CASE REPORTS

Treatment of vitiligo with autologous epidermal transplantation using the roofs of suction blisters

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We report our experience of autologous epidermal transplantation for three patients with vitiligo. The vitiligo in two patients was stable whereas that in the third was active. Autologous epidermal transplantation using suction blister roofs from normally pigmented skin was performed following the failure to repigment skin using topical steroid and/or psoralen–ultraviolet A treatment. Grafts were well taken in all three patients. Satisfactory repigmentation was noted in the two patients who had stable vitiligo; there were no complications except for mild hyperpigmentation at the donor areas. For the patient who had active vitiligo, depigmentation of the graft and concomitant Koebner's phenomenon at the donor site were observed 3 weeks after the procedure. We conclude that autologous epidermal transplantation using the roofs of suction blisters is an excellent and safe repigmenting procedure for stable, localised vitiligo and that active disease precludes transplantation.

HKMJ 1998;4:219-24

Key words: Epidermis/surgery; Vitiligo/therapy; Transplantation, autologous

Introduction

Vitiligo is a worldwide, acquired disease of unknown aetiology and is characterised by spontaneous skin depigmentation due to loss of melanocytes. The disease has a prevalence of 1% to 2%, and up to 8.8% in some countries.[1] Most afflicted patients enjoy good general health; however, the disease can have a profound psychological impact, which may lead to a disturbed social life.[2] Conventional therapies include the use of topical and/or systemic steroid, and psoralen–ultraviolet A (PUVA) treatment. These treatments achieve varying degrees of repigmentation and their response may be appreciated only after a long period of frequent and regular treatment.[3] In addition, the necessity of using prolonged treatment increases the chance of exposure to the adverse effects of these agents.[4]

Various surgical methods that aim to replenish lost melanocytes have gained popularity in recent years. Among them is autologous epidermal transplantation (AET) using suction blisters, which appears to be very promising for treating stable, localised vitiligo. We report our experience of AET using the roofs of suction blisters in three patients: two with stable, localised vitiligo lesions and one with active vitiligo. The technique of this procedure is also described.

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Epidermal transplantation technique

The donor skin at the medial aspect of the right/left arm was disinfected, as with any surgical procedure. Glass cups (or syringes) of appropriate orificial sizes were placed on the donor skin and suction was applied at a constant negative pressure. The pressure ranged from -33.3 to -40.0 kPa and was created by an SAM12 electric vacuum suction machine (MG Medical, Colchester, UK). No anaesthesia was required because the procedure was painless. Small vesicles started to form after about 1 hour of continuous suction, which enlarged and coalesced to form a bulla approximately 1 hour later (Fig 1). The roof of the bulla, which represented the epidermal graft, was separated from the surrounding skin using a pair of curved iris scissors. The graft, supported by a moistened plain fine gauze, was placed on a platform and a pair of fine forceps was used to gently spread it to its maximum size. Any fibrin clots attached to the dermal surface were gently removed. The graft was trimmed to a size and

shape appropriate to the recipient site, which had been prepared simultaneously and in the same way as the donor area. The graft was accurately implanted into the recipient site. The procedure was completed after applying antibiotic spray and covering the graft with paraffin gauze, then plain gauze, and finally semi-permeable adhesive dressing (Tegaderm; 3M Canada Inc., Ontario, Canada).

Case reports

Case 1

A 14-year-old male student was referred by a general practitioner to the Social Hygiene Clinic in 1994. A white patch had appeared spontaneously on the left side of the patient's chin about 6 months before the consultation. The lesion had started as a small white spot and had enlarged within a few months. The patient otherwise enjoyed good general health and none of his family members had a history of skin diseases. On examination, a well-demarcated, depigmented triangular patch of 2.0 by 3.0 by 4.0 cm was found abutting the lower lip on the left side of the chin (Fig 2a). Wood's lamp illumination accentuated the depigmentation and supported a diagnosis of vitiligo. There was no vitiliginous lesion elsewhere on the face, body, or limbs. The patient was treated with topical 0.05% halometasone monohydrate cream (Sicorten; Novartis, Basel, Switzerland) and 0.1% mometasone furoate cream (Elomet; Schering Canada Inc., Quebec, Canada) during the first year, with no response.

Topical PUVA treatment was given twice weekly for 6 months. The therapy was temporarily suspended due to a PUVA-induced burn; thereafter, treatment continued uneventfully. Therapy was stopped after 6 months for lack of repigmentation. Since the patient's consultation, the size of the vitiliginous patch had remained unchanged. A trial of AET using the suction blister method was suggested and consented to. Pre-operative blood tests included complete blood count, renal and liver functions, sensitive thyroid stimulating hormone and total thyroxine, and markers of auto-immune diseases. All tests gave normal or negative results. Autologous epidermal transplantation was performed in February 1997. A 1.9- by 1.1-cm epidermal graft was taken from the medial aspect of the patient's right arm as a trial. Observation after removing the dressing on day 14 revealed a very good uptake of the graft. Faint, uneven pigmentation was noted on the recipient site after the epidermal graft had sloughed off a few days later. Subsequent follow-up showed that pigmentation had spread and intensified, and that an evenly pigmented patch had gradually formed. The spread of pigmentation continued for 6 months after the grafting.

Slight hyperpigmentation was noted at the donor areas and this was accepted by the patient. Five donor epidermal sheets of smaller sizes were subsequently grafted onto the adjacent vitiliginous areas in two separate sessions. The last follow-up was 9 months after the first treatment and revealed no loss of pigmentation in the grafted area, and the more recently grafted areas showed continued improvement (Fig 2b).

Case 2

A 17-year-old male manual worker first presented to the Social Hygiene Clinic in 1996 with an 8-year history of depigmented patches that had arisen spontaneously on the right side of his neck and which had not changed during the past 5 years. The patient's skin was otherwise normal. He enjoyed good general health and had no family history of vitiligo or auto-immune diseases. Under Wood's lamp illumination, the patches appeared white, thus confirming a clinical diagnosis of vitiligo. Systemic examination was normal. The same blood tests as for the patient in Case 1 gave normal or negative results.

The patient was treated with topical 0.05% halometasone monohydrate cream for 5 months, but no improvement was noted. He refused topical PUVA treatment for lack of time. Autologous epidermal transplantation was offered and accepted. The grafting method used was the same as for the patient in Case 1. A total of three epidermal sheets (2.2x1.5 cm, 1.2x0.9 cm, and 1.4x1.0 cm) were grafted. Follow-up examinations in the first and third months after the procedure showed satisfactory repigmentation in the grafted areas. A second AET for the rest of the vitiliginous lesions was suggested but refused for lack of time and also because a satisfactory cosmetic result had already been achieved. At a consultation 10 months after the procedure for an unrelated skin problem, the pigmentation in the grafted sites persisted (Fig 3a), and faintly pigmented macules could be seen at the donor sites at the medial left arm (Fig 3b).

Case 3

A 37-year-old female purchaser first noticed white patches on the right zygomatic area and angles of the mouth in 1987. Further white patches appeared on the right lower neck, abdomen, and distal fingers. The patient was otherwise healthy and had no family history of vitiligo, thyroid, or other autoimmune diseases. Prior treatments with topical steroids had been given by private doctors; although there was temporary

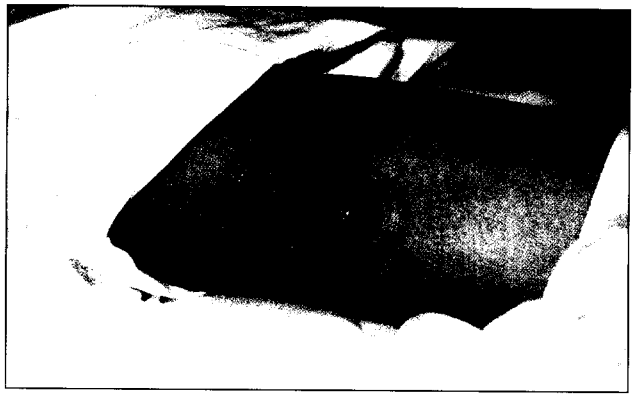


Fig 1. Case 1: photograph showing suction blister at donor site
A bulla of a size comparable to the orificial size of the suction cup formed at the donor area after 2 hours' continuous suction

improvement in some lesions, new lesions had also appeared.

The patient was referred to the Social Hygiene Clinic in June 1996. Topical PUVA treatment was instituted in August 1996 and topical steroid treatment was maintained. There was no apparent improvement after approximately 8 months of therapy and she was referred for AET. Her history strongly suggested that she had active vitiligo and thus contra-indicated any surgical repigmentation procedure. The results of blood tests for autoimmune markers and thyroid function, however, were normal or negative. At the patient's strong request and acceptance of possible complications, a single epidermal sheet of 1.8-cm diameter

2a.

2b.

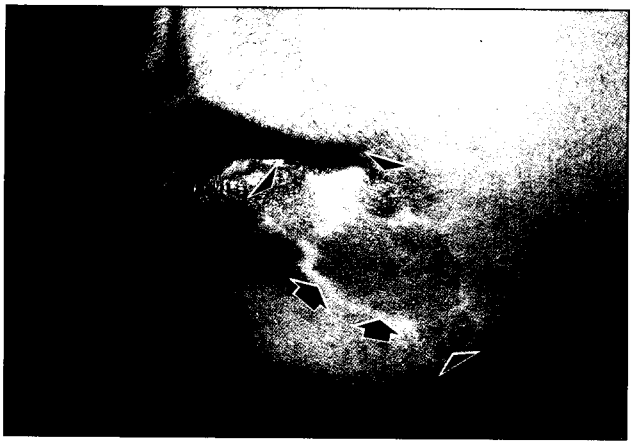
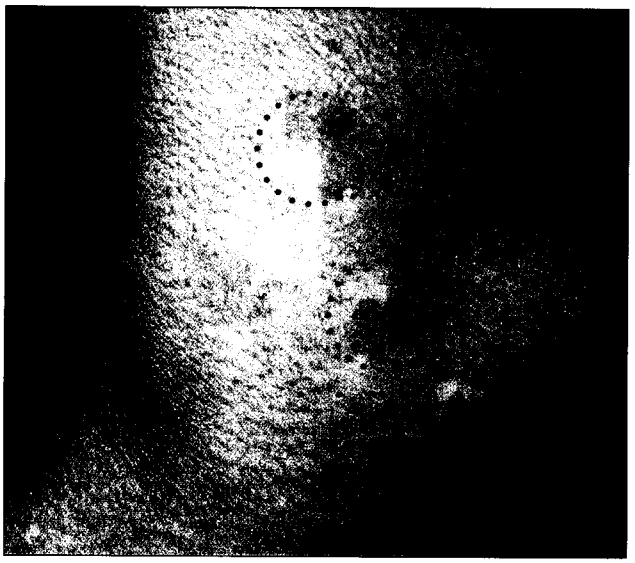


Fig 2. Case 1: photographs of vitiligo lesion before and after treatment
(2a) a triangular vitiliginous patch of 2.0 by 3.0 by 4.0 cm abuts the lower lip margin on the left side of the chin; (2b) follow-up 9 months after the first treatment revealed very satisfactory pigmentation at the first grafted area (asterisk). Arrows indicate the achromatic fissure. Repigmentation continued at the more recently grafted areas (arrowheads)

3a.



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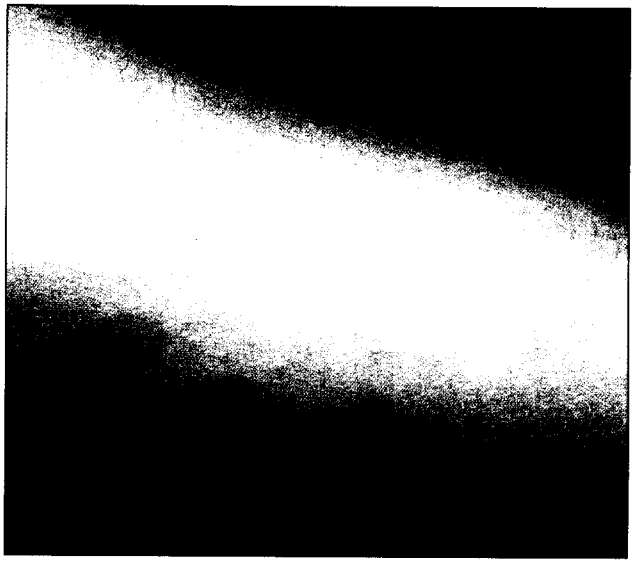

Fig 3. Case 2: photographs of recipient and donor sites after treatment
(3a) satisfactory pigmentation at the grafted areas at the right side of the neck 9 months after treatment; dotted circles indicate the estimated pretreatment vitiliginous areas; (3b) faint and inconspicuous pigmented macules without scars were noted on the donor sites on the medial left arm

was taken from a normally pigmented area on the right side of the anterior abdomen and was grafted onto a lesion on her right lower neck. Examination 8 days after the procedure revealed very good graft uptake. Three weeks after the procedure, however, the size of the pigmented area was notably reduced to an area of 1.3 by 0.9 cm. Moreover, a faint depigmentation was noted at the donor site on the abdomen which is a feature of Koebner's phenomenon. The patient's request for further transplantation was rejected.

Discussion

Vitiligo is often regarded by physicians as a disease not readily amenable to treatment and by the general public as 'incurable'. Transplantation of melanocytes is an alternative and effective way to repigment stable vitiligo that has failed steroid and/or PUVA treatments. The principle of melanocyte transplantation is simple and involves the harvesting of melanocytes (donor graft), removal of the vitiliginous skin or epidermis (recipient area) followed by implantation of the donor graft into the prepared recipient area. The harvesting of melanocytes can be accomplished by the creation of a donor graft using surgical methods or by the in vitro culture of melanocytes using special growth media. Surgical methods for harvesting normally pigmented donor skin have been practised for many years; they include the use of Thiersch's graft,[5] split-thickness skin graft,[6] and mini–punch graft[7]—all produce good results of pigmentation. These methods, however, have not gained wide popularity because they require anaesthesia. In addition, the surgery carries a risk of damage to the dermis and hence scarring.

In contrast, AET using the roofs of suction blisters is an effective, non-scarring surgical repigmentation method that has become popular since 1971, when Falabella[8] reported his success in treating four patients with leukoderma. The AET repigmenting procedure is based on the principle discovered by Kiistala and Mustakallio in 1964[9]—namely, that prolonged suction of the skin in vivo can produce dermo-epidermal separation which results in the formation of a blister. The roof of the blister comprises the whole epidermis, which includes an intact basal cell layer where most melanocytes and melanin reside, and can therefore be used as a donor graft in AET for treating vitiligo. That the immediately underlying dermis is intact explains why there is no procedural pain and why epidermal regeneration is possible without scar formation. The procedure is therefore repeatable. The results from centres that have used this method for AET are most remarkable in patients with segmental vitiligo especially on the face.[10] Incidentally, the epidermis obtained by this method has also been utilised for treating exposed dermal surfaces of patients with burns.[11]

The patient described in Case 1 was the first vitiligo patient in our service, and probably in Hong Kong, to have been treated with AET using the roofs of suction blisters. At follow-up 1 month after the procedure, pigmentation was sparse with uneven density. The density later intensified, however, and simultaneously spread towards the periphery of the original recipient area. Our observations from this graft suggested that maximum pigmentation occurred within the first 3 to 4 months; thereafter, changes were subtle. To the naked eye, no visually discernible difference could be noted between the sixth and ninth months after AET. The repigmentation process in this patient was also recorded by measuring the total area of repigmentation once every 1 to 2 months over a period of 9 months using small, regular 2-mm lattice squares. Figure 4 depicts such measurements in the first and sixth months. The repigmented area measured 112 mm^2 in the first month and 164 mm^2 in the sixth and ninth months (an increase of 46.4%).

The proliferation and in vitro migration of melanocytes account for the increase in the size of the pigmentation and the final even distribution of pigmentation. Also contributing was the transfer of melanosomes from melanocytic dendrites to the neighbouring keratinocytes within an epidermal-melanin unit.[12] The maximum area of pigmentation (164 mm^2) was nevertheless smaller than the original donor graft (209 mm^2) and this partly contributed to the formation of an achromatic fissure (Fig 2b). We therefore propose that a donor graft obtained from the roof of a suction blister should not be smaller than the corresponding recipient area and that prior accurate measurements of recipient sites can help to reduce the incidence of achromatic fissures and hence achieve a more superior cosmesis. Equally good repigmentation was seen in the patient described in Case 2 at the last follow-up, 9 months after AET. The patient in Case 3 had an ongoing active disease and failed to sustain satisfactory repigmentation. The creation of a blister also induced Koebner's phenomenon at this patient's donor area, which resulted in depigmentation.

Based on our experience with these three patients, we conclude that stable vitiliginous lesions are amenable to AET. On the other hand, patients with ongoing active depigmentation, such as the patient described in Case 3, are not suitable until their disease has become

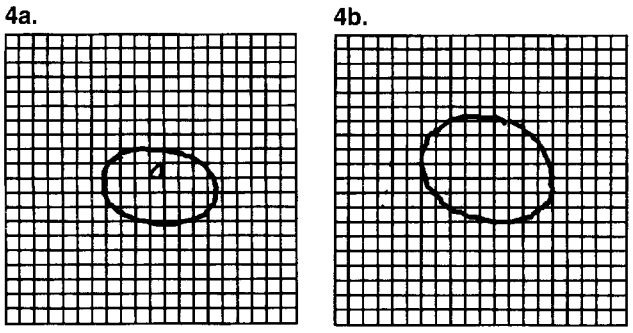

Fig 4. Case 1: records tracing the spread of pigmentation after treatment
(4a) the pigmented area measured 112 mm² in the first month and (4b) increased to 164 mm² in the sixth month (an increase of 46.4%). No further increase was noted in the ninth month. The achromia in (4a), represented by the small circle in the centre square, was not discernible in (4b). Each lattice square measures 2x2 mm

inactive. Furthermore, it should be ensured that Koebner's phenomenon does not occur, should AET be performed. This is concordant with the experience of Hatchome et al[13] who reported that 4 of 11 patients with generalised vitiligo displayed Koebner's phenomenon at their donor sites, and their grafted sites failed to repigment.

Retrospectively, our experience also supports that vitiligo can present different clinicopathological features. Two major types of vitiligo have been classified by Koga,[14] and Hann and Lee.[15] The first type (type A) is a generalised one and the second, less frequent type (type B) involves dermatomic or segmental lesions. A difference in the sweat output response to physostigmine in patients with each type of vitiligo has been noted.[14] More importantly, lesions of each type of disease differ in their clinical behaviour. Type B lesions differ from type A lesions by virtue of the rare occurrence of Koebner's phenomenon and the long quiescence of depigmenting activity after an initial short phase of vigorous activity and rapid repigmentation.[15] In contrast, patients of type A vitiligo usually have variable depigmenting activities, and the course is less predictable but tends to progress. Type B vitiligo occurs more often in younger patients whereas onset of type A can occur at any age.[14]

Reports comparing treatment response in patients of either disease type to topical steroid/PUVA are scarce and it is not yet clear if a real difference in response exists between them. Koga[14] reported that of five patients with segmental vitiligo, none responded to topical steroid, while an improvement of 60.0% to 94.4% was noted in 90 patients with non-segmental disease.[14] A recent data analysis of 73 patients with segmental vitiligo who were treated with PUVA at the Vitiligo and Pigmentation Center of Southern California showed that the repigmentation response was not significantly different from those with non-segmental disease,[16] a finding contrary to what has been generally believed. In the light of all this information, we believe that most type B and some type A patients with stable inactive lesions can be amenable to AET and that for patients with localised stable vitiligo of type B, AET should be considered with high priority.

For the three patients in this study, lesions were located on the chin and neck areas and blisters were obtained quite easily using negative pressure suction. Post-operative graft immobilisation was also not difficult. At present, suitable patients are being treated in our clinic and their results so far appear good. Practical problems from the AET procedure have occurred but are uncommon. These include the necessity for prolonged suction for blister formation (at least 2 hours), thus precluding the application of this procedure for young children; location of recipient sites in joints and uneven areas which hinder the secure application of suction cups; hairy and tight recipient skin which impedes blister formation; and premature detachment of dressing and grafts. With refinement of our skill and utilisation of modern technology, coupled with patient counselling on the treatment procedure and postoperative care, we are optimistic that these problems can be solved.

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