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Chromosomal abnormality associated with congenital macroglossia and other abnormalities

Congenital macroglossia is a rare clinical abnormality, and when found in an infant with a chromosomal abnormality, it could be a useful chromosomal marker. It is for this reason that we would like to present the following clinical and chromosomal findings.

Case report

The patient is a 5-week-old white female who was born to a gravida II, para I mother after an uncomplicated, full-term pregnancy with no history of infection or any medications during pregnancy. Amniocentesis was performed twice during the pregnancy because of a possible Rh blood incompatibility factor. At birth the child had microcephaly, macroglossia, and a heart murmur; she weighed 3500 g at birth. Since birth, she has had breathing and feeding difficulties because of her enlarged tongue.

The 21-year-old father and the 20-year-old mother are in good health. One sib, aged 1 year, is normal. There is no history of congenital anomalies in the family of either parent.

On physical examination, the infant had difficulty breathing but no cyanosis. The infant's tongue was partially protruding (Fig. 1). Her height was 56 cm (75th centile), weight 4190 g (10th centile), head circumference 36 cm (10th centile), heart rate was 140/min,

and respiratory rate was 36/min. There was marked microcephaly with 2-3 mm opening of the anterior and posterior fontanelle. The tongue was diffusely enlarged filling the entire mouth cavity and remaining partially protruding at all times. There was no evidence of a hemangioma or cyst of the tongue. There was a cleft uvula. She had a precordial thrill and a grade 4/6 holosystolic murmur at left lower sternal border. The

FIG. 1. The proposita; note macroglossia and microcephaly.

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second sound was normally split. The liver was 1 cm below right costal margin; genitalia were normal female; femoral pulses were present. There was no hypotonicity. Both feet appeared elongated. She had long slender fingers on both hands (Fig. 2). There was no

FIG. 2. The proposita's hand showing elongation of fingers.

evidence of exomphalos or an umbilical hernia. There was no organomegaly or unusual creases in the ear lobulus. There were no episodes of hypoglycemia or convulsions.

Chest radiology showed a normal size heart. Cardiac angiogram revealed a large atrial septal defect and pulmonary valvular stenosis. Skull radiology confirmed microcephaly and there were no intracranial calcifications. Her bone age was slightly advanced. The dermatoglyphic patterns on the fingertips showed 10 whorls.

Chromosome studies using a Giemsa stain and light microscopy showed that the infant had 46 chromosomes, but there was a missing G chromosome and small extra metacentric chromosomes about the size of an F-group chromosome (Fig. 3). Fluorescent chromosome studies (Fig. 4) showed that a No. 22 chromosome was missing, and a small extra metacentric chromosome was present. The long arms of the chromosome showed a minimum of fluorescence and the short arms showed moderate fluorescence. The parents' chromosomes were normal.

Discussion

Our interpretation of the chromosome abnormality in this infant is based upon our fluorescent

FIG. 3. Karyotype from the proposita showing missing No. 22 chromosome and a small extra metacentric chromosome (arrow).

FIG. 4

FIG. 4. Karyotype of fluorescent chromosomes.

FIG. 5. Fluorescent chromosomes showing a comparison of the F, G groups with the small metacentric chromosome (arrow).

FIG. 5

studies. We assume that the long non-fluorescing arms of the extra chromosome contain the missing No. 22 chromosome (Fig. 5). A minimum fluorescence is characteristic of this chromosome (Caspersson *et al*, 1971). The small fluorescing arm of the chromosome is probably extra chromosomal material. This would make the infant partially trisomic for this segment. Unfortunately, this fluorescing chromosomal segment could not be identified with a particular chromosome. The parents' chromosomes were normal and, therefore, were of no assistance in identifying the trisomic chromosomal segment. We feel that the chromosomal abnormality occurred as an isolated de-novo event in an ovum or a sperm.

Congenital macroglossia is a rare clinical finding. Occasionally it is seen in diffuse lymphangioma or muscular hypertrophy (rhabdomyoma) of the tongue. Localized enlargements of the tongue are found with hemangiomas and cysts of the tongue. In the clinical conditions of cretinism, acromegaly, and gargoylism, an enlarged tongue may occasionally be found. None of these conditions was present in this infant. So far, we have not been given permission to biopsy this infant's tongue but no obvious pathological lesions are present. The mouth cavity is normal size and the only other pathology present is a cleft uvula. The infant compensates for the enlarged tongue by keeping it partially protruded at all times.

In 1963, Beckwith reported the necropsy findings on three unrelated infants who had an association of unusual physical findings. The common findings in these infants were omphalocele, muscular macroglossia, bilateral cytomegaly of the fetal cortex, hyperplasia of the gonadal interstitial cells, renal medullary, dysplasia, and hyperplastic phenomena in several organs. All three of the infants died in the neonatal period. Gigantism, microcephaly, and hypoglycaemia were later noted to be additional clinical and laboratory findings (Beckwith *et al*, 1964).

About this time, three similarly affected patients who were sibs of consanguineous parents were described (Wiedemann, 1964; Wiedemann *et al*, 1968). Since this clinical condition is an apparently newly recognized syndrome, it has been referred to by the eponym, the 'Beckwith syndrome' or the 'Wiedemann-Beckwith syndrome'.

As with any newly recognized syndrome where only a small number of patients has been reported, the variation in the full extent of the pathology is poorly documented. This seems to be true in this condition. In addition, in this syndrome, the genetics and inheritance appear to be uncertain.

Both of these factors will remain true until an adequate number of patients is reported.

Macroglossia, microcephaly, and a large infant with poor motor development are all suggestive of the Wiedemann-Beckwith syndrome; however, this infant lacks some of the associated anomalies found in the syndrome. The infant had no evidence of exomphalos (Irving, 1967), omphalocele, or organomegaly. The blood sugar was normal and there were no episodes of hypoglycaemia (Combs, Grunt, and Brandt, 1966).

The aetiology of the Wiedemann-Beckwith syndrome is unknown but in some families a recessive type of inheritance is suspected, while in others the inheritance is considered to be dominant (Beckwith, 1969). So far there is one report of a patient with features suggestive of the syndrome and having a chromosome abnormality (Ruffié *et al*, 1966). This patient had a reciprocal translocation of part of the long arms of a group D chromosome on to a No. 9 chromosome. Extra chromosomal material was present on the short arms of a G-group chromosome. The father appeared to be a carrier for the balanced form of the translocation.

The combination of clinical findings in our patient are of such a nature that they could be a variant form of the Wiedemann-Beckwith syndrome, or the condition could be a closely related syndrome associated with the extra chromosome material on the short arms of the No. 22 chromosome. Another alternative is that there is no association between the extra chromosome material and the unusual clinical findings. An adequate explanation for the clinical findings in this patient will depend upon the reporting of future cases. The main clinical features observed in this patient were macroglossia, microcephaly, congenital heart disease, and elongated fingers and toes. We were unable to identify any biochemical genetic markers associated with the trisomic segment.

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Correction

Effects of mitochondrial inhibition by chloramphenicol on the mitotic cycle of human cell cultures. Ursula Mittwoch, D. J. Kirk, and D. Wilkie, 11, 260-266.

In Table II on p. 262, columns 2 and 3 were transposed. The correct Table is given in full below:

TABLE II
STAGES IN MITOTIC CYCLE IN INTERPHASE CELLS TREATED WITH DIFFERENT CONCENTRATIONS OF CHLORAMPHENICOL

Concentration of Drug (μ g/ml)	Duration of Culture* (hr)	Time in Contact with Drug (hr)	No. of Cells† in				G2/Total
			G1	S	G2	Polyploidy	
0	36	—	72	12	16	0	0.16
0	38	—					
10	36	15	105	14	29	2	0.19
10	38	17					
10	40	19					
100	36	15	113	8	29	0	0.19
100	38	17					
100	40	19					
500	36	15	72	12	65	1	0.43
500	38	17					
500	40	19					
1000	36	15	89	41	19	1	0.13
1000	38	17					
1000	40	19					

* Time between plating and harvesting cells.
† Fifty cells were measured from each culture; G1 corresponds to 2C, G2 to 4C, S to intermediate values.