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SHORT PAPER

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Platelet-rich plasma for male genital lichen sclerosus resistant to conventional therapy: First prospective study

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Abstract

Ultrapotent topical corticosteroids and circumcision are usually effective for male genital lichen sclerosus (MGLSc); however, refractory cases are often referred to our Male Genital Dermatology Unit. Treatment with autologous platelet-rich plasma (TPRP) has recently been advocated as a safe and effective treatment option, but there have been no prospective studies in men to date. The objective of this study is to assess the safety and efficacy of TPRP for MGLSc resistant to conventional therapy. A prospective, open-label, single-arm, therapeutic study was carried out in this study. Inclusion criteria: resistant to conventional therapy for at least 6 months. Procedure: infiltration of 0.1 mL/cm^2 PRP every 8 weeks. Monthly data recording: visual appearance with photographs and external scoring by an expert using Investigator's Global Assessment Scale (IGA scale 0-5), symptoms (scale 0-5), quality of life (QoL; Dermatology Life Quality Index [DLQI]), and complications. No. of patients included was n = 5. No. of patients excluded during treatment was n = 1. Mean initial IGA: 3.6. Mean initial DLQI: 6. TPRP n = 34 (range: 2-9; average: 6.8 per patient). Mean IGA at 18 months: 3.25. Mean DLQI at 18 months: 1.25. All patients reported being completely asymptomatic at 10 months. No. of patients with complications is n = 1 (balanitis). TPRP seems to be safe and effective, regarding symptom control and improvement in QoL; however, visual changes were minimal.

KEYWORDS

balanitis xerotica obliterans, lichen sclerosus et atrophicus, platelet-rich plasma

1 | INTRODUCTION

Male genital lichen sclerosus (MGLSc) is an acquired, chronic, inflammatory dermatosis. It affects the glans and the inner prepuce, with hypopigmented plaques, erythema, infiltration, lichenification, and deformity (phimosis, balanoprepucial adhesions, meatal stenosis, and naviculomeatal valve insufficiency). The main symptom is male dyspareunia, with a significant impact on quality of life (QoL).[1,2]

There have been no randomized controlled trials in MGLSc. Ultrapotent corticosteroids are the first line of treatment, achieving about 50% healing; however, their efficacy in reversing scarring sequelae is limited.[1-4] Retrospective studies suggest that circumcision can be curative in 90%-100% of cases, and should be offered before intralesional or systemic therapy is considered.[1-5]

The Investigator's Global Assessment (IGA) scale has been used to assess physical signs in LSc studies, and to assess response to treatment with platelet-rich plasma (TPRP).[6,7] TPRP for MGLSc has been advocated to be a safe and effective option; however, no prospective studies have yet been done in men.[7,8] The putative mechanism is promoting healthy tissue formation by releasing growth factors; an analgesic role has also been postulated.[9-12]

2 | MATERIALS AND METHODS

We conducted a prospective, open-label, single-arm, therapeutic study. It was approved by our Institutional Ethics Committee, and informed consent was obtained. Inclusion criteria: men at least 18 years of age, diagnostic biopsy, circumcised, and previously treated with ultrapotent corticosteroids for at least 6 months without complete response. Exclusion criteria: antiplatelet/anticoagulant therapy, significant systemic diseases (eg, hematologic disorders, cancer), additional local disease (eg, infections, malignant lesions).

The 6-point Investigators Global Assessment (IGA) score (0-5) was used to evaluate severity according to visual appearance (adding "deformity" to the scale used by Casabona et al in their study of TPRP for MGLSc) (Table 1).[7]

Photographs were taken monthly. These images were scored at baseline, and every 6 months of follow-up, by an expert dermatologist, with significant experience in MGLSc, not directly connected with the treatment of these patients.

Participants were questioned monthly regarding the following symptoms: pain at rest, pain on erection, dyspareunia, stinging sensation, and pruritus. They were asked to quantify these on a 6-point scale: 0 = absent, 1 = minimal, 2 = mild, 3 = moderate, 4 = marked, 5 = severe.

A Dermatology Life Quality Index (DLQI) score was computed at baseline, and every 6 months of follow-up.

An additional assessment was carried out 24 months after the first intervention, with the specific aim of ruling out clinical evidence of malignancy.

Paracetamol 1-g PO was administered 1 hour before the procedure. Topical lidocaine 2.5% + prilocaine 2.5% cream was applied under occlusion for 30 minutes. The area was prepared with chlorhexidine. Mepivacaine + adrenaline was infiltrated in the lesional area to increase analgesia and achieve vasoconstriction (less bleeding and higher concentration of local growth factors). PRP was activated and 0.1 mL/cm^2 was injected intradermally with a micro-whealing technique using a 30-G needle and a 1 mL syringe (total: 2-3 mL per TPRP). After the procedure, 1% silver sulfadiazine + lidocaine was applied every 12 hours for 3 days. Patients then applied daily petrolatum ointment; topical corticosteroids and other treatments were prohibited. They were evaluated at 24 hours, 1 week, 4 weeks, and offered another TPRP at 8 weeks. The presence of complications was assessed at each follow-up visit (eg, bleeding, hematoma, infection, other). For further PRP information, see Supporting Information (Data S1).

TABLE 1 Investigator's Global Assessment (IGA) score definition (adapted)

Score	IGA score definition
0	No evident inflammatory signs or deformity.
1	Minimal disease: minimal erythema, infiltration, lichenification, excoriation, or deformity.
2	Mild disease: mild erythema, infiltration, lichenification, excoriation, or deformity.
3	Moderate disease: moderate erythema, infiltration, lichenification, excoriation, or deformity.
4	Marked: marked disease, erythema, infiltration, lichenification, excoriation, or deformity.
5	Severe: severe erythema, infiltration, lichenification, excoriation, or deformity.

3 | RESULTS

Subject recruitment and treatment are shown in Figure 1. Two patients were excluded; one for von Willebrand's disease and the other because of anticoagulant therapy. Patient 4 was excluded during the protocol due to his inability to attend for follow-up at the required frequency.

Baseline characteristics and study participation data are summarized in Table 2.

Baseline mean IGA was 3.6 ± 0.57 considering all five patients. Baseline mean IGA was 3.63 ± 0.73 for the four patients that actually completed 18-months follow-up. Mean IGA at 6 months: 3.13 ± 0.84. Mean IGA at 12 months: 3.25 ± 0.63. Mean IGA at 18 months: 3.25 ± 0.49 (Figures 2A, 3).

Mean baseline dyspareunia severity was 2.75 ± 1.23, at 6 months 0.25 ± 0.49, and from 10 months on: 0 for all patients (Figure 2B).

The remainder of symptoms followed a similar curve; the baseline pain on erection mean was 1 ± 1.3 (range: 0-3); from 10 months on, 0 for all patients; the pruritus baseline mean was 0.8 ± 0.96 (range: 0-2); from 7 months on, 0 for all patients; the stinging sensation baseline mean was 0.8 ± 1.14 (range: 0-3); from 10 months on, 0 for all patients: not one patient reported pain at rest.

Baseline mean DLQI was 6 ± 3.51. Baseline mean DLQI for the four patients that actually completed 18-months follow-up was 6.25 ± 4.48, at 6 months 4.5 ± 5.63, and after 12 months sustained at 1.25 ± 2.45 (Figure 2C).

Patient 2 developed a balanitis that required oral treatment, without hospitalization.

An additional follow-up at 24 months showed the absence of suspicious lesions.

4 | DISCUSSION

There have been no other studies of PRP in male patients with LSc, resistant to both corticosteroids and circumcision. Therefore, there are no other data with which to compare our findings.

Despite the fact that visual appearance severity by IGA evaluation showed little to no change in our patients, we highlight the fact that all of them showed improvement in their symptoms, and by

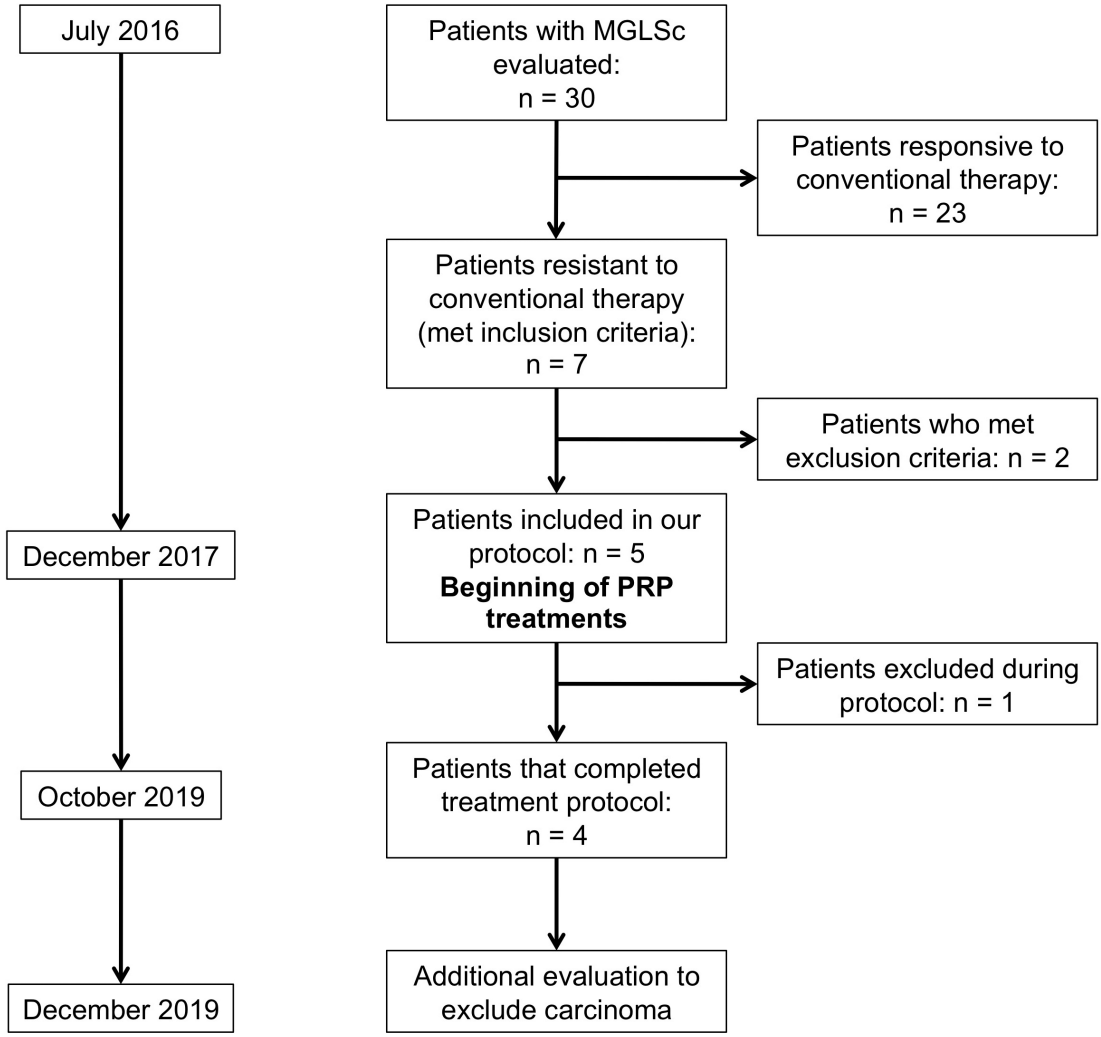

FIGURE 1 Flowchart of subject recruitment and treatment

TABLE 2 Baseline patient demographics, disease characteristics, and study participation data

Patient	Age	Years since MGLSc Dx	Years since postectomy	Total TPRP	Months of follow-up
1	66	8	5	9	20
2	67	21	17	8	21
3	46	2	1	8	18
4	80	10	6	2	2
5	68	15	15	7	18
Mean	65.4 ± 10.73	11.2 ± 6.30	8.8 ± 6.02	6.8 ± 2.43	15.8 ± 6.86

Abbreviations: Dx, diagnosis; MGLSc, male genital lichen sclerosus; TPRP, treatment with autologous platelet-rich plasma.

month 10, they were completely asymptomatic. DLQI showed a similar trend; all patients showed improvement, and four out of five achieved a score of 0 by month 12.

Squamous cell carcinoma (SCC) is the most serious complication of LSc and has been reported in 0%-12.5% of cases.[1,2] Complete filaggrin deficiency has been associated with a higher risk of developing SCC in sun-exposed areas.[13] Although work in MGLSc has not found a higher prevalence of filaggrin deficiency, its possible role in carcinogenesis merits attention.[14] Studies in vulvar LSc have shown a reduced rate of malignancy when treated with topical corticosteroids,

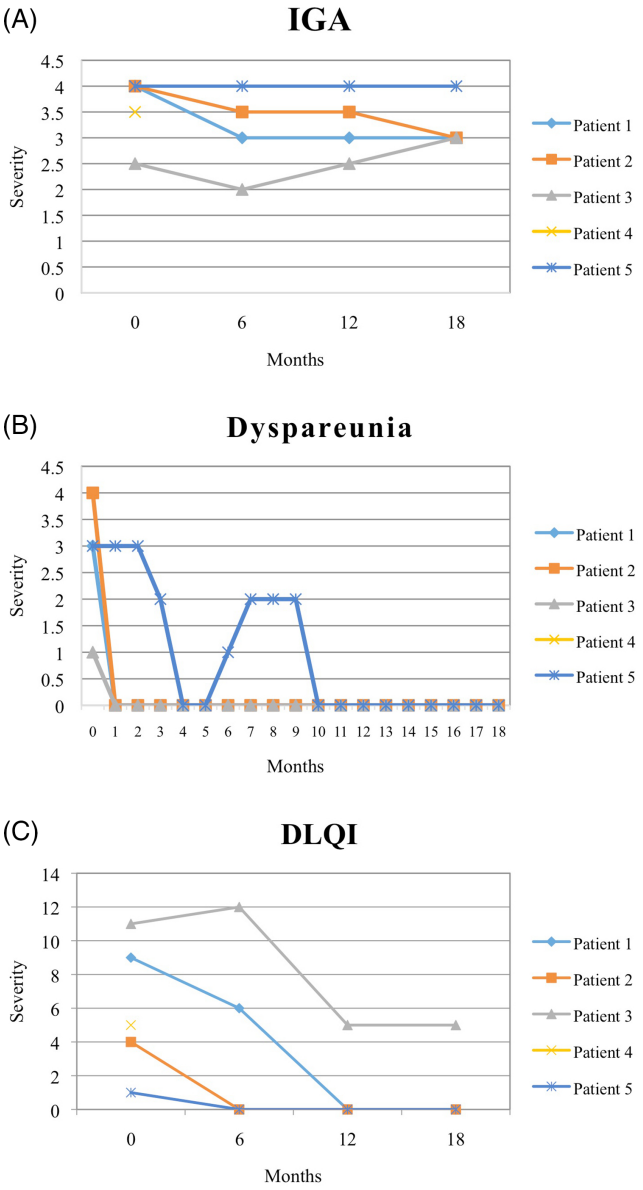

FIGURE 2 Course during follow-up of, A, Investigator's Global Assessment (IGA) score, B, dyspareunia, and, C, Dermatology Life Quality Index (DLQI) score. Patient 5 acquired adhesions with painful erosions after sex-induced trauma at 5 months follow-up that were later resolved by month 10. Patient 4 reported not having had sexual intercourse during the follow-up period

as well as a decrease in recurrence of SCC.[15] The impact of TPRP on these issues is not known. Risk of malignant transformation in MGLSc exists despite adequate therapy, and must be considered in the follow-up of patients.

Since it is known that minor trauma can have an effect on diseased tissue, future double-blind controlled studies should include a control group with saline infiltration. Other questions to address are timing, dose, and frequency of TPRP.

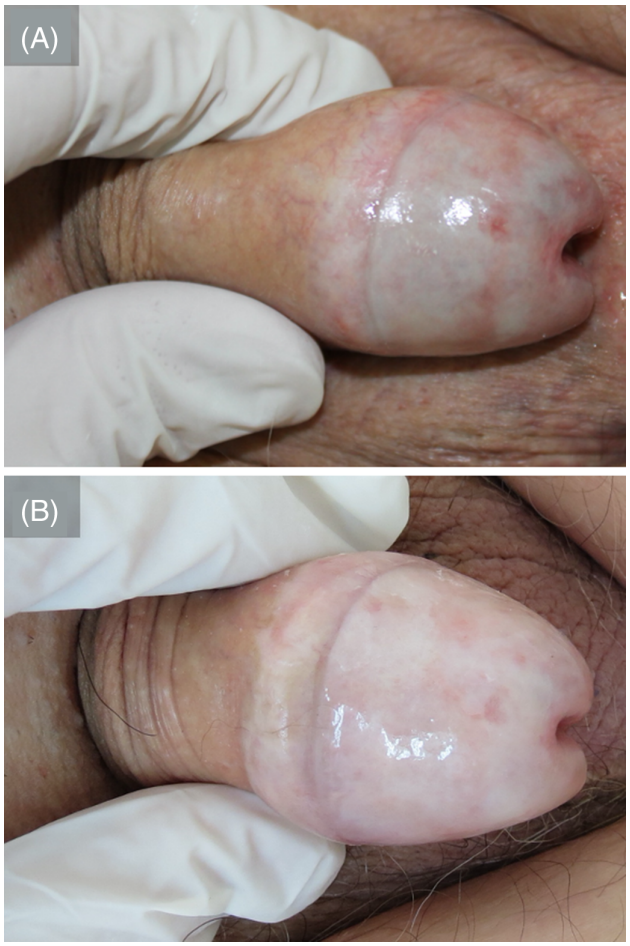

FIGURE 3 Patient 1, A, at baseline with Investigator's Global Assessment (IGA) score of 4; and, B, same patient after 20 months and 9 TPRP procedures with an unchanged IGA score of 4

5 | CONCLUSIONS

While important advances have been made in MGLSc, there remains a significant evidence gap regarding therapeutic alternatives for resistant cases. Both corticosteroids and circumcision should be offered before considering TPRP, and both remain the backbone of treatment. They could be used in combination with TPRP even in steroid-resistant cases, and warrants further investigation. Future trials with such treatment-resistant patients might be hard to conduct, given the relative rarity of severe refractory MGLSc. TPRP is costly and time-consuming, therefore, further studies could prove challenging to fund. Our results have shown that TPRP is feasible and safe; however, more patients and longer follow-up is needed. There is no evidence that TPRP lowers the risk of malignant transformation. We have offered patients a relatively novel treatment that was successful in achieving symptom control and improvement in QoL. If TPRP is to be considered, it should be done on a case-by-case basis. Expectations regarding cosmetic results must be addressed realistically.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

All authors fulfill the following requirements:

1. Have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; and
2. Been involved in drafting the manuscript or revising it critically for important intellectual content; and
3. Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; and
4. Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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