Jap. J. Human Genet. **22**, 73–78, 1977

TRISOMY / PARTIAL MONOSOMY MOSAICISM OF NO. 13 PAIR [46, XX, −13, +rob(13q13q) / 46, XX, r(13) (p11q34)]

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Summary A mentally retarded and malformed girl is described. Her karyotype was 46, XX, −13, +rob(13q 13q)/46, XX, r(13) (p11q34), *i.e.*, she was trisomic for a 13 in about 75% of the cells and partially monosomic for a distal part of 13q in about 25% of the cells. Clinical features were compared with those of cases with either trisomy or partial monosomy 13.

INTRODUCTION

A variety of chromosomal syndromes have been described, each of which was caused by either extra or deficient chromosome material (Hamerton, 1971; Makino, 1975; Lewandowski and Yunis, 1975). However, cases with both trisomic and monosomic cell lines, as to any one particular chromosome segment, have rarely been described.

In the present report, a congenitally malformed infant was described who had an extra 13 chromosome in about 75% of the cells and a ring 13 in the rest of the cells, *i.e.*, both trisomic and monosomic cell populations were detected as to the distal part of a 13q.

CASE REPORT

The proposita, a girl was born at term and weighed 2200 g. At birth, she scored 6 on the Apgar score. Congenital anomalies detected by 3 months of age included: microcephalia, hypertelorism, epicanthus, upward slant of palpebral fissures, depressed nasal bridge, low set and malformed ears, lack of uvula, simian crease (r), clinodactylia, unusually long fourth fingers and short third toes. No polydactylia, syndactylia, harelip, nor abnormality of eyes were observed (Fig. 1). She did not appear to be deaf.

At 3 months of age she weighed only 3.55 kg (average 5.6 kg). Because of very

Received June 9, 1977

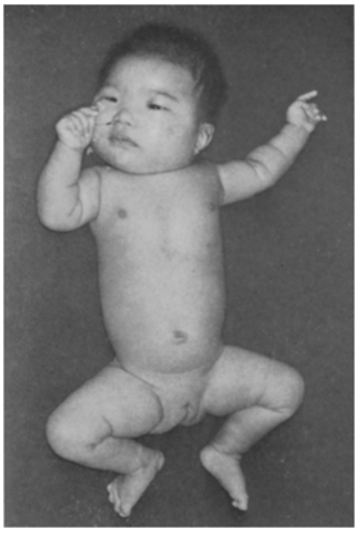

Fig. 1. The proposita at 3 months of age.

poor sucking, she needed tube feeding. Routine laboratory tests were unremarkable. Serum levels of immuno-globulins and thyroid hormones were within the normal limits. The diagnosis of patent ductus arteriosus was made by this time. The bone age was in the normal range.

She died of pneumonia at 4 months of age. The autopsy disclosed a supra-arachnoideal cyst, duplicated esophagi (one of them ended blind) and patent ductus arteriosus.

CYTOGENETIC FINDINGS

Chromosome preparations were obtained by the standard leukocyte-culture technique. Slides were aged for 7 to 10 days. They were then treated by the modified trypsin Giemsa technique (Nakagome *et al.*, 1973). Most metaphases showed 46 chromosomes, however, there were two different types of cells. In about 75% of the cells, one of the two no.13 chromosomes was replaced with a large mediancentric chromosome which represented a rob(13q13q) translocation (Fig. 2). In the rest of the cells a no.13 was replaced with a ring 13 in which points of breakage were located within bands p11 and q34 (Fig. 3). None of the rings were involved in satellite associations. The patient was monosomic for a band q34 (or a part of it) in about 25% of the cells and was trisomic for the entire length of 13q in about 75% of the cells. The karyotype was designated as 46, XX, -13, $+$rob(13q13q)/46, XX, r(13) (p11q34), based on Paris Conference system (Paris Conference, 1971). Both of her parents showed a normal karyotype.

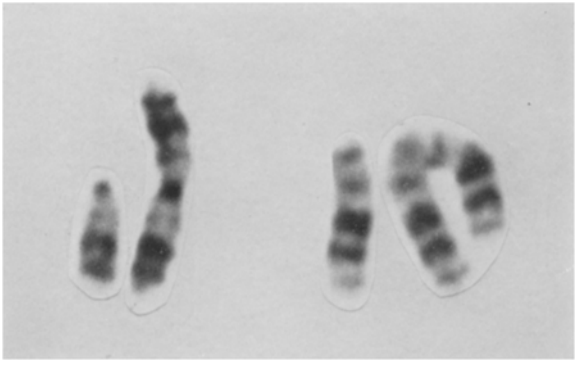

Fig. 2. Two cells with "13 trisomy." From left to right, a free 13 and a rob(13q13q) chromosomes from a metaphase and the same from another cell.

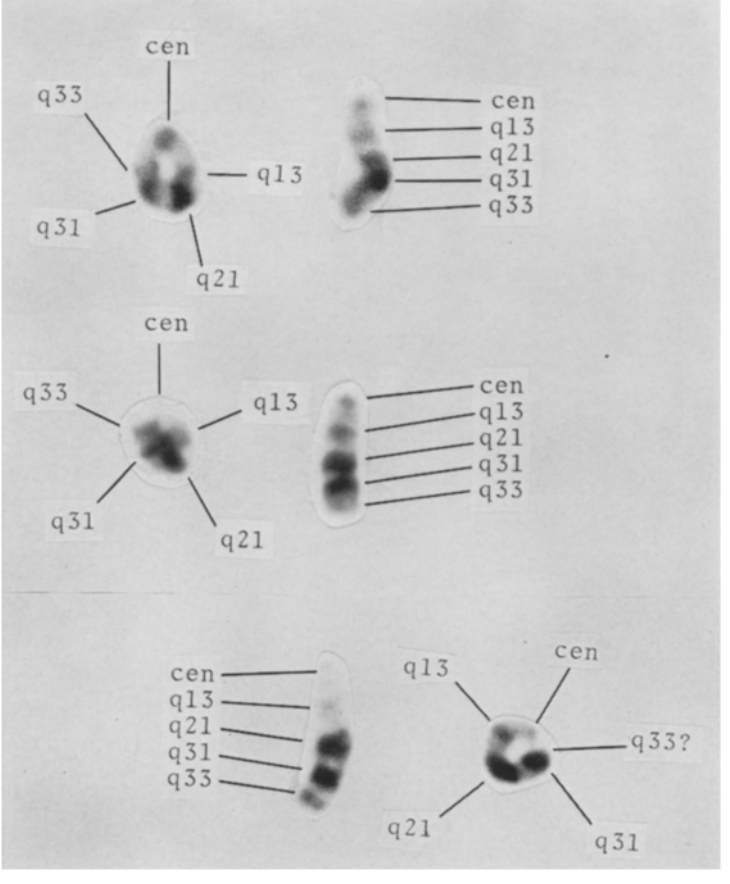

Fig. 3. A r(13) and a normal homologue from 3 cells. Points of breakage were located at bands 13p11 and 13q34.

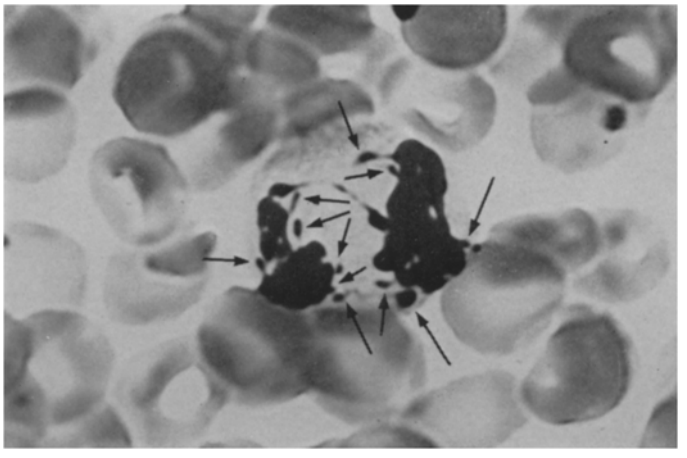

Fig. 4. A polymorphonuclear leukocyte with multiple nuclear projections.

Examination of blood films revealed that 85.9% of polymorphonuclear leukocytes had at least one nuclear projection(s) and some of them, in fact, had more than several projections (leukocytes with 2 projections, 25.3%; with 3, 16.5%; with 4, 12.2% and with 5 or more, 9.5%, the figure included drumsticks). Drumsticks were observed in 22.4% of them which in itself was very unusual (highest value observed in controls; 7.5%). An example of polymorphonuclear leukocyte with multiple projections is presented in the Fig. 4.

DISCUSSION

Clinical features of the 13 trisomy syndrome (+13) have been well established (Hamerton, 1971; Warkany *et al.*, 1966). They included microcephalia, hypertelorism, microphthalmia (anophthalmia), coloboma, cleft lip and palate, micrognathia, low set and malformed ears, congenital heart disease, polydactylia, arrhinencephalia, deafness as well as severe growth and mental retardation. When only a part of a 13q is trisomic, resulting abnormalities differ depending on the segment(s) of the 13q involved (Noel *et al.*, 1976). The lack of chromosome material, 13q- or r(13), also causes malformation syndromes. Again, depending on the segment of deletion, a different combination of abnormalities were observed (Niebuhr and Ottosen, 1973; Noel *et al.*, 1976). It was postulated that the lack of the most distal segment of a 13q (13q33 and 34) was associated with severe mental retardation, microcephalia, hypertelorism, salient frontal bosses, forward slanting of superior incisives and large and deformed ears (Niebuhr and Ottosen, 1973).

The proposita appeares to share several features with cases of 13 trisomy. Examples included depressed nasal bridge, malformed ears, congenital heart disease and multiple nuclear projections of polymorphonuclear leukocytes (Huehns *et al.*, 1968).

In addition, the absence of uvula could also be accepted as a very mild form of cleft palate. On the other hand, no specific features of distal 13q− was observed in the proposita. Exceptions included severe growth and developmental retardation, microcephalia and hypertelorism. However, they were frequently observed both in the +13 and in the 13q− (or distal 13q−) syndromes and probably were less specific in nature. In both of the cell lines in the proposita, both the short arm and the satellite were missing in the process of either r(13) or t(13q13q) formation. These regions of chromosomes were known to be free of phenotypic effects (Soudek, 1973). Some of the features observed in the present case appeared rare in both of the two syndromes (+13 and distal 13q−). They were duplicated esophagi and supra-arachnoideal cyst.

The reason why the symptoms related to the partial monosomy 13q (13q34) was absent in the proposita may be that the r(13) cell line consisted of only 25% of the total cell population (lymphocytes). In the majority of the cells, 13q34 band was triplicated, although we do not know whether phenotypic effects of monosomic cells can be cancelled by the presence of trisomic cells in a form of mosaicism. The reason why features unusual for both +13 and 13q− were observed in the present case was not clear. An anomaly like duplicated esophagi could be positioned at the extreme end of variable clinical features of either the trisomy 13 or the 13q− syndrome. Or else, it might have resulted from combined effects of both cell populations.

As far as the authors are aware of, there have been no reports of cases with either +13/r(13) or +13/13q− mosaicism. In a case of "aneusomie de recombinision" of a median or submedian centromeric chromosome, a chiasma within an inversion ring in meiosis I results a recombinant chromosome which is monosomic for a distal segment of one chromosome arm and trisomic for a distal segment of another arm (de Grouchy *et al.*, 1966; Dutrillaux *et al.*, 1973). There have been reports of aneusomie de recombinaison involving a no.13 chromosome (Surana and Conen, 1972; McDermott and Parrington, 1975). The recombinant chromosome in each case represents a "duplication/deficiency product" (Taysi *et al.*, 1973). However, as duplication or deficiency of a short arm region (p11, 12 and/or 13) of a D-group chromosome has no effects on the phenotype of an individual who carries it, they reduce to examples of partial trisomies of distal 13q. Orye and Craen (1974) described a case of 21 trisomy/ring 21 mosaicism [46, XY, −21, +t(21q21q)/46, XY, −21, +r[t(21q21q)]]. According to the authors the ring was derived from the t(21q21q) chromosome. Judging from the presented photographs, however, we are not quite sure whether their points hold.

The present case appears to provide an excellent opportunity to appreciate phenotypic effects of coexistent trisomic and monosomic cell populations.

Acknowledgements. The authors wish to express their thanks to Dr. Ei Matsunaga for encouragement, to Mrs. Masako Sakai and Michiko Yamamoto for competent technical assistance. Supported in part by a grant from the Ministry of Health and Welfare, Japan.

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