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Chromosome Aberrations in Full-Term Low Birth Weight Neonates

Andrew T. L. Chen* and Arthur Falek

Division of Human Genetics, Georgia Mental Health Institute and Department of Psychiatry, Emory University, Atlanta, Georgia 30332, USA

William Lester

Georgia Baptist Hospital, Atlanta, Georgia 30312, USA

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Summary. Chromosome analyses were done on umbilical-cord blood leucocyte cultures of 225 full-term low birth weight neonates as well as 225 normal birth weight newborn controls who were matched with the study group for sex, race and maternal age. Five chromosome anomalies were found in the study group, i.e. two male infants had 47,trisomy 21 syndrome, two female infants had 47,E_{18} trisomy syndrome and one female had an extra small chromosome which was morphologically similar to a G group chromosome with a short arm deletion. On the other hand, one boy in the controls had 47,trisomy 21 syndrome. The results suggest that chromosome aberrations play a role in the etiology of low birth weight in full-term infants.

Zusammenfassung. Bei 225 Neugeborenen, die trotz einer Geburt zum normalen Zeitpunkt ein Untergewicht aufwiesen, wurden Chromosomenanalysen durchgeführt und mit den Befunden bei der gleichen Zahl von Kontrollen mit normalem Geburtsgewicht verglichen; diese waren mit der ersten Gruppe nach Geschlechtsverteilung, Rasse und mütterlichem Alter vergleichbar. In der geprüften Gruppe wurden 5 Chromosomenanomalien gefunden: Zwei männliche Kinder hatten eine Trisomie 21, zwei Mädchen zeigten eine Trisomie 18, und ein weiteres Mädchen hatte ein kleines Extrachromosom, das wie ein G-Chromosom mit einer Deletion des kurzen Armes aussah. Unter den Kontrollen fand sich ein Junge mit Trisomie 21. Die Ergebnisse legen den Gedanken nahe, daß Chromosomenaberrationen bei der Verursachung niedrigen Geburtsgewichtes bei voll ausgetragenen Kindern eine Rolle spielen.

Among many factors that can be implicated in the etiology of low birth weight in man, an association between full-term low birth weight and chromosome aberrations has been reported in a retrospective study of a group of mentally retarded patients (Chen *et al.*, 1970). Since it has been found that there is a high death rate among low birth weight neonates (Ahvenainen and Terho, 1968; Brimblecombe and Asford, 1968) as well as patients with certain chromosome anomalies (Smith, 1964), it is possible that infants with low birth weight and chromosome disorders may have died during early infancy or *in utero*. In order to assess the role of chromosome aberrations in the etiology of low birth weight more accurately, we analyzed the chromosomes of all low birth weight neonates delivered at a private hospital which served predominantly individuals in the middle and upper socio-economic levels. The present paper deals with the chromo-

* Present address: Department of Genetics, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia 23298, USA.

some results of full-term low birth weight infants; those of a "premature" group will be the subject of another report.

Materials and Methods

Between September 1, 1969 and August 31, 1971, umbilical-cord blood was cellected from all newborn babies delivered at the Georgia Baptist Hospital in Atlanta, Georgia and refrigerated in capped centrifuge tubes containing 1 ml sodium heparin (1000 IU/ml). The blood from those newborns who weighed 5.5 lb. or less with a gestation period of 38 weeks and more (LBWN) was selected for chromosome analysis. From the same newborn population pool, a control group of normal birth weight neonates (NBWN) was chosen by matching them with the study group for sex, race and maternal age.

Blood leucocyte cultures were processed with the use of chromosome medium 1A (GIBCO). After preparation, the slides were immediately examined for quick screening for gross chromosome abnormalities. Generally, 5 to 10 cells were counted for each infant and 2 of them were examined for morphological changes. Subsequently, 4 to 5 cells from each subject were photographed and 2 of them were karyotyped. When a chromosome anomaly was detected, more cells were analyzed. During the course of the study, we found that the umbilical-cord blood stored in the refrigerator up to a 14-day period was still useful for cytogenetic study. This facilitated repeating of a small number of cultures which failed to grow.

Results

During the 2-year period of this study, a total of 8542 babies were delivered, of whom 7921 were white and 621 black. Babies with other ethnic origins were excluded from the study because of their small number. The breakdown of the sexes in the population pool was as follows: White: 4072 male, 3849 female; Black: 297 male, 324 female. Among the 8542 neonates, 227 were born with a low birth weight at term. No blood was available from 2 LBWN. Chromosome analyses were therefore performed on 225 LBWN, of whom 193 were white (71 male, 122 female) and 32 black (11 male and 21 female). The chromosomes of the same number of NBWN were examined.

Among the 225 LBWN, 5 were found to have chromosome anomalies (Table 1). Examination of the chromosomes of the parents of the patient with an extra deleted short arm G-like chromosome (Fig. 1) revealed that while the father had

Table 1. Chromosome aberrations in 225 full-term low birth weight neonates and controls

Patient	Phenotypic sex	Race	Birth weight	Gestation period (weeks)	Maternal age	Karyotype
Full-term low birth weight						
M. W.	F	W	4 lb. 3 oz.	38	42	$47,XXE_{18+}$
J. Y.	F	W	3 lb. 1 oz.	40	23	$47,XXE_{18+}$
C. H.	M	W	5 lb. 2 oz.	38	37	47,XY21+
C. C.	M	W	5 lb. 4 oz.	40	46	47,XY21+
C. M.	F	W	4 lb. 6 oz.	38	24	47,XX, ?G+(p—)
Control						
E. C.	M	W	6 lb. 2 oz.	40	34	47,XY21+

F = female, M = male, W = white.

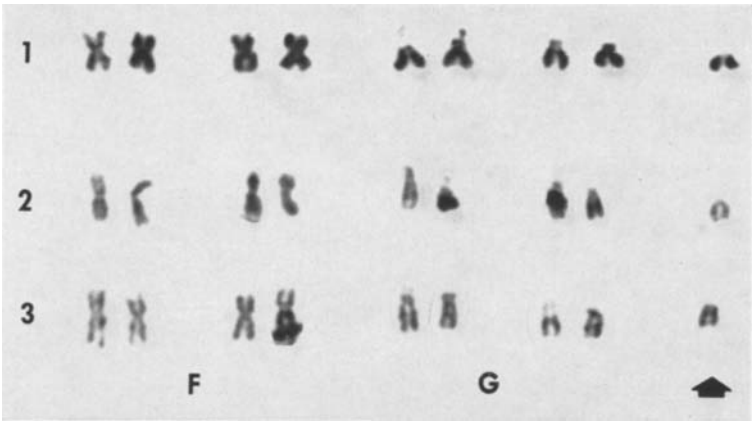

Fig. 1. Partial karyotype of female patient C.M. from 3 cells showing normal F and G group chromosomes and an extra small abnormal chromosome (arrowed)

a normal chromosome complement, the mother's blood culture on two separate occasions had 4—6% mosaicism with the abnormal G-like chromosome present in the minor cell population. Attempt was made to identify the abnormal chromosome with the use of Q banding technique but no conclusive evidence was obtained. The patient's birth weight was 4 lb. 6 oz., and she had multiple congenital anomalies including micrognathia (slight), bilateral dislocation of hips, downward deviation of left side of face and low set ears. She died 15 min after birth.

In addition to the above mentioned 5 chromosome aberrations, we observed chromosome variants in certain LBWN but have reached no conclusion about their significance. In the control group of this study only one boy had 47,trisomy 21 anomaly among 225 NBWN.

Discussion

Although the prognosis of low birth weight infants has been improved, mostly owing to better medical and nursing care (Rawlings *et al.*, 1971), the prediction of the fate of these small babies depends on an understanding of the etiology of intrauterine retardation. Clearly, many factors can be implicated.

During a period of 2 years, we have analyzed the chromosomes of 225 full-term low birth weight neonates delivered at a private hospital. Among these LBWN, 5 infants were found to be afflicted with chromosome aberrations, an incidence of one in 45 (Table 1). Two of these 5 LBWN had trisomy E_{18} syndrome, which is consistent with the observation that trisomy 18 retards birth weight significantly (Chen *et al.*, 1972). In patient C.M., although no evidence could be obtained to identify the extra small chromosome, the presence of this abnormal chromosome may lead to the low birth weight since extra chromosome material usually decreases birth weight (Chen *et al.*, 1972). On the other hand, the finding of two LBWN with trisomy 21 supports the observation that the mean birth weight of patients with Down's syndrome is significantly lower than that of controls (Chen *et al.*, 1972).

Among the 225 LBWN, there were three stillborns and their chromosome constitutions were normal. On the other hand, the patient with an extra deleted short arm G-like chromosome and two individuals with E_{18} trisomy syndrome died neonatally. The finding supports our previous observation that patients with low birth weight and certain chromosome disorders have a higher mortality rate during early infancy (Chen *et al.*, 1969). The results further suggest that the prognosis for survival of full-term low birth weight infants with chromosome abnormalities is very poor.

Although the sample size of the present study is still too small for an accurate assessment, the frequency of chromosome anomalies in full-term low birth weight newborns seems to be higher than that in the controls, even though the difference is not statistically significant ($\chi^2 = 1.52$). However, based on sample size, a significant χ^2 determination at the 0.05 level would require evaluation of approximately 330 LBWN. This conclusion is supported when the incidence of chromosome anomalies observed in the full-term low birth weight group is compared with the combined data of the incidence of chromosome aberrations reported in the consecutively born neonates (Sergovich *et al.*, 1969; Lubs and Ruddle, 1970) ($P < 0.001$). Therefore, it appears that chromosome aberrations play a role in the etiology of low birth weight in full-term infants.

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Andrew T. L. Chen, Ph.D.
Department of Genetics
Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23298, USA