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Treatment of male genital lichen sclerosus with heterologous type I collagen

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Male genital lichen sclerosus (MGLSc) is a chronic, progressive, inflammatory skin disorder that may cause itching and soreness and be complicated by phimosis, paraphimosis, urethral stricture, urinary retention or even renal failure in some cases.[1] It may also contribute to the long-term risk for squamous cell carcinoma (SCC) of the penis.

Current guidelines suggest ultrapotent topical corticosteroids as first-line treatment in MGLSc, although there are no randomized controlled trials to establish the ideal frequency or duration. Surgical treatment, cryotherapy, ultraviolet phototherapy, carbon dioxide laser and pulsed dye laser have also been used, with variable success.[2] Recurrences after circumcision or in cases where long-term use of steroids has resulted in adverse events are even more difficult to manage.

We present a patient with MGLSc who was successfully treated with injections of heterologous type I collagen (HTIC).

A 42-year-old man presented with an 8-month history of atrophic plaques involving the prepuce, frenulum and glans (Fig. 1a). He reported that for the past 12 months, he had found his foreskin difficult to retract, and he also had pruritus, soreness, discomfort and dyspareunia.

Histopathology revealed atrophic epidermis with hyperkeratosis, dermal lymphocytic infiltration and homogenization of the collagen in the upper third of the dermis. The patient had used clobetasol propionate cream twice daily for 4 weeks and subsequently once daily for 4 more weeks without clinical improvement, except for slight improvement of the pruritus. He consented to begin off-label treatment with injections of HTIC.

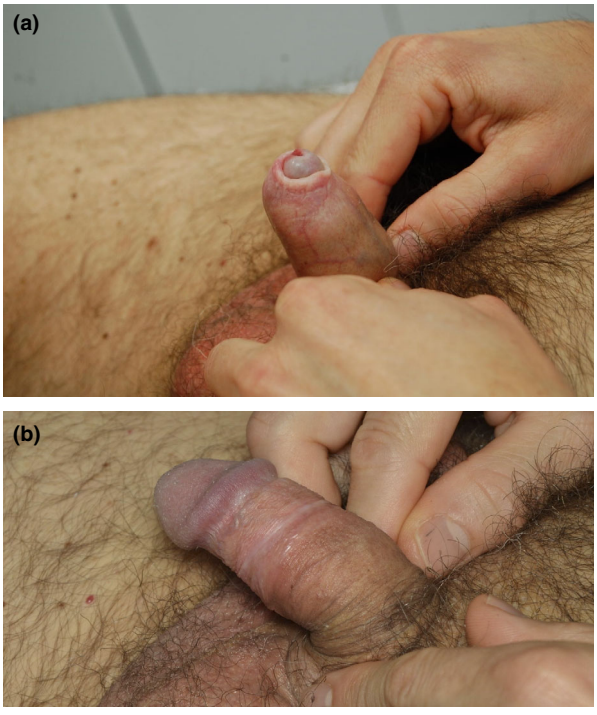

Figure 1 (a) Atrophic plaques involving the prepuce, frenulum and glans of a 42-year-old patient at the initial visit; (b) significant improvement of the lesions after three treatments with heterologous type I collagen.

Topical lidocaine 30% cream was applied to the lesional area 60 min before treatment. An injection was prepared of 100 mg heterologous type I collagen micronized, sterile powder (Linerase; Euroresearch, Milan, Italy) reconstituted in 4.5 mL of normal saline (0.9% sodium chloride solution) and 0.5 mL of lidocaine, and this was injected via a 30G needle (4 mm length) into the affected areas. The infiltration pattern

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consisted of injections of 0.1 mL of the solution per point intradermally or directly subdermal in a grid pattern at approximately 1-cm intervals over the entire affected genital area. The patient received four 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 patient reported improvement after the first treatment and significant improvement of the lesions after the third treatment (Fig. 1b). Pruritus, soreness, discomfort and dyspareunia were recorded on a visual analogue scale (VAS) at the initial visit and after each treatment session; all had resolved 10 days after the first treatment session. The patient reported minimal to moderate pain (VAS < 5) during the injection process. No adverse events were reported. The patient did not experience any relapse for the next 12 months under maintenance treatment.

MGLSc is rare in males who have been circumcised at birth, indicating that the foreskin may play a significant role in pathogenesis. Autoimmune disorders, such as thyroid disease, diabetes, vitiligo, alopecia areata, pernicious anaemia, scleroderma and rheumatoid arthritis have been reported in patients with MGLSc. Bacterial and viral pathogens, such as acid-fast bacilli and spirochaetes, *Borrelia burgdorferi*, human papillomavirus, hepatitis C virus and Epstein–Barr virus have been implicated in the disease aetiology. Exposure to the epithelium to urine due to chronic incontinence has been suggested to contribute to the disease pathogenesis.[3] Penile intraepithelial neoplasia, associated with chronic inflammation of LS is a precursor of SCC. Long-term control of the disorder includes alleviating the symptoms and preventing urethral stricture and malignant transformation.[4]

HTIC 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.[5] HTIC could restore degenerated collagen in the dermis; however, there is no indication of any modification on the inflammatory component of MGLSc pathogenesis.

Our patient had rapid complete clearance of MGLSc lesions within 6 weeks, and this was sustained for the following 12 months with minimal maintenance treatment. This suggests that HTIC could be an efficacious alternative treatment or maintenance treatment, for MGLSc, particularly when steroids fail or are contraindicated, or in cases of recurrence after circumcision.[6]

References

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CPD questions

Learning objective

To gain up-to-date knowledge on the use of heterologous type I collagen in the treatment of male genital lichen sclerosus.

Question 1

Which of the following best describes the possible mode of action of heterologous type I collagen in the treatment of lichen sclerosus?

(a) Downregulation of extracellular matrix protein antibodies.
(b) Downregulation of the lichenoid inflammatory infiltration.
(c) Modification of tissue-specific antigens that promote autoimmunity.
(d) Protection of susceptible epithelium from urine irritation due to microincontinence.
(e) Upregulation of the restoration of degenerated collagen in the dermis.

Question 2

Which of the following is the first-line treatment in male genital lichen sclerosus as suggested by current guidelines?

(a) Intralesional steroids once per month for 1–3 months.
(b) Topical calcineurin inhibitors for 1–3 months.
(c) Topical potent steroids for 1–3 months.
(d) Topical ultrapotent steroids for 1–3 months.
(e) Topical vitamin D3 analogues for 1–3 months.

Instructions for answering questions

This learning activity is freely available online at http://www.wileyhealthlearning.com/ced

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article
- Register or login online at http://www.wileyhealthlearning.com/ced and answer the CPD questions
- Complete the required evaluation component of the activity

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

This activity will be available for CPD credit for 2 years following its publication date. At that time, it will be reviewed and potentially updated and extended for an additional period.