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CHROMOSOME ABERRATIONS IN SEVERE PSORIASIS

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Abstract. An increased frequency of gaps, breaks, dicentric chromosomes and acentric fragments has been found in 10 patients with severe psoriasis, compared with 41 controls. None of the psoriatic patients were receiving systemic treatment when investigated. The results of the study may indicate that chromosomal abnormalities in psoriatics, besides being due to treatment, may reflect the severity of the disease. Further studies on chromosomal aberrations in psoriasis are needed.

Studies by Ryan and co-workers in 1965 (5) revealed an increased number of chromosomal gaps and breaks in a group of eight psoriatics treated with the folic acid antagonist methotrexate, when compared with eight non-methotrexate treated psoriatics. Other European investigators (2, 3) have also reported cytogenetic abnormalities in methotrexate-treated psoriatics. On the other hand Vorhees and co-workers (6) in 1969 found no significant differences in chromosomal abnormalities between nine methotrexate-treated psoriatics, nine non-methotrexate treated psoriatics and ten healthy adults. None of these investigators studied chromosomal abnormalities in the same patient before and after methotrexate. The conflicting data presented hitherto, prompted us to study chromosomes in leucocytes from severe psoriatics prior to methotrexate treatment in order to reexamine the same patients later during therapy. This paper reports on the unexpectedly high frequency of certain aberrations found in our premethotrexate study.

MATERIAL AND METHODS

Chromosomes were studied in leucocytes cultured for 48 hours. The chromosome analyses were made on film projections at a magnification of approximately 6 000 in combination with analysis in a Zeiss photomicroscope. All cells were analysed for gaps, breaks and other chromosomal abnormalities. Gaps are defined as achromatic lesions with no dislocation, while one of the two chromatid parts are dislocated in breaks.

Ten patients with severe psoriasis were investigated prior to methotrexate. 31 control patients from a psychiatric ward and 10 healthy volunteers (hospital staff) were also investigated.

RESULTS

In Table I it is seen that the total frequency of gaps, breaks, dicentric chromosomes as well as acentric chromosome fragments was significantly higher than in the controls. Examples of these chromosome aberrations are seen in Fig. 1.

As seen in Table I there were some other minor aberrations in the 10 psoriatic patients which were not found in the 41 controls.

There were 2 males with a relatively large Y (Y/F index above the normal range as previously described by Nielsen & Friedrich (4)) and 2 with enlarged satellites and/or short arms in a D chromosome; both are normal variations of chromosome morphology found in 1–2% of the population. The finding of 4 such cases among the 10 patients in the present study might be quite fortuitous.

DISCUSSION

When evaluating chromosomal aberrations found in a certain group of patients it is important to be aware of the many factors that may influence the frequency of such aberrations. These factors could be drugs, infections, X-rays and also the preparation technique. It may therefore be extremely difficult to compare different studies. It is worth noting that Ryan's eight patients (5), as mentioned by Vorhees (6) had received X-ray

Table I. *Chromosome aberrations in 10 patients with severe psoriasis and 41 controls*

Case no.	Sex	Age (y.)	No. of cells analysed	Gaps	Breaks	Dicentric chromosomes	Acentric fragments	Other aberrations	Type of psoriasis[a]
1	♂	10	62	15	3	—	—	1 endoreduplication	PP + E
2	♀	18	63	5	2	—	—		PV
3	♂	23	59	19	1	—	—	13 Ch	PP
4	♀	30	63	10	1	—	—	22 Ch	PV
5	♀	36	60	3	—	1	2		PV
6	♂	53	59	6	—	—	1	1 Eq	PV
7	♂	55	30	5	—	—	—		PP
8	♂	56	56	15	1	—	1	7 Ch	PV
9	♂	68	64	9	1	1	1		PP
10	♂	70	56	6	1	1	1	1 t (2p+; Bq−)	PP
Total			572	93	10	3	6		
Percentage				16.3	1.7	0.5	1.0		
41 controls			1 584	121	5	—	2	—	
Percentage				7.6	0.3	—	0.1	—	
Statistical evaluation of the difference between patients and controls				$\chi^2 = 34.925$, $P < 0.0005$	P (Fisher) = 0.0025	P (Fisher) = 0.0372	P (Fisher) = 0.0115		

[a] PV = Psoriasis vulgaris
PP = Pustular psoriasis
E = Erythroderma.

screening within the previous 6 months. Besides treatment and infection, the disease itself might also have an effect on chromosomes or the etiology of psoriasis and the chromosome aberrations might indicate the same. The differences between the various published materials on methotrexate-treated psoriatics could therefore very well be due to differences in severity of disease, and a high number of abnormalities a reflection of the severity of the psoriasis. The results of the present study show that severe psoriatics, and not only patients with erythroderma and pustular psoriasis, but also patients with severe psoriasis vulgaris, present an increased frequency of chromosomal aberrations such as gaps, breaks, dicentric chromosomes and acentric fragments. If these aberrations were present prior to treatment with folic acid antagonists, but the patients were

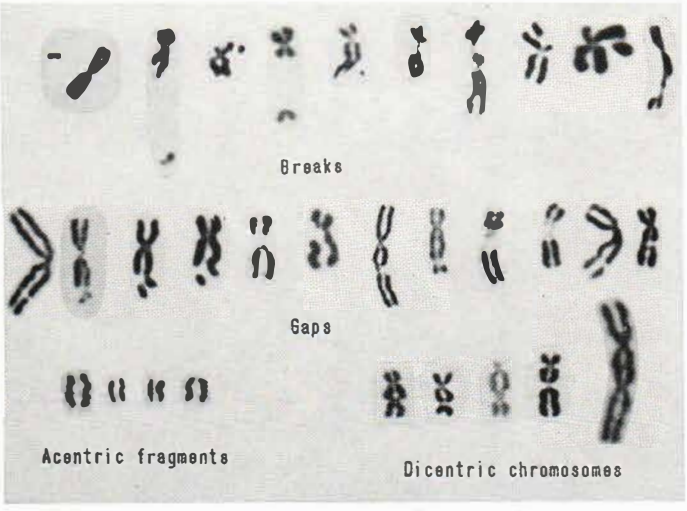

Fig. 1. Breaks, gaps, acentric fragments and dicentric chromosomes.

investigated only during treatment, the aberrations might easily have been attributed to the treatment.

Our results do not exclude the possibility that folic acid antagonists, such as methotrexate, may induce chromosome aberrations in psoriatics. In studies on a possible toxic effect of certain drugs on chromosomes, it is, however, important to use the patients as their own controls, and we will later present data on the possible effect of methotrexate on chromosomes in the patients studied in the present investigation. The importance of using patients as their own controls in such studies has previously been shown by Friedrich & Zeuthen (1), who found the same increase in the frequency of chromosome aberrations before as well as after treatment with azothioprin in patients with renal transplantations; they concluded that the increase in chromosome aberrations might be due to the uremia which was present in the patients before renal transplantation, but not to azothioprin treatment.

Further studies on the toxic effect of drugs on chromosomes in psoriasis as well as investigations on chromosomal aberrations associated with untreated psoriasis are needed.

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