

Autologous full-thickness skin graft for treating squamous carcinoma in a patient with psoriasis

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Abstract

A 31-year-old male patient with psoriasis received administration of traditional Chinese medicine (TCM) during a disease course of 14 years. He showed multiple keratoma together with squamous cell carcinoma (SCC) in left lower limbs. After admission, the conditions were stable after treatment, and received surgery for treating SCC. The skin defect was treated using full-thickness skin graft. The postoperative survival of the flap was satisfactory, and the conditions of psoriasis were well controlled. In this case, we presented the feasibility of graft in the donor site from a psoriatic lesion. Besides, we analyzed the possibility of SCC and keratinizing lesions.

Abbreviations: SCC = squamous cell carcinoma, TCM = traditional Chinese medicine.

Keywords: full thickness free skin graft, psoriasis, squamous carcinoma, traditional Chinese medicine

1. Introduction

Psoriasis, a common chronic skin disease related to inflammation, is featured by squamous erythema.^[1] In China mainland, the treatment of psoriasis is mainly relied on the conventional drugs (e.g., acitretin, methotrexate, cyclosporine and biological preparation) together with traditional Chinese medicine (TCM). Nowadays, more and more patients present psoriasis with malignancies, especially the aged population with a long disease course. Most of the patients reported oral administration of TCM. The exact mechanism of the combination of psoriasis and malignancies is still not well defined, but it is highly suspected with the administration of the presence of arsenic in the TCM.

The treatment of psoriasis combined with squamous carcinoma is mainly relied on the surgery.^[2] For the patients with large

lesions after surgical resection that could not be sutured directly, skin graft transplantation and skin transplantation are suggested. In this study, the patient showed a lesion (10 cm × 10 cm) after tumor resection. Full-thickness skin graft transplantation was utilized for the repairment, and the donor skin contained the lesions of psoriasis. During the treatment, the patient received oral administration of acitretin together with external application of agents. For the prognosis, the survival of the graft was satisfactory, and the psoriasis was well controlled.

2. Case report

A 31-year-old male patient presented to our hospital on December 31, 2018 due to systemic erythema, papule and psoriasis with no obvious causes for 14 years, together with tumor mass in the tibial side of left lower limb for 6 months. For the erythema, papule and psoriasis, no systemic treatment was given except intermittent administration of TCM that may contain the arsenic. Recurrence was frequently reported by the patient, and the injury showed gradual progression. About 6 months ago, the patient showed a tumor mass in a pink color with no causes in the tibial side of left lower limb. The mass showed a diameter of about 1 cm at first, but then was in a size of 5.5 cm × 5.5 cm rapidly. Besides, ulcer, exudation, aberrant smell, and obvious pain were reported by the patient in the lesion sites. The urination and defecation were normal. He showed no obvious loss in the body weight. Each patient signed the informed consent. The study protocols were approved by the Ethical Committee of The Second Hospital of Jilin University.

On physical examination, there were no obvious abnormalities in the systemic examination. There was no swelling in the bilateral inguinal and popliteal lymph nodes. MRI indicated slightly long T1 and slightly long T2 signals in an irregular profile in the soft tissues at the inside of right leg. Local parts showed protrusion to the skin. The adjacent soft tissues presented long T2 signals in a patchy form. There were no aberrant signals in the right tibiofibula. Diffused papule and plaques in a dark red color were observed in the facial and cervical parts, trunk and limbs. The skin tissues in these parts were covered by massive scale in a

Editor: Ediriweera Desapriya.

This study was supported by the Jilin Provincial Talent Fund (No. 2019SCZT027). The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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How to cite this article: Zhang G, Bu W, Wang S, Li X, Wang S, Li F, Yao C. Autologous full-thickness skin graft for treating squamous carcinoma in a patient with psoriasis. *Medicine* 2020;99:e22252.

Received: 18 December 2019 / Received in final form: 19 July 2020 / Accepted: 17 August 2020

<http://dx.doi.org/10.1097/MD.00000000000022252>



Figure 1. The skin lesions in the left lower limb.

silver color, especially the lower limbs. The findings for the phenomenon of membrane and dotted hemorrhage, and punctate hemorrhage were all positive. Multiple small papule (0.5 cm) in a jasmine color was observed in bilateral palms and the dorsal skin of the hand. The texture of the papule was hard, and the boundary was clear. No symptoms were felt by the patient at fist. The boundary between the mass in the left leg and the adjacent tissues was not clear, and the movement of the mass was poor. There was a black plaque with a width of 1.5 cm that wrapped the base of the peripheral mass (Fig. 1).

For the laboratory test, the urine arsenic was in a concentration of $24.67 \mu\text{g/L}$ (normal range: $<300 \mu\text{g/L}$), while the arsenic content in hair was $0.331384 \mu\text{g/g}$ (normal range: $<0.06 \mu\text{g/g}$). There were no aberrant changes in the other tests. Pathological analysis for the mass in the left lower limb indicated squamous carcinoma (Fig. 2). Pathological analysis for the black plaque in the base indicated pseudoepitheliomatous hyperplasia combined with hyperkeratosis, as well as slightly chronic inflammatory cell infiltrate in the epithelium (Fig. 3). On this basis, the patient was diagnosed with psoriasis, highly differentiated squamous carcinoma in the left lower limb, and keratoacanthoma in left lower limb, as well as areal keratosis.

The treatment regimen involved administration of Acitretin (30 mg/day), application of humectant and mometasone furoate, and anti-infection therapy, lasting for 3 weeks. The skin lesions were stable with no progression. Then the dose of Acitretin was reduced to 10 mg per day. On this basis, extensive resection and free skin grafting were performed under general anesthesia. Postoperative pathological analysis indicated no cancer cells at the margin when extending the cutting margin to a diameter of about 1.5 cm. Therefore, the intraoperative resection scale was at a position that was about 1.5 cm to the tumor margin. The deep fascia was resected, and the defect area showed a size of $10 \text{ cm} \times 10 \text{ cm}$. The full-thickness skin graft with the same sized psoriasis

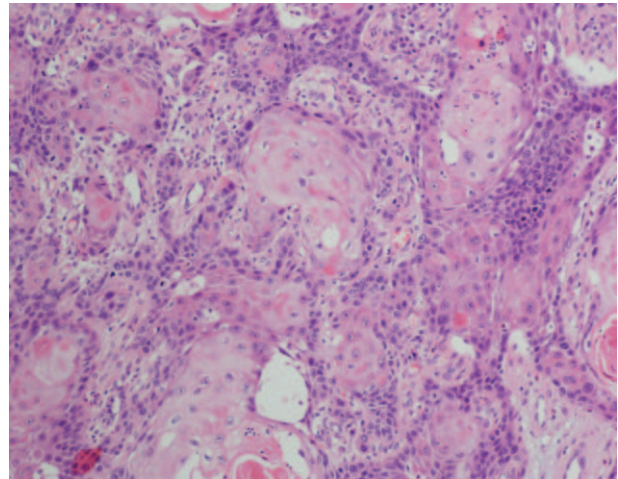


Figure 2. HE findings for the highly differentiated squamous carcinoma. The images were observed under a magnification of $100 \times$.

plaque was obtained from the homolateral abdomen, and then the donor site was directly sutured afterwards. The wound surface was covered by full-thickness skin graft, followed by packaged suturing through intermittent knot and compression. After surgery, the affected limb was elevated to 45 degree, together with anti-infection, improvement of microcirculation and regulation of epithelium (Fig. 4). On postoperative day 4, the surgical region showed isomorphic reaction of the psoriasis. The peripheral skin injury showed progression, which may be related to the surgical stress. Therefore, the dose of Acitretin was elevated to 30 mg per day. On day 14, the bandage was removed, and the transplanted graft was alive with few vesication and punctiform ulcer. The patient was followed up for 8 months with satisfactory outcome (Fig. 5). The color and texture of the free skin graft were similar with the recipient site. Additionally, the psoriasis showed attenuation and even elimination.

3. Discussion

Cutaneous squamous cell carcinoma (SCC) ranks as the second skin malignancy in the non-melanoma skin cancers, and it shows

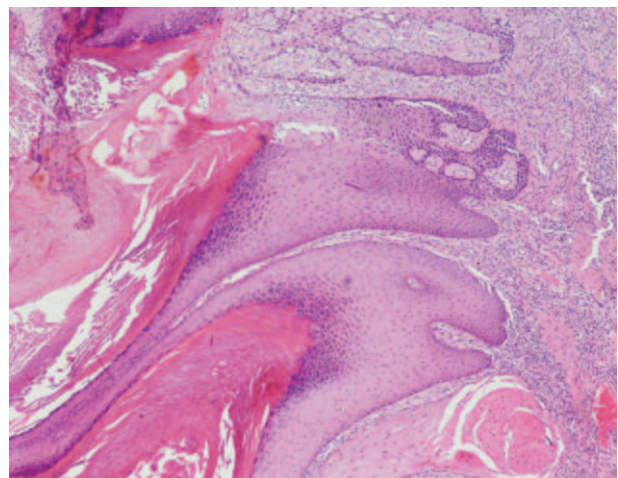


Figure 3. HE findings for the keratoacanthoma under a magnification of $40 \times$.

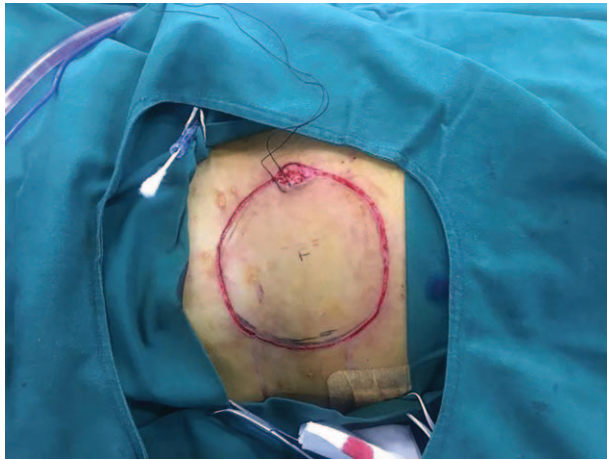


Figure 4. Design of free skin graft.

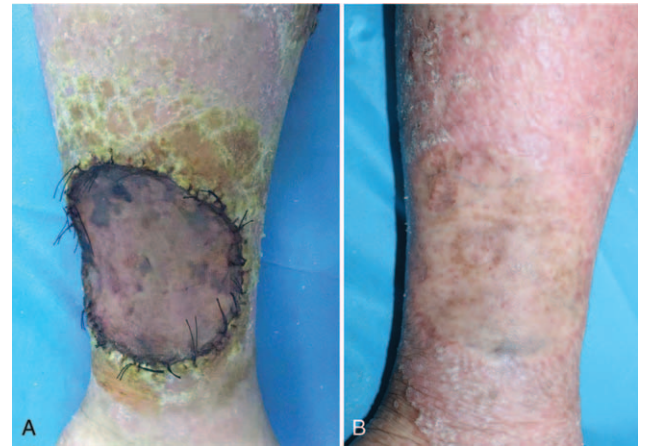


Figure 5. Cosmetic appearance of the skin lesions about 14 days (A) and 8 months (B) after surgery.

a tendency of increase worldwide.^[3] Psoriasis is a common inflammatory cutaneous disease mediated by immune response, accounting for about 2% in the whole population.^[4] The SCC combined with psoriasis is considered to be associated with the arsenicals exposure,^[5] contact with coal tar, application of immunosuppressive drugs, long-term chronic inflammation, viral infection and trauma.

Arsenic, a non-mental element, may induce multiple-organ injury upon uptake. Besides, it may affect the skin and induce dermatitis, hyperkeratosis in skin, pigmentation and verrucous hyperplasia, and even skin cancer.^[6] In China mainland, araenical keratosis is mainly caused by long-term exposure to the arsenicals and inorganic arsenic that are commonly utilized in treating psoriasis, leukemia, epilepsy and asthma. The TCM involving utilization of arsenic included white arsenic, cinnabar and realgar. Araenical keratosis is a common symptoms of arsenism.^[7] In this case, the patient showed a history of psoriasis of 14 years. Long-term administration of TCM was given to the patient, which could not exclude the possibility of arsenicals exposure. The content of arsenic in the hair showed obvious elevation, which reflected the environmental exposure and the average level in the tissues. The urine sample could only reflect the conditions in a short term. The negativity in the urine arsenic may be related to the recent termination of the TCM.^[6] Therefore, we are not sure whether the araenical keratosis and the SCC are associated with the administration of arsenicals. In future, more examinations are required.

Currently, the treatment of SCC is mainly relied on extensive resection.^[5] For the patients with moderate psoriasis, Acitretin is usually given as it could regulate the differentiation, proliferation and apoptosis of keratinocytes, and attenuate the corneum layer through inhibiting the hyperplasia in the dermal capillary. This contributed to the normalization of the cutaneous tissues.^[4] In

this case, the injury site was localized in the tibial side with poor blood supply. Besides, the skin injury and affected area were comparatively large. Moreover, the psoriasis upon admission was in a state of progression. Therefore, the patient received treatment for SCC and psoriasis including acitretin. Upon resection, there was a huge skin wound, while there was a large psoriatic injury in the donor site of the full thickness free skin graft. All these conditions may affect the survival of the graft and the outcome after resection of tumor. Fortunately, the graft survival of such case was satisfactory, and the psoriasis was well controlled.

Rare studies have been focused on the extensive resection and full thickness free skin graft transplantation in the SCC patients concurrent with psoriasis (Table 1).^[8,9] In this study, we investigated the feasibility of surgery for treating such kind of patients:

- (i) the post-resection cutaneous wound was up to 10 cm × 10 cm. On this basis, it was very difficult to find a suitable donor site in the peripheral skin without psoriatic plaque. The pathological changes of the psoriasis were mainly featured by parakeratosis and hyperkeratosis in the epiderm, while the changes were featured by thinning in the papillary layer of dermis and telangiectasis in the dermal papilla. However, there were no changes in the hypodermal cells and part of the epidermic cells.^[10] Therefore, the injury skin in the patients with psoriasis containing the dermis could serve as the donor site.
- (ii) For the coverage of the wound, several types of graft could be chosen including epidermal skin graft, intermediate and full thickness free skin graft. The epidermal skin graft was not suitable for the wound coverage in the psoriatic patients

Table 1

Summary of psoriasis patients combined with araenical keratosis and squamous cell carcinoma.

| Case | Gender | Age | Progressive or Stable Psoriasis | Application of Acitretin | Tumor size | Skin Damage in the Donor Site | Repairment | Reference |
|-------|--------|-----|---------------------------------|--------------------------|----------------|-------------------------------|----------------------|----------------|
| No. 1 | Male | 70 | Stable | None | 2.0cm × 2.0 cm | Yes | Skin transplantation | Scupham et al |
| No. 2 | Male | 46 | Stable | None | Not mentioned | No | Direct suture | Siefring et al |

as it may present contracture, intolerance to friction and obvious pigmentation, as well as the location of the pathological changes (i.e., cuticular layer). For the intermediate thickness free skin graft, it contained partial dermal tissues that caused no effects on the donor site healing of the psoriatic patients, however, there might be large-scaled hyperplastic scar in the donor site affecting the life quality and cosmetic appearance. Full-thickness skin graft, containing the dermis and the cuticular layer, was rich in elastic fibers and capillaries, which showed less contraction, normal color, satisfactory flexibility and tolerance to the heavy burden and friction upon survival. In addition, the donor site could be sutured directly only resulting in generation of linear scar.

- (iii) The complete hemostasis, compression and ligation of the wound surface contributed to the close adhesion of the graft to the wound surface, which prevented the graft transplantation failure induced by formation of dead space, subcutaneous hydrops, obstruction in the venous return, as well as the graft shift.
- (iv) For the application of full thickness free skin graft, the sebum function was recovered about few months after transplantation. Therefore, the recipient site should be smeared with hydrous wool fat and paraffin oil at the early-stage in order to prevent postoperative rupture.
- (v) There is usually an anoxic duration about 2 to 3 days after graft transplantation, until the recovery of blood circulation. Patients with psoriatic injury usually in a state of hypermetabolism and high proportion of mitosis. In a previous study, the graft used in the transplantation for the repair of active psoriasis was more likely to induce obvious anoxia compared to the normal graft, which may hamper the transplantation of the graft.^[11] In our clinical experiences, great attempts have been made for the treatment of psoriasis, and control of the pathological features of the skin in order to promote the graft survival.
- (vi) Due to stimulation of long-term chronic inflammation, part of the affected skin showed various infection. For these patients, anti-psoriatic drugs should be given before or after surgery to eliminate the postoperative infection and improve the graft survival.^[12]
- (vii) For the patients suspected with lymphadenovariex, lymph node biopsy was required. According to the biopsy results, the clinical physicians made a decision on whether to perform the lymph node dissection. In this study, the patient showed no aberrant changes in the lymph node, and therefore, no lymph node dissection was given. Finally, regular follow-up was given to the patient after surgery.

In summary, psoriatic patients with ulcerative nodule may present a high possibility of SCC. For the patients with

progressive psoriasis, surgery and full thickness free skin graft were feasible. In particular, full thickness free skin graft contributes to the cosmetic appearance and function in the patients with massive skin defect.

Author contributions

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