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Down's Syndrome with Familial G/G Translocation

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1. Introduction

Since the discovery of translocation type of Down's syndrome, the importance of karyotype analysis has increased, for the recurrence risk of translocation mongolism greatly differs from that of 21-trisomy. To identify the presence of G/G translocation, especially with familial transmission, is of particular importance, since it is here that the familial prognosis is much worse than in other cases of mongolism.

It was the question of prognosis that led to the discovery of familial G/G translocation in the case reported below.

2. Case Record

Beate K., 1 7/12-year-old girl was admitted to our Department with the diagnosis of Down's syndrome. The parents wanted to know whether it was really Down's syndrome, and if so, what recurrence risk there would be at a later pregnancy.

The patient's appearance and clinical symptoms were characteristic of Down's syndrome. She had epicanthal folds, mongoloid eyes, strabismus, small ears, a depressed nasal bridge, a high arched palate, a protruding tongue, muscular hypotony, umbilical hernia, severe mental retardation. No signs of a heart defect or other congenital malformations and no rough radiological anomalies could be observed.

Haematological examination revealed a leukocyte number of 8400 per mm^3 with a slightly elevated granulocyte alkaline phosphatase activity (78 units) and with a granulation index of 1.78. The excretion rate of BAIB was elevated, other laboratory data were within normal limits.

The index patient was the first and only child of the parents.

The father, J. K., was 29 years of age at the patient's birth. He had had no serious disease, his family history was noncontributory. He was the only child of his parents, who had already died. His intellegence, although scientifically not tested, seemed to be normal.

The mother, M. K., was 28 years of age at delivery. Her family history was also negative, she seemed to be mentally normal.

Dermatoglyphic patterns of the patient and her father are illustrated in schematic drawings (Figs. 1 and 2).

The patterns of the index patient were characteristic of Down's syndrome, and the father had also some features suspicious for mongolism.

When using the score proposed by Beckman et al (1965), the child's patterns resulted

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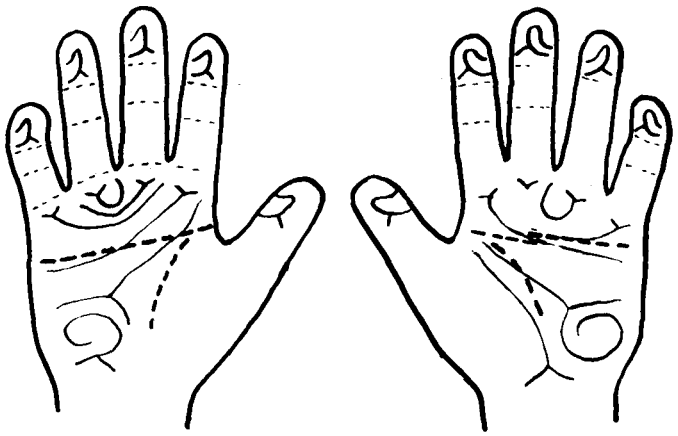

Fig. 1. Dermatoglyphic patterns of the patient.

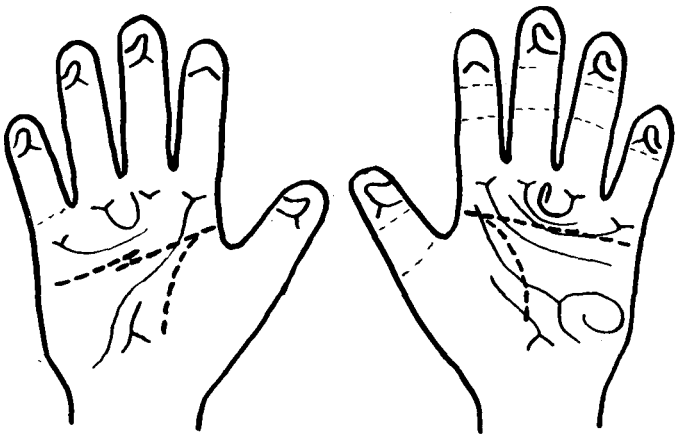

Fig. 2. Dermatoglyphic patterns of the father.

a value of 21, highly specific for mongolism ($P_{Down} < 0.99$), the father's patterns gave the number 12, representing a probability for Down's syndrome of about 95% ($P_{Down} = 0.95$). The mother's score-value was 2 ($P_{Down} < 0.001$).

Chromosome analysis of peripheral blood cultures were carried out in the child and both parents. The idiograms are presented in Tab. I.

Although she was a typical case of Down's syndrome, there were only 46 chromosomes in the mitoses of the patient, and only 45 in those of the apparently normal father. This made us conclude that we had discovered a case of translocation mongolism with paternal

Tab. I. Chromosome counts in the mitoses of the probanda and her parents

	Chromosome counts			
	44	45	46	47
Beate K.	3	1	10	—
	2	1	17	1
Father	2	28	1	1
Mother	—	1	16	—

transmission, the father being a carrier with balanced translocation. In the father's karyotypes two small acrocentric chromosomes were lacking and a mediocentric chromosome, probably originated by fusion of the two lacking acrocentric ones, was present (Fig. 3).

The analysis of the child's plates also revealed a probable G/G translocation.

The mother's karyotypes proved to be normal.

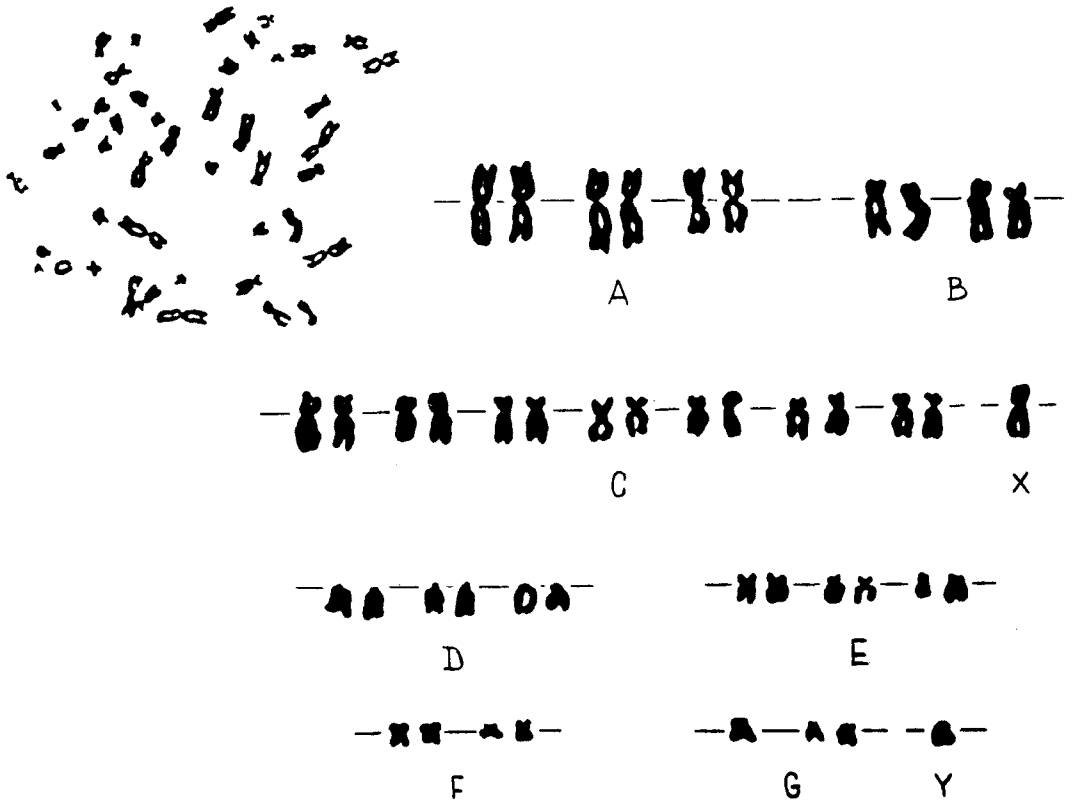

Fig. 3. The father's karyotype showing a balanced G/G translocation.

3. Discussion

The incidence of G/G translocation in mongols is about 2-4% (Mikkelsen, 1967; Ricci et al, 1967; Wright et al, 1967), and it is more common in younger mothers. The majority of G/G translocations seems to be sporadic, and a familial occurrence is seldom seen. Paternal transmission is, as in our case, particularly rare (Forssman and Lehmann, 1962). The distribution of translocations in Down's syndrome according to the father's ages has been studied by Penrose (1962), who found that the fathers were usually at a significantly higher age when their children with a G/G translocation were born. However, it is not known whether this is also true for carrier fathers with a balanced translocation.

Prognostically, all the children of a 21/21 translocation carrier would be mongols, but only 1/3 of those of a 21/22 carrier father would suffer from the disease (Gedda et al, 1967; Lejeune, 1963; Pfeiffer, 1963; Smith, 1964; Zellweger, 1962). Since it generally cannot be determined which two chromosomes are translocated, the term G/G translocation is used, and the risk figure is given as 1/3 - 1. In practice, however, the risk figure might be regarded as lower, especially in cases of paternal transmission (Jackson and Ashford, 1967; Reisman, 1967; Zellweger, 1966*a*, 1966*b*). The better chances of 21/22 translocation carrier fathers are probably due to the decreased viability and negative selection of aneuploid sperms. It is a further problem that the possibility of mosaicism in the carriers cannot be discarded, thus even 21/21 carriers may occasionally have normal children (Waxman and Arakaki, 1966).

It should be emphasized that there are no special symptoms characteristic of the translocation form of Down's syndrome. No essential differences in clinical symptoms, radiological and psychometric findings or in dermatoglyphic patterns can be found between translocation and trisomic mongols (Dallapiccola and Ricci, 1967; Ong, 1967; Rosner and Ong, 1967). Mosaic patients may show milder symptoms, but can also be indistinguishable from trisomic and translocation cases (Schuler and Gàcs, 1967; van Gelderen et al, 1967).

In a given case of Down's syndrome, chromosome studies are absolutely necessary for counselling, particularly so when young parents are concerned, or siblings and/or other relatives are affected. This principle receives support also from the cases reported here. Viz., it was only a karyotype analysis that led to a correct explanation, although the previously examined finger and palm patterns of the carrier father were also suspicious. It still remains questionable whether or not the latter can be regarded as diagnostic tools in such patients.

Summary

Cytogenetic examinations of a 7/12-year-old girl and her parents revealed a familial G/G translocation.

46 chromosomes in the mitoses of the mongoloid child and only 45 chromosomes in those of the apparently normal father could be observed. The analysis of

karyotypes revealed a balanced G/G translocation in the father and a G/G translocation mongolism in the probanda. Dermatoglyphic patterns of both the child and her father showed some features characteristic of Down's syndrome.

The mother's karyotype proved to be normal (46, XX).

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RIASSUNTO

Gli esami citogenetici di una bambina di 7 mesi e dei genitori hanno evidenziato una traslocazione familiare G/G. Sono stati riscontrati 46 cromosomi nelle mitosi della bambina mongoloide e solo 45 in quelle del padre apparentemente normale. L'analisi cromosomica ha mostrato una traslocazione bilanciata G/G nel padre e un mongoloidismo da traslocazione G/G nella probanda. Il reperto dermatoglifico della bambina e del padre ha evidenziato delle caratteristiche della sindrome di Down. Il cariotipo della madre è risultato normale (46, XX).

RÉSUMÉ

Les recherches cariologiques conduites chez une enfant, âgée de 7 mois, et chez ses parents ont montré une translocation familiale G/G. On a pu observer 46 chromosomes dans les mitoses de l'enfant mongoloïde et seulement 45 dans celles du père apparemment normal. L'analyse chromosomiale a démontré une translocation balancée G/G chez le père et un mongoloïdisme par translocation G/G chez l'enfant. L'analyse des dermatoglyphes a mis en évidence des caractéristiques du syndrome de Down. Le cariotype de la mère paraît normal (46, XX).

ZUSAMMENFASSUNG

Die zytogenetischen Untersuchungen bei einem 7 Monate alten Mädchen und deren Eltern ergaben eine familiäre G/G-Translokation. In den Mitosen des mongoloiden Kindes fanden sich 46 Chromosomen und bei dem anscheinend normalen Vater nur 45. Eine Analyse der Chromosomen zeigte beim Vater eine ausgeglichene G/G-Translokation und bei der Probandin einen Mongoloidismus nach G/G-Translokation. Der Hautleistenbefund an den Fingern ergab sowohl bei dem Kind als beim Vater die Merkmale des Down'schen Syndroms. Der Karyotyp der Mutter war normal (46, XX).

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