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A CASE OF RING CHROMOSOME 3, 46,XX,−3,+r(3)(p26q29)

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Summary We will discuss a girl with the karyotype 46,XX,−3,+r(3)(p26q29). She had growth and borderline mental retardation, craniofacial anomalies and microcephalus.

INTRODUCTION

Ring chromosome abnormalities have been reported in every pair of human chromosomes. However, ring chromosome 3 seems to be extremely rare. To our knowledge, only three cases have been reported in the literature. Here we have reported and discussed the case of a 10-month-old girl with ring chromosome 3 and its clinical and cytogenetic characteristics.

CASE REPORT

The proband was a 10-month-old female born to a mother of 34 years of age after a 39 week gestation period. She was the second child of healthy parents. The mother's first pregnancy resulted in the birth of a healthy girl and the second pregnancy aborted spontaneously. Her birth weight was 1,900 g and her length was 44 cm. Her psychomotor development was slightly delayed. She held her head at 3 months, smiled at 4 months, and sat at 9 months. She also had significant growth retardation.

On physical examinations at 10 months, her height was 67.5 cm (=3 percentile), her weight 5,680 g (<3 percentile), and her head circumference only 36.0 cm. The following congenital anomalies were noted: microcephaly, narrow face, broad nasal root, mouth with down-turned corners, widely set nipples, incurved fifth fingers, and proximally implanted thumb. Heart sounds were clear. Her development quotient was 90 by MCC Test and Tsumori Test. Routine laboratory findings were within normal limits. X-rays, EEG and ECG all gave results within the normal range. Analysis of excreted amino acid in urine was unremarkable.

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Her dermatoglyphics inspection revealed the presence of W, W, W, W, A on the left and W, W, W, W, UL on the right finger tips from thumb to fifth fingers and the presence of intermediate axial triradius on right hand.

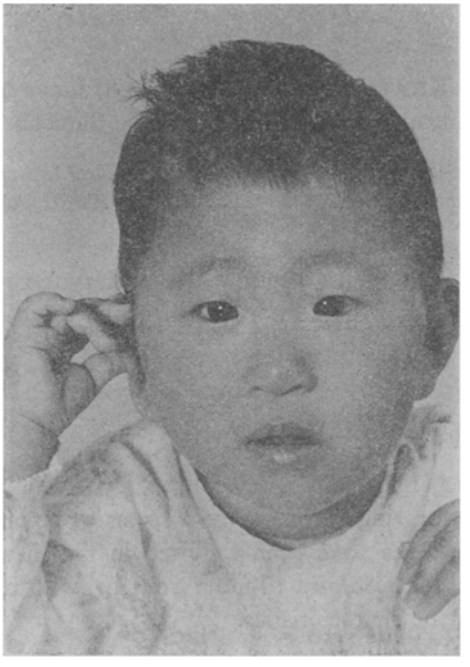

Fig. 1. The appearance of the patient at the age of 10 months.

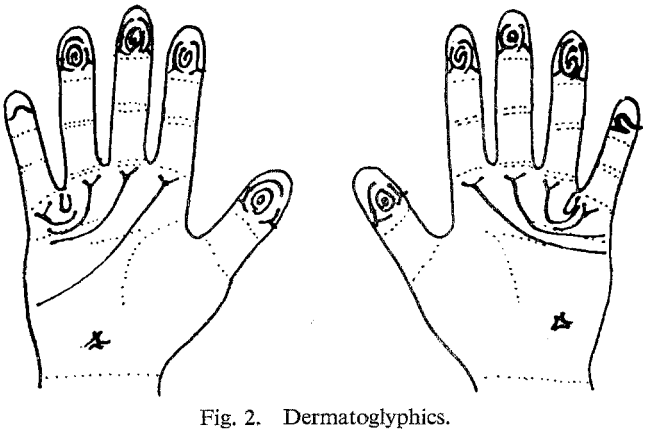

Fig. 2. Dermatoglyphics.

CYTOGENETIC STUDY

Chromosome analysis by trypsin Giemsa technique using peripheral blood lymphocytes revealed a karyotype 46,XX,−3,+r(3)(p26q29) in 77.4% of the cells.

Table 1. The results of cytogenetic analysis in 72-hr cultured lymphocytes.

Karyotype	No. of cells	%
46, XX	10	3.5
46, ring	223	77.4
46, dic ring	11	3.8
46, 3p+q−	3	1.0
45, −3	4	1.4
47, 2 rings	1	0.3
4n, dic ring	30	10.4
4n, 2 dic rings	2	0.7
Rod-shaped chromosome	2	0.7
4n, −3	1	0.3
8n, tetra centric ring	1	0.3
Total	288	100

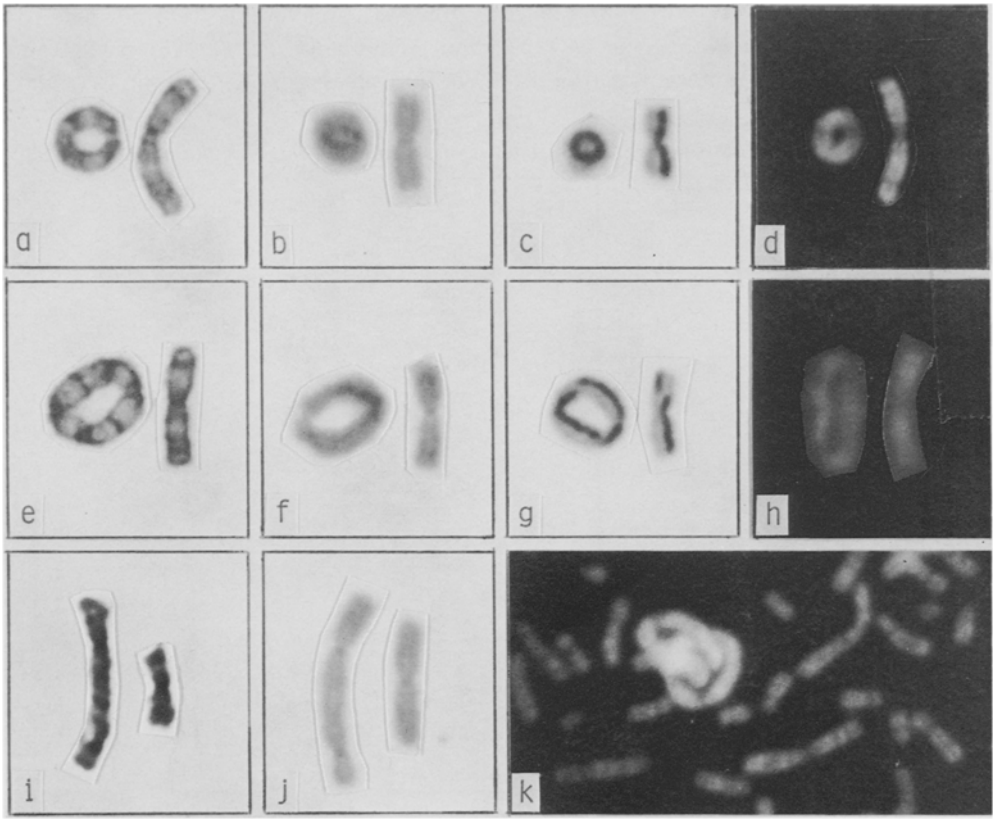

Fig. 3. The appearance of the ring chromosome 3: monocentric ring 3 and normal 3; (a) (b) (c) (d) (G-, C-, SCE and R-banded), dicentric ring 3 and normal 3; (e) (f) (g) (h) (G-, C-, SCE and R-banded), rod-shaped 3 and normal 3; (i) (j) (G- and C-banded), interlocked ring 3; (k) (R-banded).

Table 1 shows the constitution of 288 cells examined after conventional 72-hr lymphocyte culture; 87.5% of the cells were diploid or near diploid and 12.5% of the cells were polyploid. There were ten normal cells with apparently normal karyotypes. However, five cells lacked number 3 chromosomes while the remaining cells had mono- or dicentric rings, multicentric rod-shaped chromosomes, or interlocked rings.

The karyotypes of the parents were normal.

DISCUSSION

Three cases of ring chromosome 3 have been reported in the related literature (Picciano *et al.*, 1972, Witkowski *et al.*, 1978, Wilson *et al.*, 1982). In our case, chromosome analysis and breakpoints of ring chromosome using the banding technique revealed 46,XX,−3,+r(3)(p26q29) karyotype, which is exactly the same as the case reported by Wilson *et al.* (1982). However, breakpoints were not defined in cases reported by Picciano *et al.* (1972) and Witkowski *et al.* (1978). The rate of cells with single monocentric ring in 46 chromosomes is 77.4% in our case and

Table 2. Clinical and cytogenetic findings of patients with ring chromosome 3.

	Present case	Wilson *et al.* (1982)	Witkowski *et al.* (1978)	Picciano *et al.* (1972)	Total
Sex	F	M	M	M	
Prenatal growth retardation	+	+	−	+	3/4
Postnatal growth retardation	+	+	+	+	4/4
Mental retardation	+	+++	++	+	4/4
Microcephaly	+	+	+	+	4/4
Ptosis	−	+	−	−	1/4
Epicanthal folds	−	+	+	?	2/3
Strabismus	−	−	+	?	1/3
Broad nasal root	+	+	+	?	3/3
Dysplastic ears	−	+	?	+	2/3
Micrognathia	−	+	+	+	3/4
Down-turned corners of the mouth	+	+	+	+	4/4
Genitourinary abnormalities	−	+	−	+	2/4
Deep sacral dimple	−	+	?	?	1/2
Anal anomaly	−	−	−	+	1/4
Renal anomaly	?	?	−	+	1/2
Hypertonicity	−	+	?	?	1/2
Break point	p26q29	p26q29	?	?	
Rate of cells with 46,r3	77.4%	92%	100%	75%	

100%, 92%, 75% in others, respectively (Witkowski *et al.*, 1978, Wilson *et al.*, 1982, Picciano *et al.*, 1972).

Clinical features in all four cases with ring chromosome 3 are compared (Table 2). Common findings are growth retardation, mild to severe mental retardation, microcephalus and down-turned corners of the mouth. Broad nasal roots are noted in three of the four cases. Although ptosis of the eye lids and severe mental retardation were frequently found in cases of chromosome 3 deletion at p25 (Merrild *et al.*, 1981), only ptosis was found in the case of Wilson *et al.* (1982) with ring chromosome 3. Despite clinical resemblance in all cases of ring chromosome 3, the physical abnormalities found in these patients are not very specific, because they are also noted in other chromosomal disorders including rings of other chromosomes.

Dicentric, rod-shaped and interlocked ring abnormalities found in our case have been frequently reported in other ring chromosomes (Ledbetter *et al.*, 1980, Zuffardi *et al.*, 1980, Wyandt *et al.*, 1982). Our case is the first to be described to have aneuploidy of ring chromosome 3. It is well known that the normal occurrence of sister chromatid exchanges in a ring produces further chromosome anomalies and aneuploidy in a large number of cells (McClintock, 1938, Lejeune, 1968, Jansen *et al.*, 1982). These abnormal results were only found in the case of Cote *et al.* (1981) after two or more cell cycles in lymphocyte cultures. Their elimination *in vivo* results in cell death and an enormous waste of metabolism. This suggests that not only loss of specific information due to deletion of the distal end of the chromosome, but the presence of ring structure itself might have caused growth and mental retardation because of cell loss in ring chromosome 3.

REFERENCES

Cote, G.B., Katsantoni, A., and Deligeorgis, D. 1981. The cytogenetic and clinical implications of a ring chromosome 2. *Ann. Genet.* **24**: 231–235.

Jansen, M., Beemer, F.A., van der Heiden, C., Van Hemel, J.O., and Van den Brande, J.L. 1982. Ring chromosome 2: Clinical, chromosomal, and biochemical aspects. *Hum. Genet.* **60**: 91–95.

Ledbetter, D.H., Riccardi, V.M., Au, W.W., Wilson, D.P., and Holmquist, G.P. 1980. Ring chromosome 15: phenotype, Ag-NOR analysis, secondary aneuploidy, and associated chromosome instability. *Cytogenet. Cell Genet.* **27**: 111–122.

Lejeune, J. 1968. De la duplication de structures circulaires. *Ann. Genet.* **11**: 71–77.

McClintock, B. 1938. The production of homozygous deficient tissues with mutant characteristics by means of the aberrant mitotic behavior of ring-shaped chromosomes. *Genetics* **23**: 315–376.

Merrild, U., Berggreen, S., Hansen, L., Mikkelsen, M., and Henningsen, K. 1981. Partial deletion of the short arm of chromosome 3. *Eur. J. Pediatr.* **136**: 211–216.

Picciano, D.J., Berlin, C.M., Davenport, S.L.H., and Jacobson, C.B. 1972. Human ring chromosomes: a report of five cases. *Ann. Genet.* **15**: 241–247.

Wilson, G.N., Pooley, J., and Parker, J. 1982. The phenotype of ring chromosome 3. *J. Med. Genet.* **19**: 471–473.

Witkowski, R., Ullrich, E., and Piede, U. 1978. Ring chromosome 3 in a retarded boy. *Hum. Genet.* **42**: 345–348.

Wyandt, H.E., Kasprzak, R., Lamb, A., Willson, K., Wilson, W.G., and Kelly, T.E. 1982. Human chromosome 2 rod/ring mosaicism: probable origin by prezygotic breakage and intrachromosomal exchange. *Cytogenet. Cell Genet.* **33**: 222–231.

Zuffardi, O., Danesino, C., Poloni, L., Pavesi, F., Bianchi, C., and Gargantini L. 1980. Ring chromosome 12 and latent centromeres. *Cytogenet. Cell Genet.* **28**: 151–157.