A Case of Short Arm Deletion of Chromosome 18

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A case of the short arm deletion of chromosome 18 is described. This 13-year-old girl was associated with growth and mental retardation, trachoma, trichiasis, myopia, depression of nasal bridge, dental caries, and slender fingers. The syndromes associated with this autosomal deletion are discussed.

In 1963 chromosomal abnormality of the short arm deletion of chromosome 18 was first recognized by de Grouchy[1] in a six-year-old boy with mental retardation strabismus, hypertelorism, low-set ears, serrated teeth, syndactyly and clinodactyly. Numerous subsequent reports of similar deletions have been described in the literature. This paper presents a similar case of chromosomal abnormality in a 13-year-old girl with growth and mental retardation and minor physical malformations.

Case Report

A 13-year-old girl, native of Taiwan was admitted to Taipei Municipal Jen-Ai Hospital on Oct. 15, 1973 because of stunted growth. The mother, a housewife was 45 and the father, a worker was 48 years old at the time of the patient's birth. She was the youngest in the family and had four brothers and four sisters. Except for ahistory of chronic duodenal ulcer of her father, the mother and the other siblings were healthy The parents were not consanguineously related. There was no history of abortion preceding or subsequent to her birth, and no maternal irradiation or drug ingestion during the relevant pregnancy. The patient was delivered uneventfully after an uncomplicated full-term gestation, weighing 3000 gm. Her early growth and development such as sitting, standing, walking, speaking etc were slow but her mother was unable to give accurate details of postnatal history to us. Since the age of 10 she had an intermittent attacks of mild abdominal pain around the umbilical area. It was insidious in onset about once in four or five weeks, lasting for hours to days with occasional nausea and vomiting.

Physical examination on admission revealed a poorly developed and emaciated girl (Fig. 1) whose weight was 17.5 kg, height 123.5 cm, both being below the third percentile[2] The circumferences of her head and chest were 49 cm and 59.5 cm, respectively. She had trachoma and trichiasis but no ptosis, epicanthus or hypertelorism. The fundus were normal. The visual acuity was 16/20 on both eyes. The nasal bridge was slightly depressed. The ears were not low-set

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and normal in size and shape. The teeth had no anomalies but had severe dental caries. The chest was symmetric and slightly kyphotic. Examination of the heart and lungs revealed no abnormalities. The abdomen was soft and flat, without tenderness or detectable tumor mass. The liver and spleen were not palpable. The fingers were slender (Fig. 2). The external genitalia were normal for a female. No signs of puberty appeared as yet, such as engorgement of the breast, axillary or pubic hair distribution and occurrence of menses. The psychologist who evaluated the patient concluded that she had a depressive mood and had the verbal and performance scale IQ of 65 and 78 respectively.

Fig. 1: The patient, a poorly developed and emaciated girl with slight kyphosis.

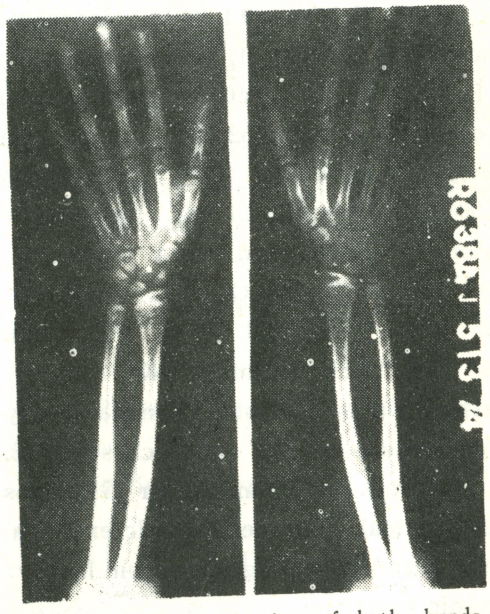

Fig. 2: X-ray examination of both hands showed slender fingers.

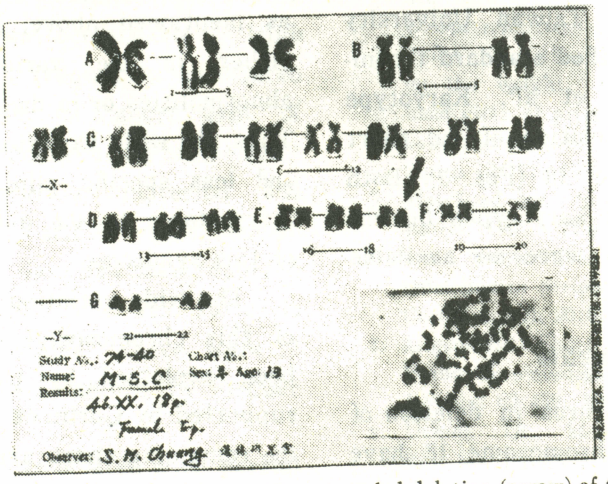

Fig. 3: Chromosomal analysis revealed deletion (arrow) of the short arm of chromosome 18.

Laboratory Studies: Except of leukocytosis found in the first few days of admission, the blood, urine and stool routine examinations were normal. Serum protein 6.8 g/dl; A/G ratio 4.2/2.6; Cholesterol 151 mg/dl; BUN 10 mg/dl; Creatinine 1.4 mg/dl; Amylase 94 U; Alkaline phosphatase 1.5 BU/L; SGOT 20 S-F U; SGPT 12 S-F U; Sodium 137 mEq/l; Chloride 99 mEq/l; Potassium 4.1 mEq/l; Calcium 9.1 mg/dl; Inorganic phosphorus 3.5 mg/dl; Iron 164 mcg/dl; P. B. I. 5.2 mcg/dl; Electrophoresis of total protein: Albumin 62.20%; α_1-globulin 1.58%; α_2-globulin 5.52%; β-globulin 15.00%; γ-globulin 15.70%. Immunoglobulin: IgG 1300 mg/dl; IgA 205 mg/dl; IgM 180 mg/dl. ASLO 12 U; CRP (−); RA test: (−); STS (−); Tuberculin test (−); EEG normal; EKG normal; Gastric juice analysis normal; X-ray examinations of the skull, chest, KUB, extremities, upper and lower GI series were normal. Gastroendoscopic examination: gastritis. Fibergastroscopic biopsy: chronic gastritis.

Cytogenetic studies: Peripherial blood cultures were performed at the Genetic Laboratory of the Taiwan University Hospital by the modified standard techniques of Moorhead et al[3]. Karyotype analysis revealed deletion of the short arm of chromosome 18 (Fig. 3). Both parents had normal karyotypes but the sisters and brothers were not available for this study.

Comments

The clinical features in deletion of the short arm of chromosome 18 have been summarized by Miegon as: 1) Significant mental retardation. 2) Short stature. 3) Absence of cardiac, renal, or gastrointestinal malformations. 4) Presence of a spectrum of minor congenital malformations such as hypertelorism, micrognathia, strabismus, epicanthi, low-set ears and rounded face. But these varied considerably from minor physical abnormalities of the eyes, nose, ears, mouth and teeth to severe central nervous system anomalies such as arhinencephaly[5] or cyclops[6~7]. Since phenotype is determined by the entire genetic composition of the individual, one might perhaps expect that loss of chromosomal segment would have certain effects upon the phenotype which may lead to some specific anomalies, as in the deletion of the short arm of chromosome 5[8] or the long arm of chromosome 18[9], which are well documented and relatively severe and can be suspected or diagnosed clinically. In contrast, the mental and growth retardation which is predominant in the deletion of the short arm of chromosome 18, has been observed in most of the chromosomal aberrations. And the minor congenital malformations, one of the other characteristic features, as mentioned above, have been found either in the various chromosomal abnormalities or in the normrl karyotype. Thus, the wide variation, relatively mild and less specific clinical features are attributable to the diagnostic difficulty of this syndrome.

The wide variation in the karyotype of this chromosomal anomaly as have been explained by Uchida et al[5] and supported by Gorlin et al[10] that genes on the remaining short arm of chromosome 18 would determine the phenotype, and that a hemizygous recessive gene in a

deficient heterozygote could account for cases of arhinencephaly. The relatively minimal clinical abnormality may be explained by the distribution of heterochromatin and euchromatin[11]. Since the centromere region often mainly consists of heterochromatin, it is possible that a large portion of the chromosomal fragment which has deleted is ordinarily heterochromatic with relatively little active genetic material[7]. The presence of similar somatic characters associated with aberrations in different chromosomes may be explained by the fact that either similar genetic material is present at different genetic loci or, more likely, that the phenotype is common to more than one genotype[4].

With few exceptions which were familial involving[5], , , most cases occurred spontaneously and this is hemizygous for genes on the homologue of the deleted fragment[14]. Although premature deliveries have been noted in some cases, in the majority, the pregnancy history was uneventful and no any consistent history of maternal illness, irradiation, drug ingestion or other complications during the gestation was remarkable[15]. High parental age was frequently associated with the deletion of short arm of chromosome 18. Jacobsen and Mikkelsen[16] reported the average maternal and paternal age of 35 and 36 years respectively, and similar data had been reported by other authors[17]. The sex ratio is predominant in females. There were 17 females to 7 males as shown by Fischer et al[17].

IgA deficiency associated with partial deletion of chromosome 18 was first reported in 1968 by Feingold et al[18], and the possible relation between the structural locus of IgA and the deleted chromosomal fragment were postulated. Since then immunoglobulin levels were studied in many patients with abnormalities of the chromosome 18. Recently it has been found that both normal or abnormal IgA levels may be present in the deletion of the short arm or long arm or in the ring chromosome 18. However, more than one locus of genes controlling the immunoglobulin on chromosome 18 were suggested[17]. Thus, multiple genes may be important in determining immunoglobulin levels, and the entire effect of the deletion may be non-specific[14].

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第18對染色體上臂脫失之一例

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第18對染色體上臂脫失的主要特徵是併有才智遲鈍、發育阻滯和一些小畸形，但無心臟、腎臟、腸胃方面的畸形。自從1963年 de Grouchy 發表這種染色體異常的病例以後，在國外陸續有許多相同的報告，但在本省則尚未有此病例報告。著者等報告在臺北市立仁愛醫院小兒科所觀察的一位13歲本省籍女孩，身高 123.5 公分，體重 17.5公斤，語言智商65，操作智商78，併有砂眼、倒睫、近視、鼻樑扁平、蛀牙、手指細長等症狀。染色體檢查發現有第18對染色體上臂脫失（18P—）的異常。

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