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Mini Review

Use of Photodynamic Therapy for a Rare Inflammatory Skin Disease: Extragenital Lichen Sclerosus

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ABSTRACT

Extragenital Lichen Sclerosus (LS) poses diagnostic and therapeutic challenges due to its rarity and varied presentations. This report presents a case of LS affecting the face, resistant to conventional therapies, successfully treated with topical 5-Aminolevulinic Acid (ALA)-Photodynamic Therapy (PDT). A literature review highlights the difficulty in diagnosing extragenital LS and discusses various treatment options, including corticosteroids, calcineurin inhibitors, surgery, and emerging therapies such as ALA-PDT and Janus Kinase inhibitors (JAKi). ALA-PDT emerges as a promising alternative for refractory cases, offering efficacy and safety, while JAKi presents a novel option for long-term management.

Keywords: Lichen sclerosus; PDT; ALA; Photodynamic therapy

INTRODUCTION

The extragenital Lichen Sclerosus (LS), successfully treated with ALA-PDT. The 36-year-old patient in this report suffered from histologically confirmed lichen sclerosus of the face. This was previously treated with topical tacrolimus and topical and systemic corticosteroids without benefit. Since the patient was resistant to conventional therapies and an exposed site was involved, topical 5-Aminolevulinic Acid (ALA)-Photodynamic Therapy (PDT) was started with a dosage of 37 J/cm^2 once a month for eight minutes per irradiation. At each follow-up the lesion improved with a reduction in the diameter of the plaque and the hypopigmentation that characterised it. Only in one case, at the fourth administration, the dose was increased to 40 J/cm^2 due to the poorer improvement found, but at the next visit the initial dose was resumed, due to the excellent result achieved. In this study, a literature review was carried out on LS cases of the face. The 8 cases found were treated with topical or systemic corticosteroids or topical tacrolimus, with good results. ALA-PDT is approved for other diseases, such as actinic keratosis, of which the face is a common site. This treatment is therefore proposed as a viable alternative against LS of this site, due to its high safety profile, compared to previously described therapies.

LITERATURE REVIEW

Lichen Sclerosus (LS) is a chronic inflammatory skin disease that most commonly affects the genital area. More rarely, in about 15% of cases, other areas such as the face are involved [1]. LS is challenging from the perspective of diagnosis and therapy. In the former case, recognition may be easier when the pathology involves its most typical site, the genital area. But if an extragenital area is affected, as in the case described, it is not always easy to reach the correct diagnosis. Moreover, it should be remembered that other mucous membranes than the genital area may also be involved. For instance, LS of the labial mucosa is very rare and can easily be misdiagnosed as lichen planus. Thirty-nine histologically confirmed cases of oral LS plus a more recent one from 2024 are reported in the literature [2]. Although it is a rare localisation requiring treatment only in the presence of symptoms, it is recommended to suspect oral LS in the presence of whitish to ivory-white macules or plaques [3]. On the extragenital skin the LS classically presents with whitish papules from whose union atrophic plaques form. In this context the follicular ostia are represented by comedo-like openings [4]. This picture can easily be confused with other diseases that enter into differential diagnosis with LS, such as morphea and atrophic lichen planus [5]. Late and less indurated lesions may also resemble vitiligo and hypopigmented mycosis fungoides [5]. A

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useful tool that can help identify LS is dermoscopy. The most common findings are white to yellow patches, followed by white chrysalis-like structures. Irregular linear vessels, rosettes and comedo-like openings are also frequent [5,6]. An example of how useful epiluminescence microscopy can be is the comparison with the dermoscopic aspects of morphea, where the typical whitish fibrotic rays are smaller, less defined and more opaque than the patches of LS [5]. However, the diagnosis of LS remains clinical and recourse to biopsy should be reserved for atypical cases, extragenital morphea-like lesions, exclusion of neoplasms (as in the case of lesions with pigmented areas that may mimic atypical melanocytic proliferations), and manifestations that are not responsive to first-line therapies [7]. For the reported case, biopsy was necessary given the extragenital localisation and the lack of response to corticosteroid and tacrolimus therapies.

As mentioned above, LS therapy is also often tough, because the disease is not curable but can only be controlled by following long-term treatment. The first line of treatment is 3 months of high-potency topical corticosteroids, preferably in ointment [1]. Topical calcineurin inhibitors, such as tacrolimus, are considered less effective than corticosteroids, so they are used as second line [1]. When the desired results are not achieved, surgery is one of the possible treatment options [1]. For male in particular, circumcision is considered curative, with regression of symptoms 4-8 weeks after surgery, although the rate of recurrence of the disease is not well known [8]. Available systemic therapies such as cyclosporine, methotrexate and corticosteroids have lower levels of evidence and degrees of recommendation than topical therapies, with a risk-benefit ratio too high. So their use is limited only in refractory cases [8].

DISCUSSION

In the reported case, when the diagnosis was obtained with histological examination, the issue of treatment arose. As mentioned, the patient did not respond to first-line therapies and surgery was ruled out to avoid scarring that would disfigure an exposed site such as the face. PDT was chosen because it is non-invasive and because of the extensive experience of dermatologists in its use against actinic keratoses and basal cells carcinomas, which are very common on the face. It is part of the proposed treatments for LS [9], and a meta-analysis was recently carried out to evaluate its efficacy and safety. Qing, et al. [10], considered four Randomised Controlled Trials (RCTs) with a total of 184 patients with a follow-up of at least 6 months. Three of these RCTs compared ALA-PDT with topical corticosteroid therapy, while the fourth compared it with a topical calcineurin inhibitor. In all cases ALA-PDT showed higher response rates and longer remission periods than controls. With regard to safety, no long-term effects, as may occur with corticosteroid therapy, were reported. Pain and swelling during and after treatment are the most common adverse events seen with ALA-PDT [10]. Given this, some concerns are associated with this meta-analysis. The studies considered are only from China, so other areas need to be considered [10]. Furthermore, these RCTs only evaluated ALA-PDT on genital LS since there are no works in the literature on the use of ALA-PDT for extragenital LS, other than the one we published. Recently, Wang et al. published a case report on a 10-year-old patient with vulvar and extravulvar LS and Turner syndrome, where ALA-PDT was used against vulvar lesions, but not for extragenital disease, where a topical calcineurin inhibitor was used, with clinical benefits. However, this case report adds one more element on the safety of ALA-PDT in paediatric patients and patients with significant comorbidities such as Turner syndrome [11]. In addition, ALA-PDT is an outpatient procedure and is not very expensive [10], so it is easy to manage and further studies are needed to increase its uptake among physicians. In spite of this, there are some cases in which it is unthinkable to take advantage of this treatment. In the paper published in 2023 by Kryshtalskyj, et al. [12], a case of eyelid LS is described in a 5-year-old patient who was successfully treated with tacrolimus 0.1% ointment and clobetasol 0.05% ointment. In this case, PDT was impossible to use for two reasons: The first is the age of the patient, who was unlikely to remain still for the duration of the irradiation, making the therapy less precise and with a high risk of affecting healthy skin; the second reason is the eyelid site of the disease, where it is inadvisable to use PDT due to the risk of ocular adverse effects, in fact patients must always be protected with goggles. Indeed, the eye is sensitive to PDT, which is why it is used for some of its pathologies [13]. It is worth mentioning the most innovative therapies for LS, because as in all chronic diseases, treatments can lose efficacy over time, including PDT. Moreover, although considered very safe, it is not always tolerated by patients because, as seen, it can bring pain and burning in the irradiation area. Improvements in signs, symptoms and in quality of life are reported with CO_2 laser ablation, although supporting data are not yet many or long-term [14]. For unresponsive cases of LS, regenerative therapy for scarring and atrophy, in particular with Platelet Rich Plasma (PRP), is under investigation. Its regulatory effect on inflammatory cytokines and promotion of angiogenesis is exploited to improve the clinical picture of LS, but the level of evidence is currently poor due to lack of standardization [15]. Janus Kinase inhibitors (JAKi) are drugs that are increasingly used for inflammatory dermatoses. None of them are currently approved for LS, but there are a few cases described in the literature. Zundell, et al. [16], described 4 cases of different dermatoses, including that of an LS in a 9-year-old patient who had been suffering from the disease for 6 years in the vulvar region, with itching and dysuria. The patient had failed treatment with topical corticosteroids, tacrolimus and crisaborole. Therefore, therapy with ruxolitinib 1.5% cream had been started and after 6 weeks there was a reduction in the erythematous patch and in itching and dysuria [16]. Jiang, et al. [17], instead published a case series on generalised extragenital LS and a 69-year-old female patient with an affected breast was treated with ruxolitinib 1.5% cream twice daily. After 2 months of therapy, there was improvement in plaque hardening and reduction of itching. Bao, et al. [18], also published a study on the efficacy of oral baricitinib 4 mg against LS, evaluating not only clinical but also dermoscopic and confocal microscopy parameters. The study included 26 patients evaluated every 2 weeks until week 8, then every 4 weeks until week 24. Pain and itch scores improved throughout the treatment, all patients achieved soft skin at week 4 and disease control at week 20. At dermoscopy, the first parameter to improve was the white areas

without structure as early as week 2, followed by others, such as the vessel score which improved from week 8. The treatment proved safe in the patients studied, with hypercholesterolemia (11.54%), thrombocytosis (7.69%) and increased liver enzymes (7.69%) as the most common but transient effects [18].

CONCLUSION

In conclusion, studies on extragenital LS need to be implemented to improve the specialist's diagnostic capabilities. This exhortation should also be extended to the treatment of this pathology, which in most cases is limited to corticosteroids and topical calcineurin inhibitors. ALA-PDT has proven to be an effective and safe treatment in this respect and should be considered in cases refractory to first-line therapies. Finally, the increasing uptake of JAKi offers an important alternative for the long-term management of these patients.

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