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Trisomy 18 Syndrome in Chinese Infants

Clinical Findings and Incidence*

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The trisomy 18 syndrome was first described in 1960 (Edwards *et al.*, 1960). Since then, numerous cases have been reported in Caucasoid children from the United States, Canada, and Europe (Hecht *et al.*, 1963; Townes, DeHart, and Ziegler, 1964; Zellweger, Huff, and Abbo, 1965; Taylor, 1967, 1968), but only a few cases have been reported in other racial groups. 8 African children with this syndrome were recently reported from the Democratic Republic of the Congo (Cornu *et al.*, 1968). The anomaly in an American Negro child has been reported (Rohde, Hodgman, and Cleland, 1964), and an affected Chinese child from Canada has been reported (Uchida, Bowman, and Wang, 1962).

While the physical features have been well described, there are only four studies with sufficient data to assess the incidence rate of this anomaly (Smith, 1964; Conen and Erkman, 1966; A. I. Taylor and E. C. Moores, unpublished observations, and A. I. Taylor and J. A. F. Roberts, unpublished observations, cited in Taylor, 1967), and these have been in Caucasoid populations. This communication describes four affected Chinese infants born at Taipei hospitals participating in a large epidemiological survey of congenital malformations (Emanuel *et al.*, in preparation), and derives an incidence rate for this population.

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Materials and Methods

During the three-year period, 11 January 1965 to 10 January 1968, six major obstetrical hospitals in Taipei participated in the Taipei Collaborative Study of Congenital Malformation (Emanuel *et al.*, 1970). During this period there were 25,814 liveborn and stillborn pregnancies, including both single and plural births. Hospital physicians examined all newborn babies (liveborn and stillborn) and all infants with definite or suspected malformations were reported to the study physicians who then examined these babies. Chromosome preparations (Arakaki and Sparkes, 1963) were done on babies suspected of having a chromosomal anomaly.

Dermatoglyphic inspection was performed with a magnifying glass and illumination.

Clinical Data

Table I summarizes birth characteristics for the four cases. There was no family history of congenital malformations or consanguinity. For Case 4, the father's father's mother was a twin. Table II summarizes the history of radiation and significant medical problems of the parents.

TABLE I

BIRTH CHARACTERISTICS OF THE CASES OF TRISOMY 18

	Case 1	Case 2	Case 3	Case 4
Birth date	6/65	9/65	9/65	4/66
Sex	F	F	M	M
Gestation (wk.)	41	40	42	32
Birthweight (g.)	2480	1960	2040	900
Birth length (cm.)	48	—	42	33
Placenta weight (g.)	—	350	440	250
Head circ. (cm.)	35·0	32·0	34·4	27·0
Maternal age (yr.)	26	25	38	23
Paternal age (yr.)	42	28	52	29
Previous pregnancies (total)	2	1	2	1
Previous foetal deaths	0	0	1	0
Age at diagnosis	1 mth.	1 dy.	1 dy.	1 dy.
Age at death	73 dy.	4 dy.	3 dy.	1 hr.
Polyhydramnios	—	—	+	+

The four cases are presented in Fig. 1, and Table III summarizes the physical findings of the four cases. In addition, early hydrocephalus was probably present in Case 1, but it was not possible to follow the patient long enough to fully document it. Case 2 had a right-sided cleft of the lip, hard and soft palates. Case 3, in addition to restricted hip abduction, also had a slight extension contracture of the left hip. The right thigh and leg were shorter

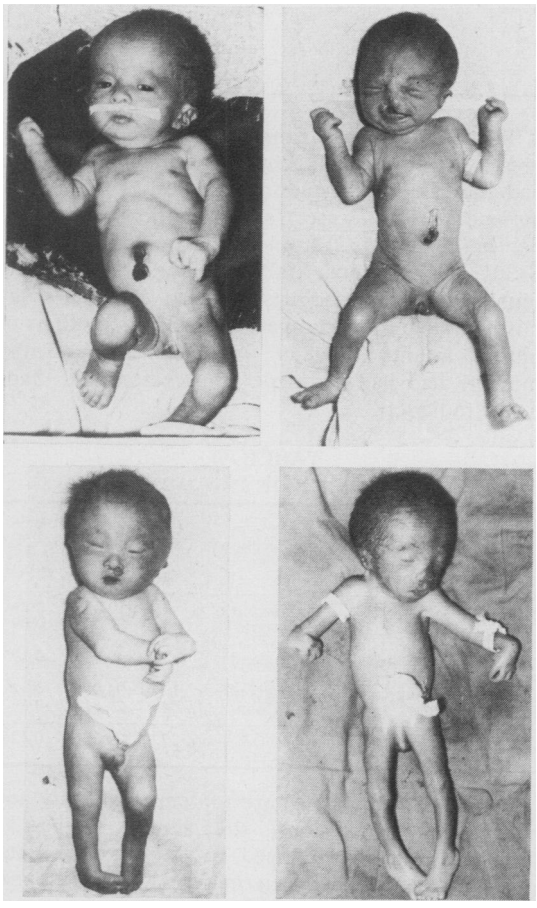

FIG. 1. Trisomy E syndrome in Chinese infants. Upper left, Case 1; upper right, Case 2; lower left, Case 3; lower right, Case 4.

than the left and there was a pronounced right talipes equinovarus. There was also a flexion contracture of the wrist. Case 4 had anal atresia and reduction deformities of the upper extremities. The right upper arm was small, the elbow was malformed, and there was a rudimentary forearm and absent thumb. The left upper extremity had a rudimentary thumb and a flexion contracture of the wrist.

TABLE II

PREGESTATIONAL RADIATION AND MEDICAL PROBLEMS OF PARENTS

Case No.	Maternal Radiation	Paternal Radiation	Medical Problems of Parents
1	Myelography, age 8 yr.; plain film of abdomen 4 yr. ago	None	Mother—Pott's disease
2	*X*-ray pelvimetry, 1½ yr. ago	Plain chest film, 0, 1, and 2 yr.	Both deliveries by caesarean section
3	Upper G.I. series, 2 yr. ago; plain chest film, 1 yr. ago	None	2 deliveries by caesarean section
4	None	Plain chest film, 1½ yr. ago	None

Dermatoglyphs

Case 1 had a total of 7 arches on the fingertips, while Case 2 had 8 and Case 3 had none. Adequate visualization of the fingerprints was not possible for Case 4. A simian line was present unilaterally in Case 2 and Case 3, bilaterally in Case 4, and was absent in Case 1. All finger flexion creases were absent in Case 4, and all finger creases were absent from 4 fingers in Case 3. Single flexion creases were present in Case 2 (8 fingers) and Case 3 (6 fingers).

TABLE III

PHYSICAL FEATURES OF TRISOMY 18 SYNDROME IN CHINESE BABIES

	1	2	3	4
Hypotonia at birth	−	−	+	+
Tremors	−	−	+	−
Prominent occiput	−	+	+	+
Narrow palpebral fissures	+	−	−	−
Small eyes	+	−	+	−
Epicanthic folds	−	−	−	−
Upward slanting eyes	−	+	−	−
Facial palsy	+	−	−	−
Low-set and deformed ears	+	+	+	−
Small mouth	+	−	+	+
High palate arch	+	−	+	+
Micrognathia	−	−	+	+
Short and webbed neck	−	−	−	+
Widely spaced nipples	+	+	+	−
Short sternum	+	+	+	+
Inguinal hernia	−	−	+	−
Short perineum	+	+	−	+
Hypoplastic male genitalia	−	−	+	+
Hypospadias	−	−	−	+
Cryptorchidism	−	−	+	+
Enlarged clitoris	−	+	−	−
Hypoplastic labia majora	+	+	−	−
Finger flexion	+	+	+	−
Ulnar deviation of hands	+	+	−	+
Hypoplastic thumb	−	−	+	+
Hypoplastic nails	+	+	+	+
Webbed fingers	−	−	+	−
Clinodactyly fifth fingers	−	−	+	−
Hypoplastic fifth fingers	−	+	−	−
Limited hip abduction	+	+	+	+
Rockerbottom feet and heel protrusion	+	+	+	+
Short great toe	+	+	−	+
Dorsiflexed great toe	−	−	−	+
Syndactyly toes II–III	−	−	−	+
Redundant skin	+	+	−	−
General hirsutism	+	−	−	+

Cytogenetics

Cytogenetic results appear in Table IV. Three cases had modal counts of 47 chromosomes each with an extra number in Group E (Case 1 and 2: 47,XX,E+; Case 4: 47,XY,E+). Case 3 had a normal/trisomy E mosaic pattern (46,XY/47,XY, E+) in the ratio of 62/39 cells. Partial karyotypes showing the 'E' group of the cases are presented in Fig. 2.

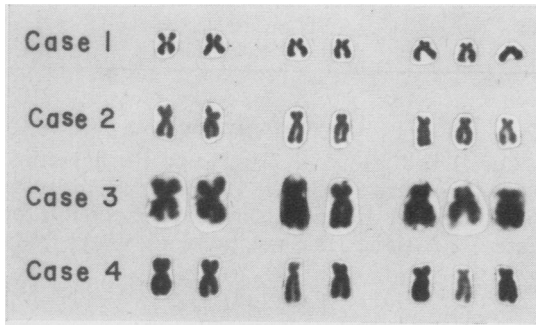

FIG. 2. Partial karyotypes showing 'E' group of patients.

Discussion

These four cases further show both the comparability of the physical findings of this syndrome in different racial groups and the variability of the clinical features (Taylor, 1967, 1968; Cornu *et al.*, 1968; Rohde *et al.*, 1964; Uchida *et al.*, 1962). This small series includes several of the specific major malformations associated with this syndrome, such as anal atresia, cleft lip and palate (Townes *et al.*, 1964), hydrocephalus (El-Alfi, Biesele, and Smith, 1964), and reduction deformities of the extremities (Zellweger *et al.*, 1965). That three of the four cases were clinically diagnosed on the first day of life suggests that there should be no particular problem in detecting this syndrome in Chinese infants.

Dermatoglyphic findings are similar to those previously reported (Hecht *et al.*, 1963) including an excess of arches on the fingers, simian creases, and absent flexion creases of the fingers. It is of interest that Case 3, a mosaic with about 60% normal cells, had no arches on the fingers.

Townes *et al.* (1964), in reviewing the published reports of trisomy 18 syndrome, presented evidence suggesting that there might be an excess of pregestational irradiation in the parents of affected children. In a partially prospective study by Uchida, Holunga, and Lawler (1968), there was an elevenfold increase of autosomal anomalies in children of irradiated women compared to a control group. The irradiated group had 8 cases of Down's syndrome, 2 cases of trisomy 18 syndrome, and 1 case with a ring chromosome and translocation.

TABLE IV
CYTOGENETIC RESULTS, TRISOMY 18

Case No.	No. of Chromosomes per Cell				No. of Cells Counted	No. of Cells Karyotyped	Karyotype
	44	45	46	47			
1		1	3	99	103	12	47,XX,E+
2			2	61	63	8	47,XX,E+
3	1	2	62	39	104	33	46,XY/47,XY,E+
4			3	47	50	14	47,XY,E+

There is additional suggestive evidence from the present small series. Fathers of affected children had the same pregestational medical radiation experience (2 of 4 cases) as did fathers of normal babies (53% of 732) from the Taipei Collaborative Study of Congenital Malformations. Two of the four mothers of trisomies had had complex diagnostic radiography, compared to 1·2% in mothers of normal infants (N = 856). Only 28% of normal mothers had had any type of pregestational diagnostic radiation.

TABLE V
INCIDENCE OF TRISOMY 18

Author	Location	Cases	No. of Births	Rate per 1,000 Births
Smith (1964)	Wisconsin	3	10,345	0·29
Conen and Erkman (1966)	Ontario	8	89,309	0·09
A. I. Taylor and E. C. Moores (unpublished)	England	1	9,688	0·10
A. I. Taylor and J. A. F. Roberts (unpublished)	England	11	94,000	0·12
Present study	Taiwan	4	25,814	0·15
Total		27	229,156	0·12

While all these series are too small to draw any satisfactory conclusions, the similar suggestive findings indicate the need to study further the possible relation between maternal pregestational radiation and trisomy 18.

Table V summarizes the incidence data for this syndrome in Canada, England, Taiwan, and the United States. These are the only large series for which incidence data are available. There are no statistically significant differences among these studies (χ^2 test for the Poisson distribution = 1·34, $0{\cdot}3 < p > 0{\cdot}2$).

All 4 infants show significant intrauterine growth failure compared to normal Chinese newborns (Lin and Emanuel, in preparation) and the known reduced viability of this syndrome.

Summary

Four cases of the trisomy 18 syndrome in Chinese infants are presented. This small series further shows both the variability of the physical findings in this syndrome and their comparability in different ethnic groups. The positive history of pregestational complex radiography in two mothers, compared to its rarity in a large control series, is consistent with the hypothesis that radiation may be an important aetiological factor. The incidence rate for Taiwan is 0·15/1,000 births, which is not significantly different from series from Canada, England, and the United States.

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