Vulvar Lichen Sclerosus: Consider Treatment With Heterologous Type I Collagen

Vulvar lichen sclerosus (VLS) is a chronic inflammatory dermatosis characterized by ivory-white commonly affecting the anogenital region. It may cause substantial discomfort due to the intractable itching and soreness, while thinning and shrinkage of the genital area make coitus, urination, and defecation painful. The lesions occur on the inner aspects of labia majora, labia minora, and clitoris, while perianal lesions occur in 30% of cases. Common extragenital sites are sites of pressure.[1]

Various treatment modalities have been tried in the management of lichen sclerosus (LS) with varied results. Current guidelines suggest ultrapotent topical corticosteroids as first-line treatment, although there are no randomized controlled trials to establish the ideal potency, frequency, and duration of steroid application.[1]

Other topical treatment options include calcineurin inhibitors, retinoids, vitamin D analogs, or intralesional therapy with triamcinolone acetonide or adalimumab. Systemic agents used in the treatment of LS include retinoids, hydroxychloroquine, cyclosporine, dietary supplements with vitamin E, and para-aminobenzoic acid. Phototherapy, photodynamic therapy, cryotherapy, tissue-vaporizing CO_2 lasers, or nonablative lasers, such as pulsed-dye and Nd-YAG, has also been used with success. Surgical treatments which involve vulvectomy have also been reported.[2] Recent publications suggest the injection of platelet rich plasma and stem cells used along with fat transfer as a novel technique in the management of VLS.[3]

We evaluated the safety, symptom resolution, and clinical improvement in 3 patients diagnosed with VLS, after an innovative, regenerative treatment, which is based on injection of heterologous Type I collagen (HT1C).

Patients and Methods

Three female patients aged 36, 47, and 61 years presented to the outpatient clinic with porcelain-

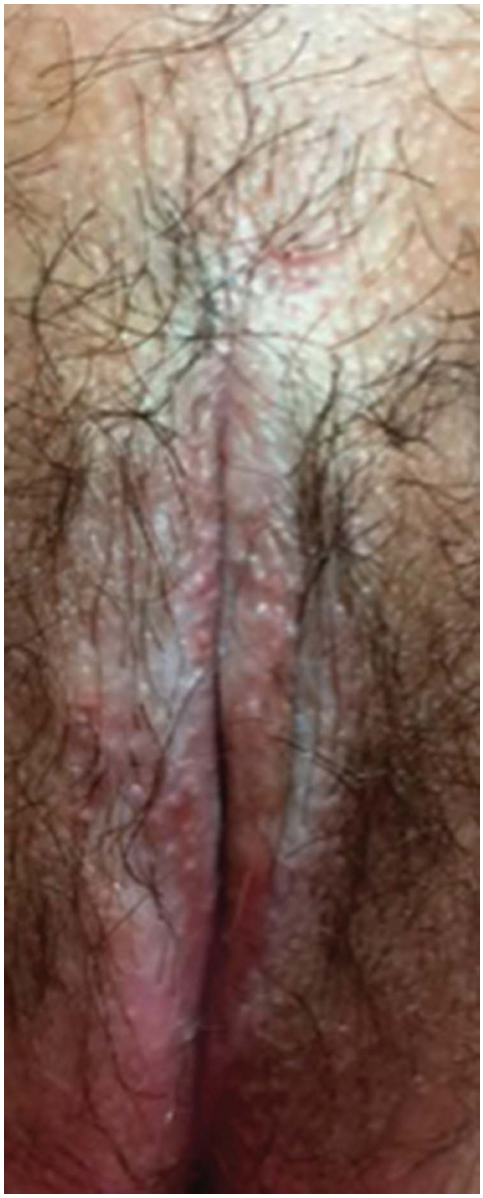

Figure 1. A 47-year-old patient with vulvar lichen sclerosus at the initial visit.

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white atrophic, confluent plaques with fragile surface in the labia minora, interlabial sulci, and perineal area since 6 to 12 months (Figure 1). All 3 patients reported soreness, discomfort, erosions, and dyspareunia. A biopsy specimen obtained from the lesional areas revealed features typical of VLS in all patients including thinning of epidermis and hyperkeratosis, a white homogenized collagen band below the dermoepidermal junction, and lymphocytic infiltrate in the dermis. A diagnosis of VLS was made based on the clinical and histological features. The patients were prescribed clobetasol propionate cream to apply twice daily for 3 weeks and subsequently once daily for 3 more weeks. A follow-up visit after 6 weeks showed no amelioration of the lesions, although 2 of the patients reported improvement of pruritus.

One hundred milligrams of heterologous Type I collagen micronized, sterile powder (Linerase; Euroresearch, Milano, Italy) reconstituted in 4.5 mL of normal saline (0.9% sodium chloride solution) and 0.5 mL of lidocaine was injected to the affected areas. The infiltration pattern was to inject 0.1 mL of the solution per point intradermally or directly subdermally at approximately 1-cm intervals over the entire affected area of the external genitalia, including the labia majora, the labia minora, and the perineum plus the posterior vaginal forchette. The injection was performed using a 30-gauge needle of 4 mm. The patients received 4 treatments at 2-week intervals and continued with a maintenance treatment once every 2 months. Maintenance treatment was initiated 3 months after the fourth treatment.

The patients evaluated pruritus, soreness, discomfort, and dyspareunia on a visual analog scale (VAS) after each treatment session. The lesions were evaluated clinically at each session. The patient were also asked to rate the pain during the injections on a VAS.

Results

The patients exhibited a decrease of the surface area of the lesions after the first treatment with complete resolution after the third treatment (Figure 2). Pruritus, soreness, discomfort, and dyspareunia improved 50% to 75% for the 2 patients and were completely resolved for the third, 10 days after the first treatment session. All patients reported no symptoms 10 days after the second treatment session. All patients reported minimal to moderate pain (VAS <5) during the injection process. No adverse events were reported. The patients did not experience any relapse for the next 12 months under maintenance treatment (Figure 3).

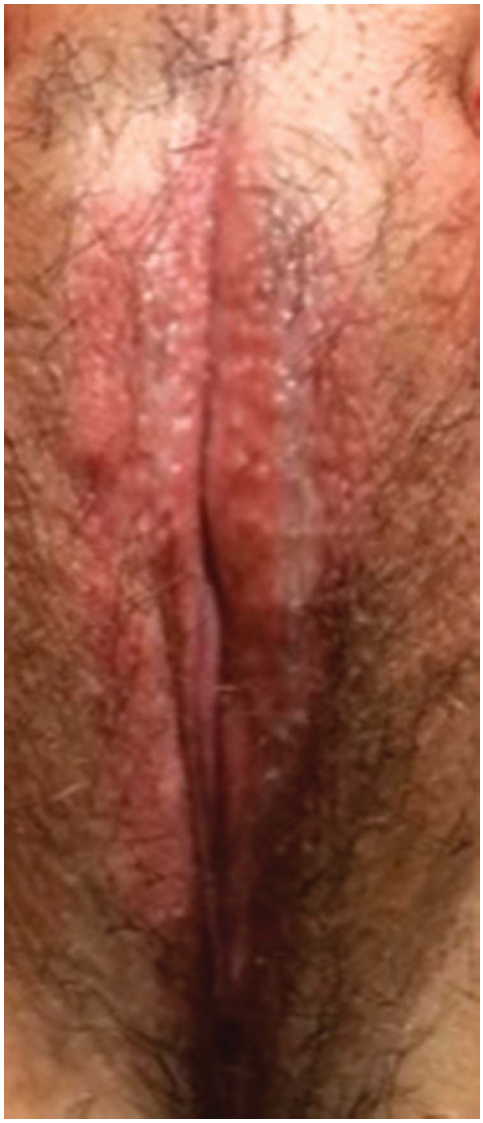

Figure 2. Complete resolution of the lesions 14 days after the second treatment (28 days after the initial visit).

Discussion

Vulvar lichen sclerosus' true incidence is unknown and possibly underestimated because there is often a delay

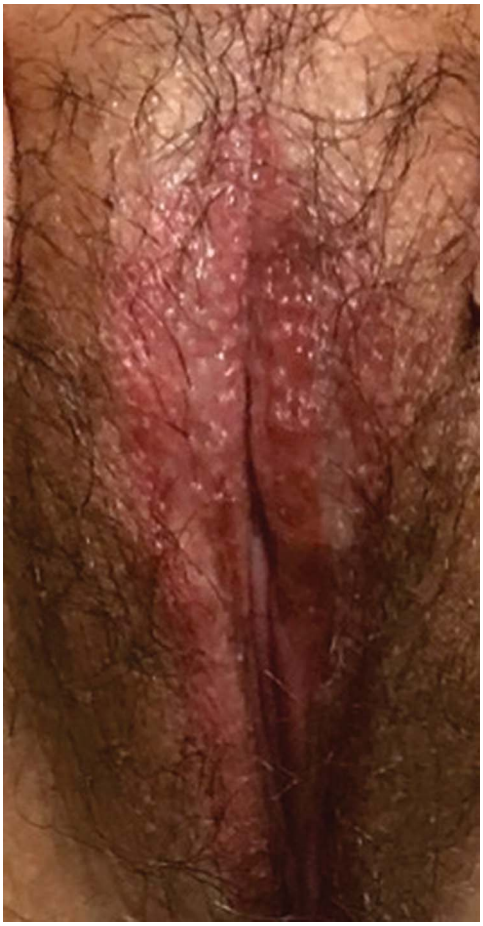

Figure 3. Excellent maintenance of clearance after the second maintenance treatment (7 months after the initial visit).

in diagnosis due to its asymptomatic nature. Etiopathogenesis of LS is not fully illuminated, but several theories have been postulated. A genetic predisposition, based on family clustering, is apparent. A strong association with autoimmune disorders, such as alopecia areata, vitiligo, thyroid disease, diabetes mellitus Type I, and pernicious anemia, has been reported in 21.5% to 34% of patients. Lichen sclerosus is not contagious, but both bacterial and viral pathogens have been implicated in its etiology. There are also linkages between hormones, cell kinetics, local skin changes, and the pathogenesis of LS. Advanced disease has a considerable impact on patients' quality of life. Moreover, it has been associated with increased risk of vulvar squamous cell carcinoma with a 4% to 5% risk.

HT1C, in the form of a lyophilized collagen patch, has been used for almost 30 years in dermatology, angiology, and vascular surgery for the treatment of skin ulcers, open wounds, scars, and bedsores.[4,5]

HT1C has been reported to stimulate the production of new fibroblasts to create native Type III collagen. It supplements dermal biorevitalization and assists the regeneration and reconstruction of connective tissue in the dermis providing perfect conditions for the physiological neoformation of collagen.[4,5]

The 3 patients treated with HT1C experienced relief of symptoms and complete amelioration of VLS lesions within 6 weeks. Furthermore, they maintained complete resolution of the lesions for the next 12 months with minimal maintenance treatment. HT1C could restore degenerated collagen in the dermis of patients with VLS; however, there is no indication of any modification on the inflammatory component of VLS pathogenesis. That is why maintenance treatment should be provided to preserve the improvement. None of the patients reported any adverse events, and the pain associated with the injections was well tolerated. The main limitation of these case series is the lack of a control group, as part of the improvement could be due to the tissue needling involved in the collagen injection process. Although the patients were asked to consent for a post-treatment biopsy to assess connective tissue changes, they all declined.

HT1C is minimally invasive and can be performed in an office setting under local anesthesia. It is a promising treatment option for VLS, which needs further assessment in randomized controlled trials.

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