Graft Exchange in Vitiligo

Studies on the Outcome of Exchanging Biopsies from Vitiliginous Skin to Normal, Pigmented Skin and Vice Versa

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In 27 patients with vitiligo punch biopsies from vitiliginous skin to normal skin and vice versa were performed. Of the vitiligo grafts 69% showed donor dominance and 31% receptor dominance. When normal skin was transplanted 74% showed receptor dominance and 26% donor dominance. In 13 patients (52%) blood screening pointed towards an autoimmune disease. *Key words: Punch biopsy; Autoimmune disease; Melanocytes.* (Received December 5, 1985.)

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Vitiligo occurs in about one per cent of Caucasians (1).

Several hypotheses have been set forward to elucidate the cause of damage following disappearance of melanocytes and invasion of Langerhans' cells. Among the most convenient theories concerning pathogenesis of vitiligo the hypothesis of self-destruction (2) has recently been supported by further observations (3).

Since Haxthausen (4) made his first studies in 1947 only few transplantation experiments have been published (Table I).

The latest investigation was made in 1982 by Schmidt (11) who found that the vitiliginous grafts stayed depigmented in all 11 patients. A further investigation of a larger material was found to be of interest.

MATERIAL AND METHODS

Exchange biopsies were performed in patients coming to our clinic for vitiliginous disorders. Before entering the study patients were asked for a family history as to the disease, duration of vitiligo and Koebner phenomenon. Patients with focal vitiligo, vitiligo caused by Koebner response, trichrome vitiligo, inflammatory vitiligo, early malignant melanoma, pregnancy and patients under systemically hormonal therapy, were excluded.

At the examination the special localization of vitiligo was noticed: localized, segmental or generalized vitiligo (acrofacial, vulgaris, universal). A 4 mm punch biopsy was taken after local freezing with chloretyl from both normally pigmented and from vitiliginous skin and these were exchanged. The biopsies were taken simultaneously. The biopsy was removed from its basis by a pair of scissors and transferred directly to its new site. One of the biopsies was kept by a pair of tweezers while the other was placed. However, the full procedure took less than two minutes. The biopsies were kept for six days in their position by means of OpSite® adhesive membrane. In relation to exchange of grafts a third biopsy from vitiliginous skin was taken to study the presence or absence of melanocytes. A special melanine colouring procedure was performed. Electronmicroscopy was not performed.

As vitiligo may be associated with autoimmune diseases, a screening for thyroidea antibodies (TA), microsomal thyroidea antibodies (MTA), and parietal cell antibodies (PA) was performed.

The following examination was performed: erythrocyte sedimentation rate (ESR), hemoglobin, s-electrolytes, s-thyroxine, alanine transaminase (ALAT), alkaline phosphatase, lactic dehydrogenase (LDH), s-cobolamine, s-iron, and urine for sugar.

The patients were examined in the clinic at least after 3 and 6 months and the pigmentation state was scored: No pigmentation, partial pigmentation or complete pigmentation. The examination was supplied with a photo.

RESULTS

Our material consisted of 12 males and 15 females. The males ranged in age from 18–66 years (mean 40 years), the females from 11–62 years (mean 39 years). One woman was excluded, because she did not appear for control.

The localization of the vitiligo was the same in both sexes. Six patients had noticed Koebner phenomenon. The duration of vitiligo was in the male group 1–30 years (mean 10

Table I. *Previous investigations*

DD = donor dominance, RD = receptor dominance

Author	Ref.	Number of patients	Grafts		Observation time (months)
			Vitiligo	Pigmented	
Haxthausen, 1947	(4)	3	2 RD/1 DD	3 RD	9–12
Comel, 1948	(5)	4	4 RD	4 RD	Several
Spencer, 1952	(6)	1	1 DD	1 DD	16
Orentreich, 1959	(7)	2	2 RD	2 RD	12
Behl, 1961	(9)	10	9 DD/1 RD	–	3–12
Behl, 1961	(9)	84	–	80 DD/4 RD	3–12
Behl, 1964	(8)	107	–	95 DD/12 RD	?
Copinathan, 1965	(10)	5	3 DD/2 RD	3 RD/1 DD	5–12
Schmidt, 1982	(11)	11	11 DD	8 RD/2 DD	1–5

Table II. *Results of the transplantation with vitiligo and normal skin in relation to antibodies*

AB = antibody, + = positive, – = negative and (H) = number of grafts with a depigmented ring

Clinical observation	Male		Female		Number
	+ AB	– AB	+ AB	– AB	
Vitiligo grafts					
No pigmentation	3	4	10 (1 H)	1 (1 H)	18
Partially pigmentation		2	1		3
Complete pigmentation	1	2 (1 H)	1	1 (1 H)	5
Failed		1			1
Total number					27
Normal skin grafts					
No pigmentation	3	3	11	0	17
Partially pigmentation	1	1 (1 H)			2
Complete pigmentation		3 (1 H)	1 (1 H)		4
Failed		2		2	4
Total number					27

years) and in the females 4–25 years (mean 12 years). Eleven patients (40%) had a family history as to vitiligo.

Provided that the graft kept its colour/lack of colour when removed to its new place the definition donor dominance (DD) was used. However, when the graft behaved as its surroundings meaning e.g. that the pigmented biopsy bleached or the vitiliginous biopsy became pigmented, it was characterized as recipient dominance (RD).

From Table II it will be seen that one of the vitiligo grafts and four pigmented grafts failed to grow.

In 18 of the 26 patients the vitiligo graft showed DD. Three became partially pigmented and five became completely pigmented. However, in four further cases the vitiligo biopsy did not only remain depigmented but showed a white halo around the biopsy.

Concerning the pigmented graft 17 patients showed RD. Two remained partially and four completely pigmented. In this series three grafts showed a white halo around the biopsy.

The distribution of the pigmentation of the grafts seemed to be equal for both sexes.

Examination of the blood showed that two patients had elevated thyroxine and one showed elevated ALAT and LDH.

Twenty-five patients were screened for autoimmune diseases. Thirteen patients (52%) had at least one positive test. Twelve were negative. The distribution of the positive antibodies in relation to sex and the two kinds of transplantation is shown in Table III.

The histological examination in 17 patients showed that 9 had no melanocytes whereas 8 showed a decreased number of melanocytes.

In 8 patients a gastrin test was made. All had normal values. The clinical observation of the patients gave no evidence of suspecting vitiligo to be a skin marker of internal malignancy.

DISCUSSION

In the present study contrary to previous investigations (2, 9, 10) we found that the vitiligo develops in an older age. In our investigation the women ranged in age from 11–62 years (mean 39 years) and the men from 18–66 years (mean 40 years). Both men and women had, when entering into the study, been suffering from vitiligo for about 10 years. The vitiligo

Table III. *Distribution of the antibodies in relation to the results of the grafts*

TA = thyroglobulin antibody, MTA = microsomal thyroidea antibody, PA = parietal cell antibody

Clinical observation	Male			Female		
	TA	MTA	PA	TA	MTA	PA
Vitiligo grafts						
No pigmentation	1		2		5	5
Partially pigmentation					1	
Complete pigmentation			1		1	
Number positive	1	0	3	0	7	5
Normal skin grafts						
No pigmentation	1		2		7	4
Partially pigmentation			1			
Complete pigmentation						1
Number positive	1	0	3	0	7	5

was uncontrolled in 76%. Exchange of the grafts showed DD in 69% of the cases and RD in 31%, when vitiliginous skin was grafted to normally pigmented skin. Our results are in accordance with those of Schmidt (11) in 1982, where he found 100% DD for vitiliginous grafts, but are in contrast to most of the previous studies which showed RD in all cases (Table I). The exchange of normally pigmented grafts to vitiliginous skin showed RD in 74% of the cases. In this case Behl (8) only found RD in 11% of 107 patients studied.

The discordance between these studies are difficult to explain and our explanation is purely speculative. In the evaluation of behaviour of grafts including pigmentary changes several factors, known to influence such behaviour, have to be taken into consideration, namely scar formation, local circulatory changes, migration of epithelial cells from underlying hair follicles and sebaceous glands.

Behl (9) made the observation that in vitiligo the results of transplantation depend on the progressive or not progressive condition of the affection. The patients in Behl's study showed no progression at all of their vitiligo for at least 12 months which is in contradiction to our study where 76% were active. This consideration has not been taken into account in previous studies.

Thirty-one per cent of our vitiligo grafts showed RD and 26% of the normal skin grafts showed DD at exchange transplantation. An explanation might be that the skin of these vitiligo patients had started being controlled. The supposition of trauma as the precipitation factor of depigmentation could be discarded. We observed that in 4 of our patients, in whom a pigmented biopsy was exchanged with another pigmented biopsy, both biopsies maintained their pigmentation.

At control after 6 months we found that 4 vitiligo grafts had developed a further depigmented halo, an observation which previously was made by Behl (9, 11) and Spencer (6). The reason for that could be the presence of antibodies against melanocytes in the vitiligo. However, we found only a few showing this phenomenon. Another explanation mentioned by Behl (8, 9) was that if the transplant is smaller than the recipient hole scar tissue develops which is interpreted as depigmentation. This is in accordance with our observation that the biopsy to some extent shrinks and the recipient hole dilates due to elasticity of the surrounding normal skin. Another explanation could be a Koebner phenomenon but the halo observation was seen only in one of the 7 patients. In one patient with a Koebner phenomenon a control transplantation was done with pigmented skin at the abdomen. No depigmentation occurred.

In order to investigate the importance of antibodies TA, MTA, and PA were examined. From Table III is seen that the presence of these antibodies were prevailing among women with DD of vitiligo grafts and RD for normal skin. Fifty-two per cent of the patients had at least one positive test which indicates the presence of an autoimmune disease. This amount is larger than that previously reported by Koransky (12), who found 8–15% in contrast to 1% in the normal population. Our observation supports the suggestion that antibodies may play a role in active vitiligo. In spite of this there was no specific distribution of antibodies in relation to the 17 histological examinations. In 9 biopsies there were no melanocytes, 3 had antibodies while 6 had none. In the last 8 biopsies with a reduced amount of melanocytes 4 had antibodies.

It was not possible to demonstrate a correlation between activity in the vitiligo, the amount of melanocytes, and the presence of antibodies.

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