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CHROMOSOME ABERRATIONS IN AFFECTED AND UNAFFECTED SKIN OF PATIENTS WITH PSORIASIS

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Abstract. The karyotypes were analysed in preparations from skin cultures of affected and unaffected skin from 12 patients with psoriasis. Regardless of treatment, an increased frequency of structural rearrangements was found in affected as well as in unaffected skin, on comparison with controls. The overall frequency of rearrangements was 10.5%, 2.0% and 0.4%, respectively. The majority (approx. 90%) of the structural abnormalities appeared as clones of cells with balanced translocations. It is concluded that the disease of psoriasis and the chromosome abnormalities found most likely have a common unknown etiology, although treatment effects in patients of this type are difficult to exclude with absolute certainty.

Up to the present, few investigations have been performed (3, 4) on chromosomes in tissue cultures from affected and unaffected skin in patients with psoriasis and the chromosome patterns found have been normal.

In this paper we present our own results which show that certain structural abnormalities of the chromosomes may be found.

MATERIAL AND METHOD

A total of 12 patients with psoriasis were investigated, 8 of whom had been treated locally for the disease before the investigation, and 4 who had fresh, untreated psoriasis. The treatment given, the age and sex of the patients and the duration of the disease are set out in Table I.

Two biopsies were taken from each patient: one from a fresh and—if possible—untreated psoriatic lesion, and one from unaffected skin. The skin was washed with a 70% solution of ethylalcohol; no analgesia was used. The biopsy from the psoriatic lesion was simply excised as superficially as possible, and that from unaffected skin was taken according to the method of Edwards (1).

At least three primary cultures were made from each of the specimens. The technique used for making the primary cultures and the subsequent subcultivation have been described elsewhere (7). If possible, chromosome preparations were made from all three primary cultures from each biopsy. As controls for the evaluation of the number of chromosomal aberrations, we used all metaphases analysed from skin cultures investigated in the laboratory during the same period. The skin biopsy specimens were taken from patients with various diseases indicating cytogenetic investigation, as well as from normals.

RESULTS

The chromosome counts of all metaphases analysed are listed in Table II. A total of 1 322 metaphases were analysed in the cultures from affected skin and 1 154 from unaffected skin. The frequency of aneuploid cells was 10.1% and 9.1%, respectively. The average frequencies of structural abnormalities appear in Table III, which shows that the frequencies of chromatid and

Table I. *Composition of the material. Twelve patients with psoriasis grouped according to treatment*

Treatment	Culture No.	Age	Sex	Duration of psoriasis
X-rays and corticosteroid ointment	H 284	25	♂	10 years
	H 285	51	♀	Several years
	H 312	72	♂	Several years
Corticosteroid ointment with oxychinoline	H 313	42	♂	6 weeks
	H 315	54	♀	24 years[a]
	H 327	10	♀	1 week
Corticosteroid ointment without oxychinoline	H 334	15	♀	4 months
	H 353	65	♂	8 months
Untreated	H 328	39	♂	1 week
	H 332	7	♂	2 weeks
	H 347	47	♀	4 months
	H 352	26	♂	5 weeks

[a] Previously treated with X-rays but never at the biopsy site.

Table II. *Chromosome counts in cultivated cells from affected and unaffected skin. Total for 12 patients with psoriasis*

	<44	44	45	46	47	48	Aneuploid cells %
Affected	20	20	89	1 188	5	–	10.1
Unaffected	13	20	66	1 049	4	2	9.1

isochromatid gaps and breaks, as well as deletions with fragments, are approximately the same in affected and unaffected. The frequency of structural rearrangements is significantly higher in affected than in unaffected skin, and the frequency of rearrangements is significantly higher in both affected and in unaffected skin than in controls.

The frequencies of structural rearrangements in cultures from affected and unaffected skin in each of the 12 patients appear from Table IV, which shows that most rearrangements are found in the cultures from affected skin, but that structural rearrangements are also found in the cultures from unaffected skin in some patients—in one case (H 328) with high frequency. It must be stressed that the disease in this case was progressing very rapidly at the time of biopsy, spreading from a few lesions on both hands to the entire body during one week.

The frequencies of structural rearrangements for the 4 untreated patients are shown in Table V. Subcultures of three different primary cultures from affected as well as unaffected skin were investigated in each patient. It appears that structural rearrangements were found in eight of the 12 cultures from affected skin, but only in one of 12 from unaffected skin, and again it must be stressed that the one culture with rearrangements

Table III. *Average frequencies (%) of cells with structural abnormalities in cultures of affected and unaffected skin from patients with psoriasis and in cultures of skin from "controls" (see text for explanation)*

	Chromatid gaps and breaks	Isochromatid gaps and breaks, deletions with fragments	Structural rearrangements
Affected	4.9	2.3	10.5
Unaffected	4.4	2.8	2.0
"Controls"	4.2	1.5	0.4

Table IV. *Frequency (%) of cells with structural rearrangements in cultures from affected and unaffected skin in patients with psoriasis*

Culture No.	Affected	Unaffected
H 284	5.6	2.9
H 285	8.5	0
H 312	11.1	0
H 313	18.4	3.1
H 315	12.7	1.8
H 327	1.8	0
H 328	13.6	16.9
H 332	27.0	0
H 334	1.6	2.2
H 347	20.7	0
H 352	11.1	0
H 353	4.3	0
Mean	10.5	2.0

was from the above-mentioned patient with rapidly spreading psoriasis (H 328).

The majority (approx. 90%) of the structural rearrangements were balanced translocations (two examples are shown in Figs. 1 and 2), but the type varied from patient to patient and also between primary cultures from the same patient. The types of translocations as well as other structural abnormalities (deletions and inversions) are set out in Table VI. It also appears that the same rearrangement was often found in several cells from the same culture (numbers in parentheses), showing that clones of cells with structural rearrangements (especially balanced translocations) were present in the cultures.

The numbers of chromosomes from the various groups involved in the structural rearrangement appear from Table VII. The number expected was calculated on the hypothesis that the events leading to the structural rearrangements involved the chromosomes at random, but with a prob-

Table V. *Frequency of cells with structural rearrangements in various primary cultures of affected and unaffected skin from 4 patients with untreated psoriasis*

Culture No.	Affected			Unaffected		
	A	B	C	A	B	C
H 328	1/30	0/21	10/30	15/30	0/29	0/30
H 332	2/7	16/41	0/26	0/15	0/45	0/10
H 347	23/78	4/45	10/56	0/90	0/45	0/59
H 352	0/58	18/58	0/46	0/52	0/59	0/42

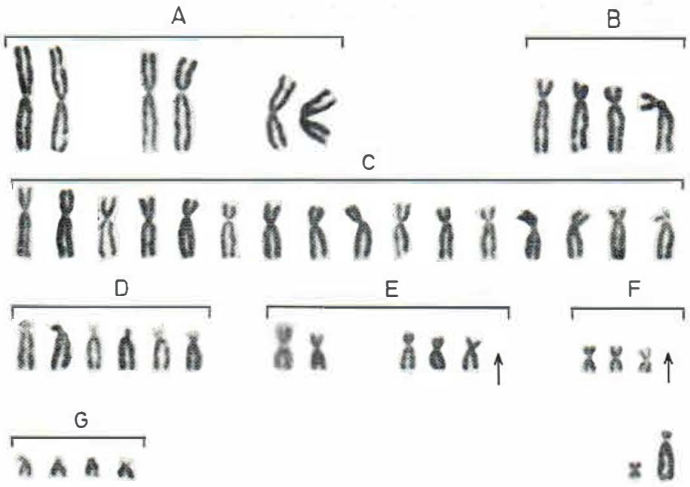

Fig. 1. Balanced translocation between an E_{17-18} and an F chromosome from affected skin of patient No. H 347. Arrows indicate missing chromosomes. Rearranged chromosomes in the lower right corner.

ability proportional to chromosomal length. Only one metaphase from each clone was counted. The probability of getting the results by chance was between 5 and 10%, and although the result is statistically insignificant, it is worth noting that the greatest deviations from the expected result were in groups C, D, F, and G, with too many D and G chromosomes involved and too few C and F chromosomes.

DISCUSSION

The average frequency of cells with gaps or breaks or deletions with fragments are the same in cultures from affected and unaffected skin, and lower than the average frequency which has been found in lymphocyte cultures from normal subjects (5), but of the same size as in skin cultures grown in our laboratory (Table III).

The average frequency of cells with structural rearrangements (especially translocations) is significantly higher in cultures from affected skin than in cultures from unaffected, and in both types of cultures the frequency of cells with rearrangements—especially halanced translocations—is higher than in cultures from controls. In lymphocyte cultures from normals only two cells with reciprocal translocations among 3 720 cells

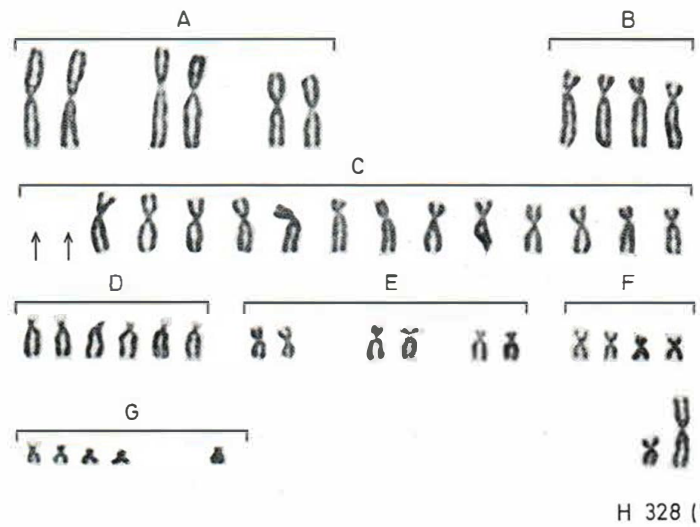

Fig. 2. Balanced translocation between two group C chromosomes from unaffected skin of patient No. H 328. Arrows indicate missing chromosomes. Rearranged chromosomes in the lower right corner.

Table VI. *The types of structural rearrangements indicated for each patient in each of the primary cultures*

If nothing else is stated, the type is a balanced translocation between the chromosomes mentioned
Figures in parentheses denote the number of cells with the rearrangement in question

Culture No.	Affected skin, primary culture			Unaffected skin, primary culture		
	A	B	C	A	B	C
H 284	3/C/D (5) inv 1 (1)	1/2 (2)	3/C (1)	B/D (1)	—	2/D (2)
H 285	C/D (1)	3/B (3)		—		
H 312	1/G (3) 1/D (1) D/E_{17-18} (1)	—	inv B (2)	—	—	
H 313	B/B (7)	3/D (1) 2/D (1)	—	B/C (1)	C/G (1)	—
H 315	inv 1 (5) 1/2 (1) 2/E_{17-18} (1)	3/16 (3) C/C (3)		—	2/G (1)	
H 327	—	C/C (2)	—	—	—	—
H 334	—	C/16 (1)	D/E_{17-18} (1)	B/C (1) D/C (?) (1)	—	—
H 353	—	D/16 (4) E_{17-18}/G (1) D/C (?) (2)	—	—	—	—
H 328	1/B (1)	—	D/E_{17-18} (10)	C/C (13) B/C (2)	—	—
H 332	C/G (2)	1/D/G (1) 2/C/D (1) 2/C/D/D (6) B/D (1) C/C (1) inv B (6)	—	—	—	—
H 347	1/C (2) 3/E_{17-18} (1) C/C/C (2) E_{17-18}/F (4) del Bp (14)	1/C (1) 3/C (3)	1/B/C/E_{17-18} (2) 1/B (1) 2/C (1) B/C (1) C/D (5)	—	—	—
H 352	—	2/D (1) C/D (12) D/F (1) G/C (?) (4)	—	—	—	—

Table VII. *The numbers of chromosomes from the various groups involved in independent rearrangements, compared with the expected numbers*

Chromosome No. or group	Number of chromosomes involved in independent rearrangements		
	Observed	Expected	χ^2
1	12	10.32	0.2735
2	10	9.60	0.0167
3	7	8.02	0.1297
B	15	14.41	0.0242
C	33	44.11	2.7983
D	22	12.00	8.3333
E	11	10.39	0.0358
F	2	5.51	2.2360
G	7	4.63	1.2132
Total	119	118.99	15.0606

$f = 8$; $0.05 < p < 0.10$.

studied were found (5). Among 1 129 cells studied in our laboratory in 75 skin cultures from normals and patients with various diseases, only four doubtful translocations were found (Table III). Clones of cells with a translocation were not observed and have never been observed in our laboratory during the period of approximately 11 years in which skin cultures have been used regularly for cytogenetic investigations.

The etiology of the translocations found in the cultures from our patients is open to discussion.

It is well known that X-rays as well as various chemicals may induce the formation of chromosomal aberrations including translocations. Oxychinoline, which in some of our patients was used locally added to corticosteroid ointment, has also been shown to have such an effect (2). Therefore, in some of our patients the translocations might

be caused by treatment. However, such an explanation cannot be valid for translocations found in the 4 patients who convinced us during our thorough interrogation that they were untreated.

We therefore find it more likely that the disease of psoriasis and the translocations found have a common etiology. So far, the etiology of psoriasis has remained largely unknown, but as stated by Shuster in 1971 (6) "the feeling at the moment is that psoriasis is a disease of faulty epidermopoiesis possibly due to impaired autocontrol mechanisms".

It is difficult to say whether the higher frequency of structural rearrangements in psoriatic skin is in any way causally related to the fact that the cell cycle, and especially the S-phase, is shorter in psoriatic cells than in normal cells (8). In this connection it is worth pointing out that the generation time of normal human fibroblasts in our tissue culture system is about 18 hours, i.e. about half that of a psoriatic cell in vivo.

The clarification of the etiology of the chromosome aberrations found in affected and in unaffected skin from patients with psoriasis must await further investigations.

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