



Facial angiofibromas treated by rapamycin 0.05% ointment and a combined laser therapy

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Summary

Background: Tuberous sclerosis is an autosomal dominant genodermatosis characterized by nonmalignant hamartomas in multiple organs. Facial angiofibromas are most commonly located on the face and have the potential to cause disfigurement. Facial disfigurement negatively affects the quality of life of patients and their families, often leading to negative psychosocial outcomes. Nowadays there are no treatment guidelines for facial angiofibromas but due to the progressive nature of facial angiofibromas a safe technique offering good results is needed.

Objective and Results: We report the case of a 40-year-old female affected by tuberous sclerosis, whose facial angiofibromas were satisfactorily treated by rapamycin 0.05% ointment, and a combined laser therapy.

KEYWORDS

combined laser therapy, facial angiofibromas, rapamycin, tuberous sclerosis

1 | INTRODUCTION

One of the dermatological hallmarks of tuberous sclerosis (TS) is the presence of facial angiofibromas (FA), often leading patients to ask clinicians for cosmetic treatment to improve their aesthetic appearance.¹ If there are few lesions and they are <4 mm in diameter, the treatment is quite simple, consisting of an excisional method or rapamycin ointment, but the problem is when the lesions are larger and/or several.² What should be done? How should the anesthetics be performed? How long is the postoperative period? The challenging task for physicians is to identify sufficiently aggressive methods but with no complications or long postoperative period because many patients are children or young adults.¹ Furthermore, patients must be informed of the progressive nature of the condition and the probable need for further treatment sessions.¹

The lack of guidelines has meant that various treatments for FA have been proposed including surgical excision, curettage, radiofrequency ablation, cryosurgery, chemical peel, dermoabrasion, shave excision, 13-cis-retinoic acid, copper vapor, argon, pulsed dye, liquid nitrogen, electrocautery, pulse KTP (potassium-titanyl-phosphate), photodynamic therapy, Er:YAG, ultrapulse CO₂, fractional CO₂, medical treatment, tranilast, podophyllotoxin, and rapamycin.³⁻⁶

We present a case demonstrating the efficacy of topical rapamycin 0.05% ointment followed by a combined laser treatment in one time.

2 | CASE REPORT

We report the case of a 40-year-old female affected by tuberous sclerosis (Figure 1A-B). Topical rapamycin 0.05% ointment twice daily was applied for 5 months (Figure 2A-B). Anesthesia was achieved by application of a lidocaine/tetracaine cream (15G 70MG/G + 70MG/G) 45 minutes prior to treatment and a local injection of lidocaine during treatment if necessary. Metal glasses were placed on the patient, and we performed a combined laser technique in one time (in this succession ablative CO₂, fractional CO₂, Nd:Yag 1064 nm, 595-nm pulsed-dye laser). The total treatment time was about 30 minutes. Postoperatively there was an intense purpura, and we covered the treated area with antibiotic cream which the patient continued at home for 1 month. We recommended to avoid sun exposure for up to 3 months after the treatment, wear a sunscreen, and covering the area with a hat in order to prevent side effects such as pigmentation.

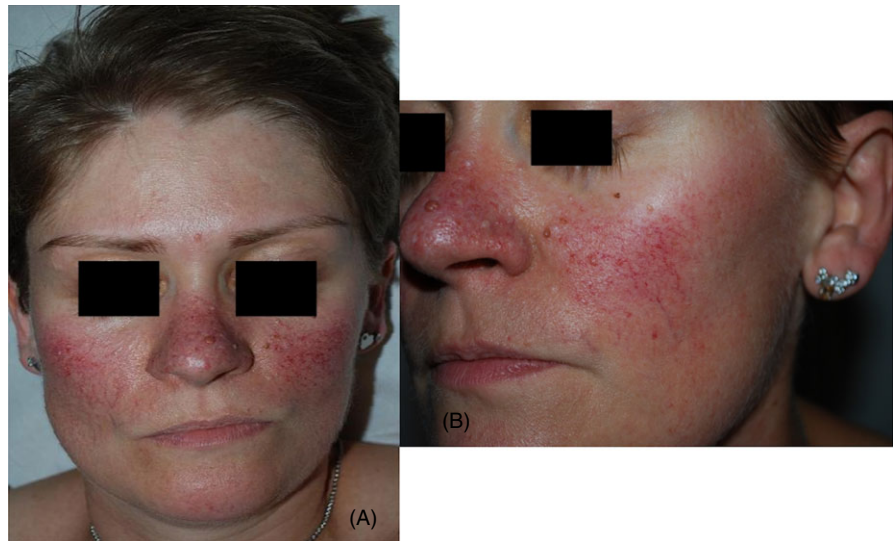


FIGURE 1 (A-B) Facial angiofibromas

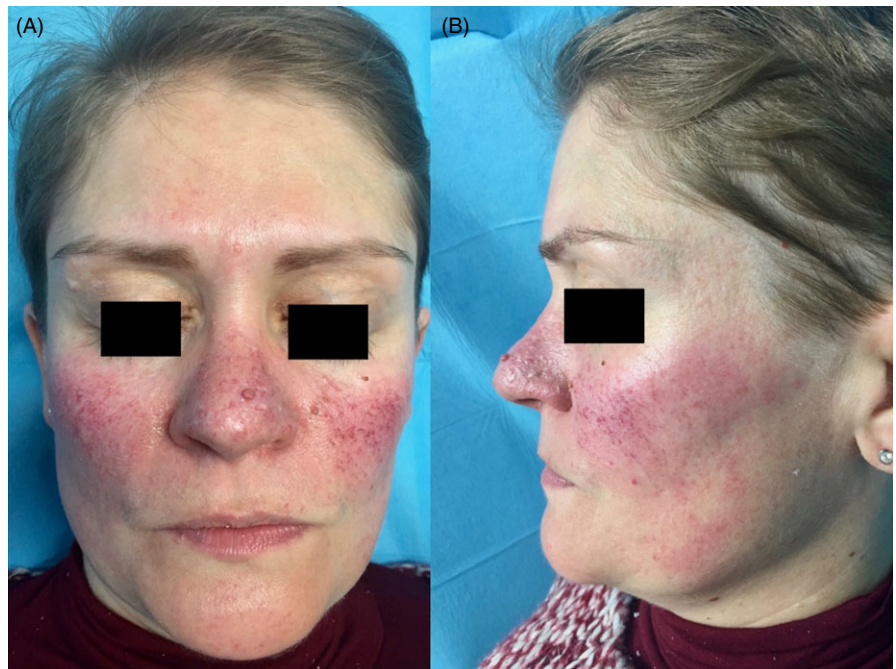


FIGURE 2 (A-B) FA after topical rapamycin 0.05% ointment twice daily for 5 months

Photographs and Antera 3D® carried out before and after the laser therapy were used to evaluate the efficacy of the treatment (Figure 3A-B). Her wound healing was uncomplicated, and the patient showed remarkable improvement after 1 month (Figure 4A-B).

Follow-up at 1 year showed very good cosmetic results, and the patient was satisfied.

3 | DISCUSSION

The lack of guidelines for the treatment of facial angiofibromas is probably due to the low incidence of this pathology. Rapamycin is today a still off-license treatment with good outcomes, but open questions are drug concentration, vehicle, and dosage.² Salido et al proposed 0.4% rapamycin ointment 3 times a week for 36-week

period concluding that this low concentration with fewer applications improves patient comfort, adherence, and safety.⁷ They also write a review and as there was only one randomized controlled trial and a few small case series or isolated case reports, they proposed an algorithm for the treatment of FA.⁴

As regards the proposed algorithm,⁴ we believe it is interesting but in our opinion topical rapamycin is always a good first choice and afterwards, if FA are still present (both in children and adults, and in mild but high emotional impact cases⁸), a laser approach is useful, while curettage dermabrasion and electrocoagulation are now outdated. The use of laser therapy for the management of FA in TS has, in fact, been described since 1988⁹ with good response, but long-term follow-up suggests high recurrence rates (a mean recurrence time of 3 years).¹⁰ Ablative CO₂ laser has been used to flatten elevated lesions because is ideal for precise, safe ablation with good

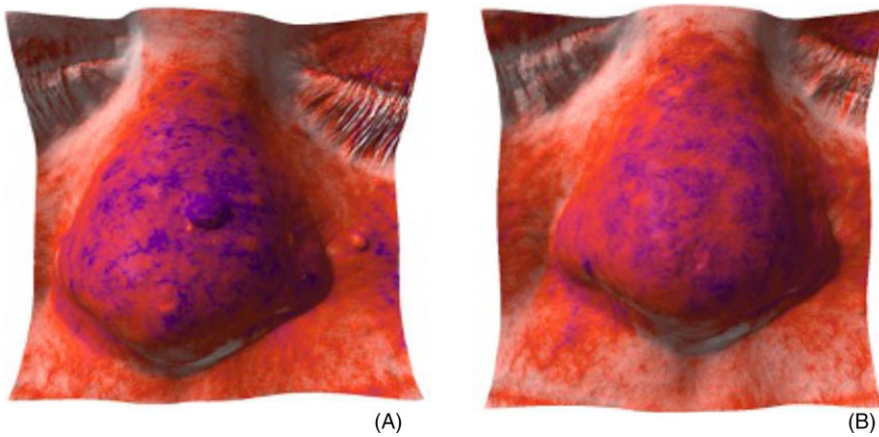


FIGURE 3 (A-B) Antera 3D® carried before (A) and after (B) the laser therapy

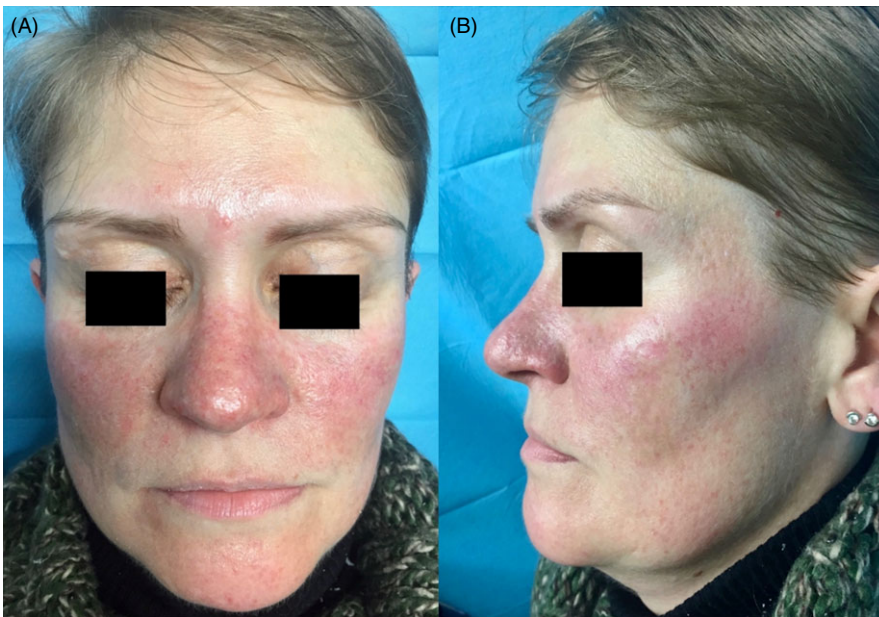


FIGURE 4 (A-B) 1 month after laser therapy [Color figure can be viewed at wileyonlinelibrary.com]

hemostasis, fractional CO₂ lasers produce a matrix-shaped microthermal injury, stimulating both the epidermis and in the dermis the basic repair process which results in skin regeneration and repair, while pulsed-dye laser and Yag has been applied to reduce the vascularization of the dermis (these lasers act at different levels because pulsed-dye laser penetrate approximately until 1 mm, while YAG until 5 or 6 mm improving the outcome¹¹), which is the cause of the unaesthetic erythema.¹ Weiss et al reported a pinpoint approach combining electro surgery, pulsed-dye laser, and ablative fractional resurfacing.¹ A recent review also shows how most cases are treated under general anesthesia.¹² In addition, all methods are subjective except for the clinically evaluated improvement obtained by comparing photographs and using a rating scale, the FA severity index (FASI), based on erythema, size and extension of the FA.⁷ Unfortunately, it is difficult to understand how this is calculated and so it is not easily reproducible. To date, there appear to be no other articles in the literature where FASI was used.

Some groups combined laser and topical rapamycin. A case report reported a 26-year-old female treated with a combination approach

using laser surgery followed by twice daily 0.2% rapamycin ointment for 3 months.¹³ Park et al started with twice daily 0.2% rapamycin and CO₂ laser and after did a maintenance schedule for a period from 8 to 17 months with rapamycin 0.1% ointment 3 times weekly.¹⁴ They recommended regular monitoring of lipid profiles and serum rapamycin levels during prolonged maintenance treatment but did not specify the cutoff time.¹⁴ Our choice is to recommend 0.05% rapamycin ointment twice daily for 5 months as early treatment to reduce FA, because for big FA (>4 mm) topical rapamycin is less likely to be effective.² However, if a patient is first treated when adult and there are large FAs, rapamycin first and combined laser therapy seems to be the best choice. We do not use the pinpoint laser approach¹ because of the long time needed to *restitutum ad integrum* so patients will have to be away from work or school for too many days. Considering the high recurrence rate with these approaches in our clinical practice, we always try to avoid general anesthesia. We believe the combined laser approach to be a useful solution because we cannot permanently clear FA due to their nature but we can offer a satisfying outcome to patients. Open questions are recurrence rate

(our follow-up is 1 year) and when and how long maintenance with rapamycin to prevent recurrence. In conclusion, topical rapamycin can be considered a useful treatment for facial FA, particularly if it is started at an early stage. After if a patient is dissatisfied or there are large FA, combined laser therapy is the best choice.

CONFLICT OF INTEREST

The authors report no declaration of interest.

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