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Case report

Photodynamic therapy in a patient with facial angiofibromas due to tuberous sclerosis complex

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ABSTRACT

The facial angiofbromas due to tuberous sclerosis complex produced significant social and emotional distress for affected individuals, but there is no specific therapeutic strategy up to now. Herein, we report a case of facial angiofibromas successfully treated by 5-aminolaevulinic acid-mediated photodynamic therapy (ALA-PDT) with no recurrence for 6 years, thus providing a promising therapeutic option.

1. Introduction

Tuberous sclerosis complex (TSC), also known as Bourneville disease, is a genetic neuro-cutaneous disorder with various clinical manifestations [1]. Facial angiofibromas is one of the major features of TSC [2], which is usually proliferative and disfiguring. Treatment options offered by the 2012 International Tuberous Sclerosis Complex Consensus Conference included: topical mammalian target of rapamycin (mTOR) inhibitor, vascular laser surgery, ablative laser surgery and surgical excision [2]. However, all the therapeutic approaches have limitations. Herein, we report a case of facial angiofibromas due to TSC successfully treated by 5-aminolaevulinic acid-mediated photodynamic therapy (ALA-PDT) with no recurrence for 6 years.

2. Case report

A 17-year-old boy presented with multiple lesions on his face came to our outpatient clinic. The lesions started to appear in his infancy and progressed as he get older, gradually affecting the whole face, neck, chest and back, without itch and pain. Physical examination revealed large amounts of red papules and nodules, about 1-10 mm in diameter, clustered on both sides of the nose and lower jaw, some of which were verrucous-like hyperplasia (Fig. 1a), while scattered on the chest and back. In addition, several shagreen patches could be seen in the abdomen (Fig. 1b) and lumbosacral region (Fig. 1c). Biopsy of the facial lesion showed mild hyperkeratosis of the epidermis, hyperplasia and dilation of the capillaries in the dermis, proliferation and densification of perivascular collagen, as well as inflammatory cells infiltrated around the blood vessels, which indicated angiofibromas secondary to TSC combined with the clinical manifestation. On the basis of all the above findings, though the patient had no neurological and any other symptoms, we made a diagnosis of facial angiofibromas due to TSC according to the diagnostic criteria updated in 2012 [2].

Since the facial angiofbromas represented a significant cosmetic problem for this adolescent patient, he once received carbon dioxide (CO_2) laser treatment in another hospital. Unfortunately, the lesion relapsed in less than one month after the therapy. Therefore, he come to our department asking for cosmetic treatment to improve his aesthetic appearance.

3. Methods/description of treatment

In view of the fact that there is no specific therapeutic strategy up to now, we performed only microwave ablation of the lesion on the left side of his lower jaw, but combined with ALA-PDT on the right lower jaw after he signed the consent form. The preparation included routine disinfection and local anesthesia by injection of lidocaine. For the left side, we used microwave with a power of 20 W by a microwave therapeutic instrument (WB-3100 AIII, Xuzhou Baoxing Medical Equipment Co., Ltd., Xuzhou, China) to remove the lesions until there was no visible lesion. For the right side, immediately after microwave ablation (the same as above), a solution of 20% 5-ALA (Fudan Zhangjiang Bio-

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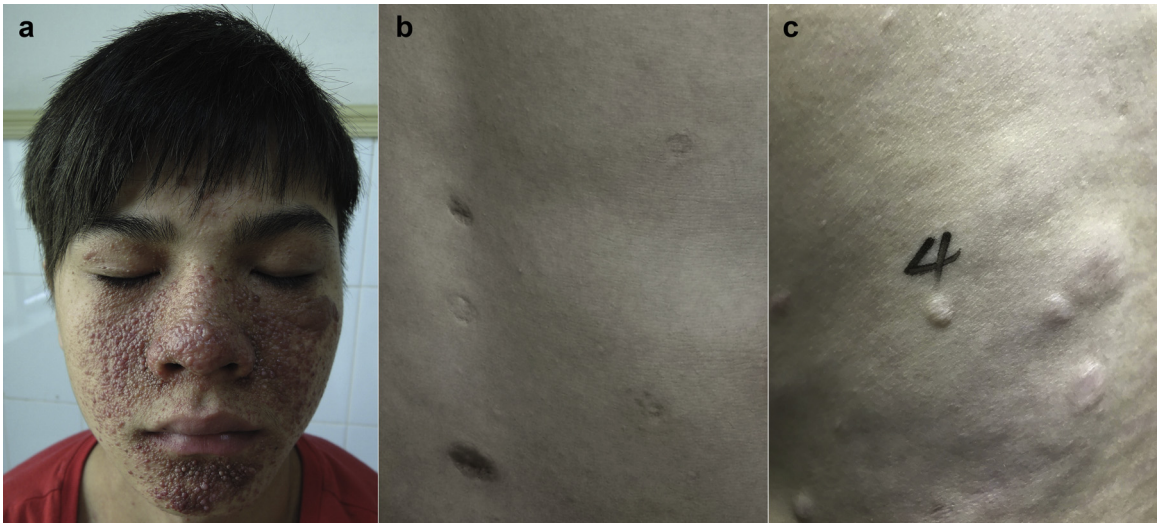

Fig. 1. Clinical features.
(a) Multiple angiofibromas on his face. (b) Shagreen patches on his abdomen. (c) Lumbosacral shagreen patches.

Pharm Co., Ltd., Shanghai, China) was applied on the lesion area, and then covered by a lightproof film for 4 h. Light irradiation of 633-nm at 80 mW/cm [2] via a semiconductor laser therapeutic apparatus (LED-IB, Wuhan Yage Optic and Electronic Technique Co., Ltd., Wuhan, China) was conducted 8-cm far away from the lesions for 30 min.

4. Results

We selected two areas of the lesions as experimental treatment regions (Fig. 2a) after obtaining the patient's consent. The lesions of both treated regions disappeared and cured with crust at first (Fig. 2b), and no adverse events happened. After two months, however, the lesion on the left lower jaw recurred, while the right lower jaw remained smooth without side effects or complications (Fig. 2c). Two and a half years later, there was still no recurrence on his right lower jaw. Considering the satisfied efficacy of the right side, the patient strongly asked us to treat his whole chin by the same method. Therefore, he took another 6 times of ALA-PDT on the chin, once a week, and for the first time with pretreatment by microwave ablation. At present, the lesions didn't recur in a follow-up of six years (Fig. 2d). What's more, the patient regained confidence and lived a happy life now.

5. Discussion

The central facially localized angiofbromas, as one of the dermatological hallmarks of TSC, produced significant social and emotional distress for affected individuals and proposed therapeutic challenge for clinicians. The consensus guidelines suggested treatment as appropriate for the lesion and clinical context [2]. Many dermatologists have published the application of surgical and laser removal of the lesions, but such invasive approaches might predispose the patients to scarring, hyperpigmentation, hypopigmentation or other adverse events. Bittencourt, R. C. et al [3] retrospected 10 cases of facial angiofbromas in TSC treated by scanning CO_2 laser and concluded that the long-term results of CO_2 laser treatment were unpredictable, of which the majority of all treated patients experienced recurrence. Besides the traditional therapeutic modality, mTOR inhibitor, such as sirolimus (also called rapamycin) and everolimus (RAD001) [2], is a new and promising treatment option. Several clinical studies have demonstrated that topical 0.2% sirolimus gel [4] and 1% rapamycin [5] were effective and safe for treatment of facial angiofibromas linked to TSC. Although most patients were well-tolerated to topical mTOR inhibitors, the 12-week [4] and 6-month [5] duration of the trial, respectively, were too limited to estimate the long-term efficacy, particularly considering the recurrent nature of angiofibromas. Therefore, refinement of therapy strategies, capable of reducing the subsequent recurrent risk, should be sought.

Photodynamic therapy has been widely used in many diseases in recent years. It contains light activation of the photosensitizer, which reacts with local oxygen to generate reactive oxygen species, thus leading to subsequent tissue injury that may include blood vessel wall damage. But there are few published literatures about facial angiofibromas treated by ALA-PDT. Weinberger, C. H. et al [6] reported six patients with centrofacial angiofibromas treated by ALA-PDT followed by immediate pulsed dye laser (PDL). In this case series, the results of patients who received combined treatments were significantly better than that of either modality alone [6]. Nevertheless, two of the patients experienced mild recrudescence in 4 years [6]. In contrast, our patient received microwave ablation followed by ALA-PDT, and kept no recurrence for 6 years. The reasons why we conducted microwave

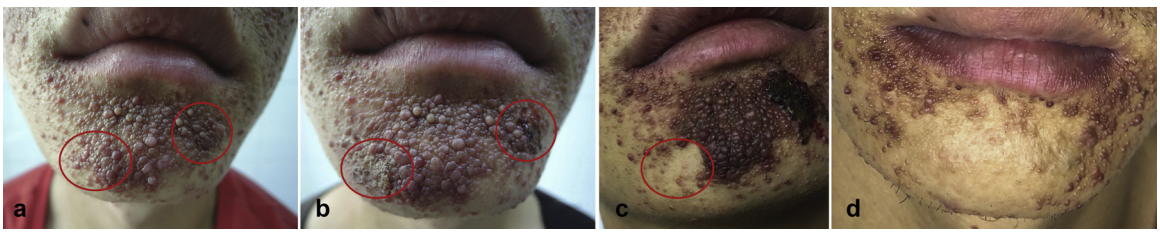

Fig. 2. Manifestations of the lesions during the treatment.
(a) Before treatment. (b) Three days after the experimental treatment. The left side: only microwave ablation. The right side: microwave ablation followed by immediate 5-aminolaevulinic acid-mediated photodynamic therapy (ALA-PDT). (c) Two months after the experimental treatment. The left side: the lesions recurred. The right side: remained smooth. (d) Six years of follow-up after 6 times of ALA-PDT on the chin. (a–c) The red circles indicate the selected treatment areas.

ablation before the first time of ALA-PDT were as follows. First, it helped to remove the visible lesions and reduce the total times of ALA-PDT. Second, it could disrupt the epidermal barrier enough to enhance penetration allowing better uptake of the ALA. Third, microwave ablation has better hemostasis effect than CO_2 laser or other photoelectric therapy, which was more conducive to postoperative recovery. What's more, our team has successfully applied microwave ablation combined with ALA-PDT to cure many cases of refractory condyloma acuminata [7,8]. Compared with microwave ablation, peeling agents and/or pretreatment with retinoids are more easily available around the world. However, they are too weak to achieve the purpose of pretreatment. And the agents couldn't promote the absorption of photosensitizer. Therefore, we chose microwave ablation instead of peeling agents. We speculated that the combination of microwave and ALA-PDT could overcome the limitations of either therapy, and multiple times of ALA-PDT could enhance the vascular damage as well as reduce the risk of recurrence.

In summary, this case illustrated that ALA-PDT showed significant clinical benefit for facial angiofibromas due to TSC, thus providing a promising therapeutic option.

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