Repigmentation of Vitiligo with Autologous Blister-induced Epidermal Grafts

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Abstract

Treatment of vitiligo can sometimes be difficult and disappointing. PUVA treatments give fairly good results. However, acral regions like the hands or feet or areas over bony prominences like the elbow, are resistant to PUVA. Blister-induced epidermal grafts have been used to repigment vitiligo skin. This study was carried out on patients with vitiligo areas unresponsive to either PUVA treatments or who had segmental vitiligo. PUVA treatments were resumed after skin grafting.

Twenty-five patients with stable vitiligo were grafted with blister-induced epidermal grafts. Up to 70% of the whole vitiligo areas were grafted in one sitting.

A total of 105 grafts were done. In 9 grafts, no repigmentation was seen. The remaining 96 grafts resulted in pigmentation. Twelve had partial and 84 had complete repigmentation. No Koebner phenomenon was noted in both the recipient sites or the donor sites.

Blister-induced epidermal graft is an effective alternative to repigment stable vitiligo areas. It is easy to do and results are good. In this study, 96 out of 105 (91%) grafts had repigmentation.

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Key words: Epidermal grafts, PUVA, Suction blisters, Vitiligo

Introduction

Treatment of vitiligo can sometimes be difficult and disappointing. Medical treatment includes topical or systemic steroids and psoralen with ultraviolet A light (PUVA). However, some sites like the hands and feet or areas over bony prominences like the elbows are resistant to treatment. Surgical treatments to repigment stable vitiligo macules include micropigmentation or tattooing,[1] dermabrasion followed by topical 5-fluorouracil,[2] autologous skin grafts[3-10] and transplantation of cultured epidermis[11] or melanocytes.[12] Skin grafts using full-thickness graft," Thiersch's graft,[4-6] minigrafts,[7] punch graft[5] and blister-induced epidermal graft[9,10] had been reported.

In this study, the results of 25 patients (total 105 grafts) with stable vitiligo grafted with blister-induced epidermal grafts are presented.

Methods and Materials

Twenty-five patients of Asian origin (18 males and 7 females) with stable vitiligo (vitiligo macules which have been stationary in size for at least 3 years) were included in this study. Eight had segmental vitiligo, 4 had localised vitiligo and 13 had generalised vitiligo. The sites treated were the forehead (3), cheeks (5), chin (4), neck (3), trunk (3), upper limbs and arms (6), dorsum of hands (11), fingers (10) and legs (2). Twenty patients were receiving oral PUVA treatments up to the time of skin grafting. The vitiligo sites grafted were resistant to PUVA treatments (varying from 100 to 384 treatments).

The recipient sites within the area of vitiligo were frozen with liquid nitrogen for 5 to 10 seconds the day before surgery. Most of the vitiligo skin were thick from PUVA treatments and liquid nitrogen was used to facilitate the production of blisters. The epidermal graft donor sites were the deltoid region. Blisters were created on both the donor sites using variable sized disposable syringes attached by tubing to a suction apparatus (Eschmann VP35) exerting a negative pressure of 200 to 300 mmHg. The sizes of the blisters obtained varied from 0.7, 1.0, 1.5, 2.0, and 3.0 cm depending on the areas to be grafted. After 3 to 4 hours of suction, dermo-epidermal separation occurred and the blisters roof became available for grafting.

The roof of the blisters on the recipient sites were removed and discarded. The normal epidermis from the donor sites was harvested by cutting around the periphery of the blisters with an iris scissors. These were reflected onto metal spatula with the dermal site up and any serum or "debris" removed. The donor grafts were then placed on the denuded recipient sites and secured with tegaderm dressings for a week. The donor sites

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were dressed with tetracycline ointment and tegaderm dressings.

After one week the dressings were removed. Patients who were on PUVA prior to surgery resumed PUVA treatments. The grafted areas received PUVA treatments one month after surgery.

Results

Twenty-five patients (18 males and 7 females) with therapy-resistant vitiligo (vitiligo that failed to respond to PUVA treatments or topical steroids) were treated. The duration of disease varied from 1 to 26 years. The age of the patients ranged from 14 to 64 years (mean 36.8 years, median 37 years). Four had localised vitiligo, 8 had segmental vitiligo and 13 had generalised vitiligo. Table I shows the patient profile, the grafted sites and the outcome of treatment. Figures 1 and 2 show response to treatment.

A total of 105 grafts were done. Of these, 9 (8.6%) had no repigmentation as the grafts slipped off during the healing process. In 12 grafts (11.4%), some repigmentation (20% to 50%) was seen as part of the grafts were displaced (Table I). A total of 84 (80.0%) grafts had 100% repigmentation after 2 months post surgery. The pigmented areas spread beyond the originally grafted areas within 3 to 4 months and merged with each other and the surrounding skin with good colour match. No line of demarcation was seen and there was no scarring. The donor sites healed satisfactorily without scarring and achieved normal colour within 2 to 3 months (Fig. 3). There was no recurrence of vitiligo at the donor nor the recipient sites during follow-up (from 12 to 36 months). Spread of pigmentation beyond the grafted areas were the same whether PUVA was continued after the surgery.

Table II shows the outcome of treatment in the different types of vitiligo. Treatment failure in localised vitiligo was higher at 33.3% compared to segmental vitiligo at 8.0% and generalised vitiligo at 4.4%. The sites where grafts were placed also determined the treatment outcome (Table III). Five grafts (15.2%) on the face failed to repigment compared to 3 grafts (3.5%) on the limbs and 1 graft (6.7%) on the trunk.

Discussion

Repigmentation of vitiligo using skin grafts has been practised since 1984.[4] At that time, thin split thickness skin grafts were used. Since then, other types of skin

TABLE I: PATIENT PROFILE AND OUTCOME OF TREATMENT

No.	Patient	Age	Sex	Duration (years)	Type segmental	Localised	Generalised	PUVA	Sites grafted	Total grafts	Post grafts PUVA	0% repigmentation	Partial	100% repigmentation
	TYJ	14	M	2	neck/face			+	chin, neck	4	4			4
2	LH	14	M	9	neck/chin			+	chin, neck		3			3
3	CCK	22	M	2	chin				chin	2		1 (infected)	1 (20%)	
4	LLP	23	F	3	forehead			+	forehead	4	4	1	-	3
5	LSW	23	F	2		face		+	cheeks	4		2	2 (50%)	
6	YSR	23	M	2			+	+	dorsum hands	4			-	4
	KKY	24	M	2	chin				chin	4			-	4
8	LEL	29	M	2	forehead			+	forehead	4			-	4
9	HHS	30	M	2			+	+	fingers	4	4		-	4
10	SYHJ	32	M	10	left face			+	cheeks	2			-	2
11	CWP	33	M	5			+	+	hands, wrist	4	4		-	4
12	LBS	35	M	10			+	+	back, neck	4	4	2	2 (40%)	
13	LHW	39	M	1		chest			chest	4			-	4
14	MK	41	F	12			+	+	hand, fingers	4		1	3 (30%)	
15	LMK	42	M	10			+	+	foot, wrist	6	6		-	6
16	EML	43	M	3			+	+	chest, shoulder		7		-	7
17	CMK	45	F	10		face, leg			forehead	2	2		-	2
18	PTL	46	M	11			+	+	shoulder, shin	4	4		-	4
19	QCH	46	F	1			+	+	hands	4			4 (30%)	
20	TMH	47	M	6			+	+	hands	4	4		-	4
21	WSK	48	F	2		elbow			elbow	2	2	2	-	
22	THP	48	M	13			+	+	arm, hand	17	17		-	17
23	TSC	50	F	13			+	+	hand	2			-	2
24	PKK	59	M	10	cheek			+	cheek	2			-	2
25	BTG	64	M	26			+	+	fingers	4	4		-	4
										105	69	9	12	84
										100%	65.7%	8.6%	11.4%	80.0%

PUVA: psoralen with ultraviolet A light

TABLE II: TYPE OF VITILIGO AND OUTCOME OF TREATMENT

Type	Total grafts	Repigmentation		
		100%	Partial	0%
Segmental	25 (100%)	22 (88.0%)	1 (4.0%)	2 (8.0%)
Localised	12 (100%)	6 (50.0%)	2 (16.7%)	4 (33.3%)
Generalised	68 (100%)	56 (82.4%)	9 (13.2%)	3 (4.4%)
Total	105	84	12	9

TABLE III: SITE OF VITILIGO AND OUTCOME OF TREATMENT

Site	Total grafts	Repigmentation		
		100%	Partial	0%
Face/neck	33 (100%)	24 (72.7%)	4 (12.1%)	5 (15.2%)
Limbs	55 (100%)	45 (81.8%)	7 (12.7%)	3 (5.5%)
Trunk	17 (100%)	15 (88.2%)	1 (6.7%)	1 (6.7%)
Total	105	84	12	9

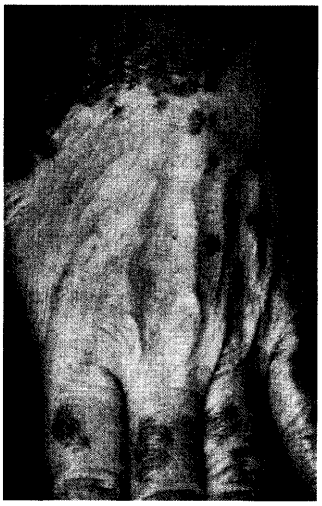

Fig. la.

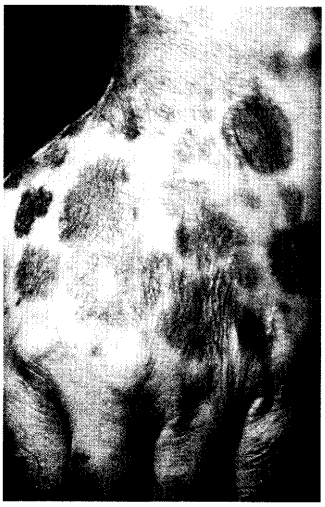

Fig. lb.

Fig. la. Vitiligo on dorsum of hands unresponsive to PUVA. Before skin grafting.

Fig. lb. Repigmentation seen 2 months after skin grafting. Picture taken before 2nd skin grafting, showing blisters induced by liquid nitrogen

grafts *viz* mini-grafts,[7] punch grafts,[8] full-thickness skin grafts,[3] and epidermal grafts[9,10] had been used. Each method had its advantages and setbacks.

Autologous blister-induced epidermal grafts provide pigmented skin for grafting. Liquid nitrogen and negative pressure suction (using sophisticated suction equipments[12,13] or manually operated suction pumps[10]) were used to create the blisters. In this study, disposable syringes were used as "cups" attached by 3-way taps and tubings to a vacuum pump graft of various sizes (0.7, 1.0, 1.5, 2.0, 3.0 cm) could be produced and up to 10 blisters at each sitting. Where possible the whole achromic areas were grafted in one sitting. The whole procedure was associated with minimal discomfort and was done on an outpatient basis. No anaesthesia was required. Donor skin was taken from the deltoid region. This site was chosen as it was convenient for the patient. The patient could lie supine during the suction process.

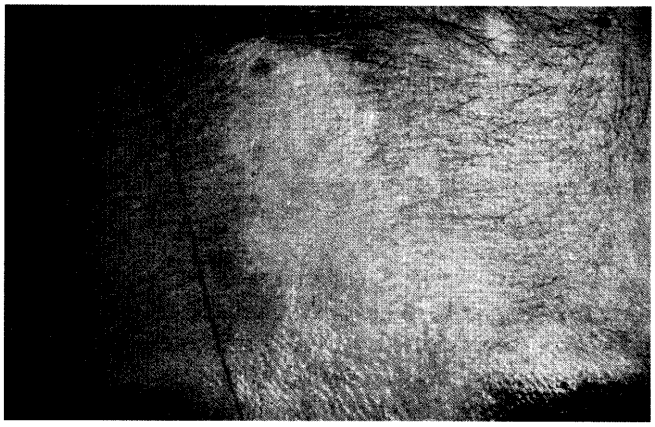

Fig. 2a. Segmental vitiligo before skin grafting.

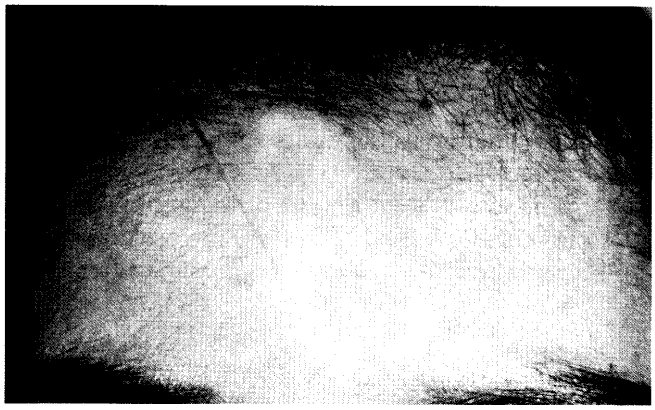

Fig. 2b. Repigmentation seen 2 months after skin grafting.

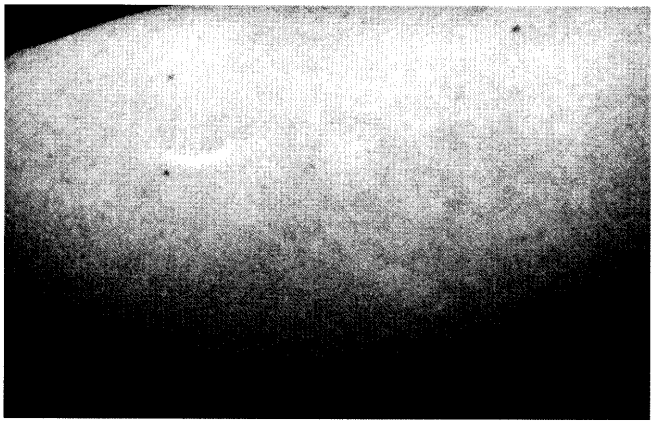

Fig. 3. Donor sites—complete recover?; 2 months after skin grafting

Methods using full-thickness grafting, punch grafting and minigrafting may result in scars or cobble-stone effect at the recipient sites. Keloids had been reported when thin split thickness skin grafts were used. With epidermal grafts, scarring or keloids had not been re-

ported at both recipient or donor sites.

The disadvantage of this method is the time taken to create blisters at the donor site. This usually takes up to 3 to 4 hours. The blistering process could be shortened by using heat during suction.[13,14] Liquid nitrogen cannot be used on the donor site as this is toxic to the melanocytes.

Blisters were easily created on the recipient sites (vitiligo sites) by applying liquid nitrogen a day before surgery. In most patients, blisters were seen on the day of surgery. Areas that do not produce blisters easily were vitiligo skin that has been treated with PUVA or areas on the forehead, chin and fingers. To overcome this, suctions were applied on the liquid nitrogen-treated sites as well. Another alternative is to remove the epidermis using the carbon dioxide or Erbium YAG laser.

Disposable syringes of various sizes were used to create the blisters on the donor sites. This enabled blisters of various sizes to be created and the size of the syringe used was determined by the size of the vitiligo macules. A 3 cc syringe will provide a blister of diameter 0.7 to 1.0 cm and this is suitable for grafting onto small areas of vitiligo like those on the fingers or eyelids. Another advantage of using disposable syringes is that these are discarded after each use and they are easily available.

Once the grafts are in place there is no guarantee that repigmentation will occur. As the grafts are not sutured down they may easily slip off, especially when there is exudation of serum over the next few days, or if the grafted areas are subject to repetitive movements. In 6 patients (total of 9 grafts), no repigmentation was seen as the grafts had slipped off during the healing stage. No grafts were seen at one week follow-up. In another 5 patients (total 12 grafts), some repigmentation was seen as part of the grafts had moved from the original position. To ensure that the grafts do not move position as a result of exudation, two puncture holes were created in the transparent dressing to allow the resulting serous fluid to drain off. This also reduced the risk of infection occurring in accumulated exudation. Patients should also be advised to minimise movements of the grafted areas to reduce the risk of dislodging the grafts from the recipient sites. Finger cots could be worn over the transparent dressing if grafts were placed on fingers.

In this study, repigmentation was seen in 96/105 (91.4%) grafts, with 84 grafts (80.0%) having 100% repigmentation and 12 (11.4%) grafts having partial (20% to 50%) repigmentation. This is comparable with results from other studies. Mutalik[10] reported total repigmentation after 4 months in 48/50 (96.0%) patients, while Skouge et al[14] reported repigmentation in 90% of grafts. Results from suction blister grafts also compares well with results using epidermal autografts bearing melanocytes. Falabella et al[11] reported repigmentation varying from 30% to 100% in 8 patients and no repigmentation in 1, while Gauthier et al[12] achieved 70% to 100% repigmentation in 3 patients (66.7%) and no repigmentation in 4 patients (33.3%).

The success of repigmentation was dependent on the contact between the grafted epidermal and the recipient vitiligo skin. The type of vitiligo or the sites of skin grafting also affect treatment outcome. Localised vitiligo repigment less often compared to generalised or segmental vitiligo. Grafts on the limbs or trunk repigment better compared to those on the face.

It has been reported that additional PUVA treatments to the grafted area may enhanced repigmentation and coalescence of pigment between grafts.[14,15] Fourteen patients had PUVA treatments on the grafted areas (total 69 grafts) while 11 patients (total 36 grafts) did not. The grafted areas continued to repigment evenly irrespective of whether PUVA treatments were given or not.

Conclusion

Epidermal skin graft is an effective treatment to repigment stable vitiligo areas. These grafts can be obtained from suction blisters and are useful for repigmenting segmental vitiligo or vitiligo on acral areas where PUVA therapy is usually not effective. Unlike other skin grafting method, epidermal grafts repigment with good cosmetic result and good colour match. In most cases, the repigmentation was complete and it was impossible to detect any vitiligo or even the site where grafting was done. The donor sites healed without scarring. The risk of inducing vitiligo[16] (Koebner phenomenon) was not seen in this study.

REFERENCES

1. Halder RM, Pham HN, Breadon JY, Johnson B A. Micropigmentation for the treatment of vitiligo. J Dermatol Surg Oncol 1989; 15:1092-8.
2. Tsuji T, Hamada T. Topically administered fluorouracil in vitiligo. Arch Dermatol 1983; 119:722-7.
3. Bonafe JL, Lassere J, Chavion J I', Baro J P, Jeune R. Pigmentation induced in vitiligo by normal skin grafts and PUVA stimulation: a preliminary study. Dermatologica 1983; 166:113-6.
4. Behl P N. Treatment of vitiligo with homologous thin Thiersch's skin grafts. Curr Med Pract 1984; 8:218-21.
5. Kahn A M, Cohen M J, Kaplan L, Highton A. A vitiligo: Treatment by dermabrasion and epithelial sheet grafting-a preliminary report. J Am Acad Dermatol 1993; 28:773-4.
6. Agrawal K, Agrawal A. Vitiligo: Repigmentation with dermabrasion and thin split-thickness skin graft. Dermatol Surg 1995; 21:295-300.
7. Falabella R. Treatment of localised vitiligo by autologous mini-grafting. Arch Dermatol 1988; 124:1649-55.

8. Orentreich N, Selmanowitz V J. Autograft repigmentation of leukoderma. Arch Dermatol 1972; 105:734-6.

9. Koga M. Epidermal grafting using the tops of suction blisters in the treatment of vitiligo. Arch Dermatol 1988; 124:1656-8.

10. Mutalik S. Transplantation of melanocytes by epidermal grafting. An Indian experience. J Dermatol Surg Oncol 1993; 19:231-4.

11. Falabella R, Escobar C, Borrero I. Treatment of refractory and stable vitiligo by transplantation of in vitro cultured epidermal autografts bearing melanocytes. J Am Acad Dermatol 1992; 26:230-6.

12. Gauthier Y, Surleve-Bazeille J E. Autologous grafting with noncultured melanocytes: A simplified method for treatment of depigmented lesion. J Am Acad Dermatol 1992; 26:191-4.

13. Peachey R D G. Some factors affection the speed of suction blister formation in normal subjects. Br J Dermatol 1971; 84:435-52.

14. Skouge J W, Morison W L, Diwan R V, Rotters S. Autografting and PUVA. A combination therapy for vitiligo. J Dermatol Surg Oncol 1992; 18:357-60.

15. Hatchome N, Kato T, Tagami J. Therapeutic success of epidermal grafting in generalised vitiligo is limited by the Koebner phenomenon. J Am Acad Dermatol 1990; 22:87-91.

16. Suga Y, Butt K I, Takimoto R, Fujioka N, Yamada H, Ogawa H. Successful treatment of vitiligo with PUVA-pigmented autologous epidermal grafting. Int J Dermatol 1996; 35:518-21.