly frustrated, agitated and anxious regarding the causation and significance of these refractory skin lesions. On examination, well-demarcated white-to-yellow plaques with intermingled erythema and epidermal atrophy were identified in the distribution mentioned above. Notably, the central areas were blistered and ulcerated (Figures la and 1b).

No other abnormalities were identified on full skin examination, which included inspection of the genital region. The patient's past medical history was unremarkable except for mild gastro-oesophageal reflux, which was well-controlled on long term omeprazole. There was no history of diabetes mellitus or peripheral vascular disease.

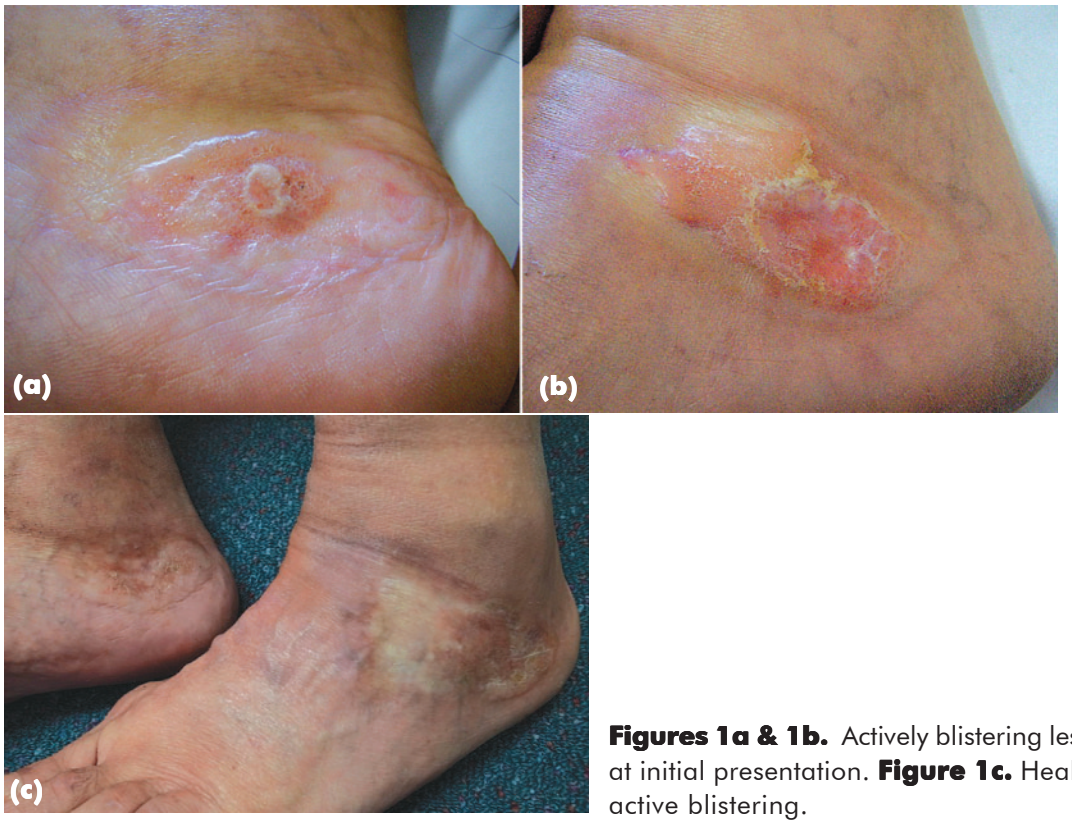
The main clinical differential diagnoses for his skin lesions included extragenital LS and morphoea. In some patients, truncal lesions of both extragenital LS and morphoea can co-exist. However, morphoea does not blister and diagnostically LS was favoured. Nevertheless, necrobiosis lipoidica, discoid lupus erythematosus and recurrent fixed-drug eruption were also considered as diagnostic possibilities.

Several punch biopsies were obtained. The histological findings were most consistent with the favoured clinical diagnosis of bullous extragenital lichen sclerosus. There was no histological evidence to suggest malignancy or localised bullous pemphigoid. The diagnosis of localised bullous LS was made. The patient was commenced on topical betamethasone diproprionate 0.5 mg/g (Diprosone™) ointment twice daily and the lesions improved impressively after several weeks. They were almost asymptomatic at his next review (Figure 1c). This also resulted in an obvious reduction in the patient's anxiety and overall improvement in his mental state. At the time of writing of this case report, the skin lesions are asymptomatic and trouble-free, though dry and sclerotic.

Case 2

A 69-year-old female was referred by the Immunology team at our institution, with a working diagnosis of progressive morphoea. The patient presented with a three-year history of multiple, enlarging sclerodermoid plaques on her trunk and limbs. The lesions were a source of both itch and considerable frustration due to the disfigurement. In the six months prior to attending Concord Dermatology Centre, the patient also developed erythema and intractable itch in the anogenital region. The past medical history was significant for transient global amnesia and antiphospholipid antibodies. Atorvastatin, cholecalciferol and fish oil were the only regular medications.

On examination, well-demarcated sclerotic creamy yellow plaques, with surrounding rims of prominent ivory-white epidermal atrophy were identified across the torso, upper and lower limbs (Figures 2a and 2b). The largest lesion on the central lower back contained prominent flaccid bullae along its inferior margin, filled with translucent straw-coloured fluid (Figure 2c). The skin surrounding the external gentialia and peri-anal region displayed poorly-demarcated



Figures 1a & 1b. Actively blistering lesions on the ankles at initial presentation. **Figure 1c.** Healed lesions without active blistering.

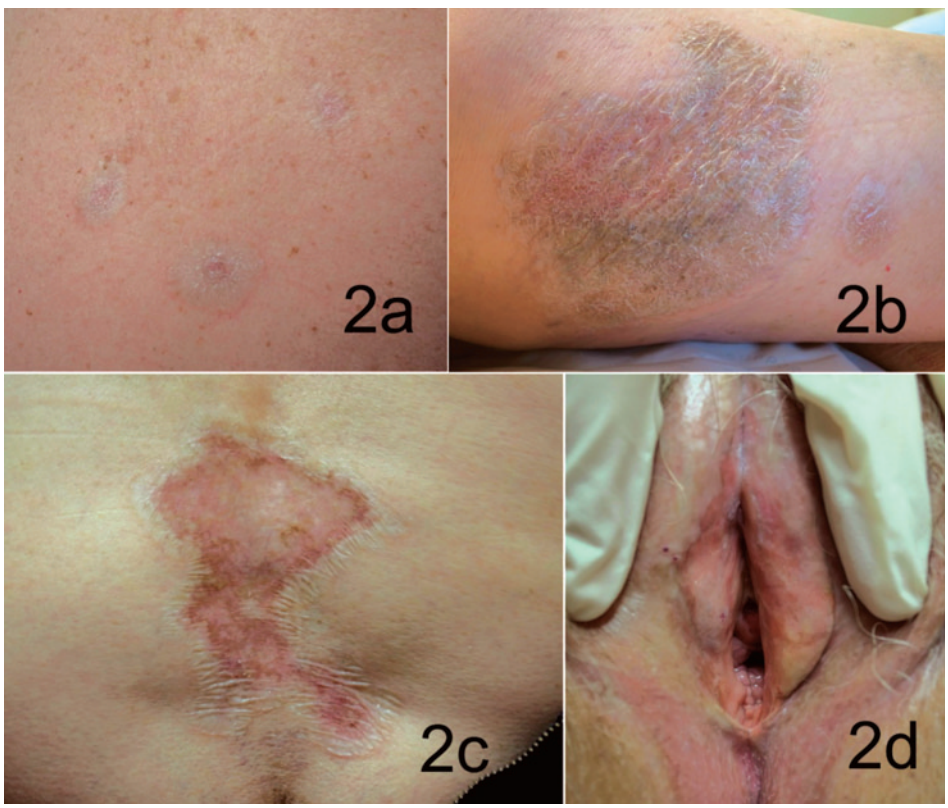


Figure 2. (a) Whitened small plaques on the trunk. (b) Flaccid bullous lesions on the lower limb. (c) Bullous lesion on the lower back. (d) Itchy erosions and inflammation around the introitus.

erythema and mild epidermal atrophy. Several small superficial erosions were evident at the introitus (Figure 2d). There were no clinical features suggestive of malignant transformation.

The favoured clinical diagnosis was genital LS with bullous extragenital involvement. The differential diagnosis included discoid lupus eryhtematosus, necrobiosis lipoidica diabeticorum and lichen planus. Skin biopsies demonstrated features consistent with LS and her diagnosis was revised to genital LS with bullous extragenital involvement.

A previous therapeutic trial by Immunology team of oral hydroxychloroquine 400 mg daily was ceased due to the development of a widespread drug eruption at week 5 of the therapy. The patient was then commenced on topical betamethasone diproprionate 0.5 mg/g (Diprosone™) ointment twice daily and both the genital and extragenital lesions were asymptomatic at her dermatology review appointment six weeks later. The patient continued with regular dermatology and gynaecology review to monitor for new skin developments and symptom recurrence, and features suspicious of the development of genital squamous cell carcinoma.

Discussion

Lichen sclerosus is a chronic inflammatory dermatosis which usually affects the anogenital region. It is about ten times more common in females than males.[1] In females, there are two peak age groups: prepubertal girls and postmenopausal women.[2] In males, there are also two peak ages of presentation: young boys and adult males.[3] The majority of patients with LS have anogenital involvement.[2] Extragenital lesions rarely affect males but are found in about 20% of female patients.[2] The prevalence of bullous LS is unknown.

The aetiology of LS remains unclear. However, this curious and potentially life changing dermatosis has been linked with autoimmune diseases such as alopecia areata, diabetes, autoimmune thyroid disease, vitiligo and pernicious anaemia.[2] It is estimated that between 21.5%-35% of patients with LS have an autoimmune condition, whilst a study in 2000 showed that 56% of patients with LS had at least one relative with an autoimmune diasese.[2,4] Genetics are also thought to play a role in the susceptibility of patients to LS with strong associations with HLA class II antigens, especially HLA DQ7.[4] Infections such as Epstein Barr virus, human papilloma virus and Borrelia have been considered as a possible causal factor for LS. However these conjectures have not been validated.[5,6]

Genital LS in women characteristically presents as ivory coloured plaques or papules.[3] Patients typically present with symptoms of pruritus or pain in the vulval area, dysuria, pain on defecating and dyspareunia. However the skin lesions may also be asymptomatic.[2,3] In young girls, the problem may be confused with signs of sexual abuse.[2] Genital LS in men usually affects the foreskin or glans penis and it may result in pruritus or phimosis.[3] The diagnosis of LS can usually be made on clinical grounds.[3] Skin biopsies may be indicated in unusual cases or cases not responding to initial treatment.[3]

Extragenital LS usually affects the trunk, neck and axillae but can occur anywhere on the body.[1] In our first patient, the location of his bullous LS was unusual although the clinical features of the lesions were quite suggestive and the histology was consistent with the diagnosis. Had this patient been diabetic with impaired peripheral circulation or immune compromised, his clinical progress might have been quite different indeed. For example, ulceration and subsequent osteomyelitis not infrequently develops in this setting. In our second patient, the extragenital features preceded the

genital involvement by two and a half years, but the clinical and histological features were again in keeping with the clinical diagnosis.

It would be well to bear in mind that extragenital LS often co-exists with genital LS and this should not be overlooked in patients presenting with extragenital lesions. Furthermore, the favourable response to trauma avoidance, topical steroids and emollients is an encouragement for doctors to have an interest in this curious and challenging dermatosis. In general, potent topical steroids are useful in the early treatment of extragenital LS and should be tried first.[3,7] Other therapies such as topical vitamin D analogues and topical calcineurin inhibitors can be used as adjuncts if necessary. A recent meta-analysis has shown no evidence to support the use of topical androgens or progesterones.[7] Specialist referral is recommended for recalcitrant or extensive cases since phototherapy and systemic therapies such as methotrexate, cyclosporine and retinoids may need to be considered.[2] Long-term follow-up by a dermatologist is desirable for patients whose LS is difficult to control.[3]

Psychological issues and functional impairment may complicate anogenital LS.[2,8] Moreover, anogenital LS is associated with malignant transformation to squamous cell carcinoma (SCC).[5] The risk of SCC has been shown to occur in 4-6% of female patients with this condition.[9] Interestingly, there is no known increase in the risk of SCC in extragenital LS.

In conclusion, bullous extragential LS is an uncommon, intriguing and sometimes anxiety-provoking dermatosis which should be considered in the differential diagnosis of sclerodermoid skin lesions. This will ensure that correct management can be commenced without undue delay. As yet there is no known cure unfortunately but prompt and appropriate management can control both physical and emotional symptoms, and limit or ameliorate otherwise lasting scarring.[7,10]

References

1. Goodfield MJD, Jones SK, Veale DJ. The 'Connective Tissue Diseases'. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology, 8th edition. Oxford, UK: Wiley-Blackwell 2010. doi:10.1002/9781444317633.ch51.
2. Tasker GL, Wojnarowska F. Lichen sclerosus. Clin Exp Dermatol 2003;28:128-33.
3. Neill SM, Tatnall FM, Cox NH. Guidelines for the management of lichen sclerosus. Br J Dermatol 2002; 147:640-9.
4. Powell J, Wojnarowska F, Winsey S, Marre P, Welsh K. Lichen sclerosus premenarche: autoimmunity and immunogenetics. Br J Dermatol 2000;142:481-4.
5. Powell JJ, Wojnarowska F. Lichen sclerosus. Lancet 1999;353:1777-83.
6. Aide S, Lattario FR, Almeida G, do Val IC, da Costa Carvalho M. Epstein-Barr virus and human papillomavirus infection in vulvar lichen sclerosus. J Low Genit Tract Dis 2010;14:319-22.
7. Chi CC, Kirtschig G, Baldo M, Lewis F, Wang SH, Wojnarowska F. Systematic review and meta-analysis of randomised controlled trials on topical interventions for genital lichen sclerosus. J Am Acad Dermatol 2012; 67:305-12.
8. Lansdorp CA, van den Hondel KE, Korfage IJ, van Gestel MJ, van der Meijden WI. Quality of life in Dutch women with lichen sclerosus. Br J Dermatol 2013;168: 787-93.
9. Val I, Almeida G. An overview of lichen sclerosus. Clin Obstet Gynecol 2005;48:808-17.
10. Tausch TJ, Peterson AC. Early aggressive treatment of lichen sclerosus may prevent disease progression. J Urol 2012;187:2101-5.