Hemihypertrophy: 10 Years Follow-up and Chromosomal Study

By

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Hemihypertrophy (congenital asymmetry) is a rare malformation, the incidence of which seems to have increased in recent years. Since its first description in 1839, 174 cases have been published. Of these 106 cases were observed in the 108 years from 1839 to 1947 [17] and 68 in the 16 years 1947 to 1963. The same increase in frequency appears from our own material of 21 cases [5, 6] of which 11 cases were recorded in the period 1954 to 1960, and 10 cases in the past 3 years.

Hemihypertrophy, the cause of which is unknown, appears in the earliest phase of intrauterine development. Asymmetry has been recorded in a 10 mm long embryo [11] and was shown to exist in the earliest phase of cell division [8]. This has given basis to the view of hemihypertrophy being an atypical, incomplete twin formation.

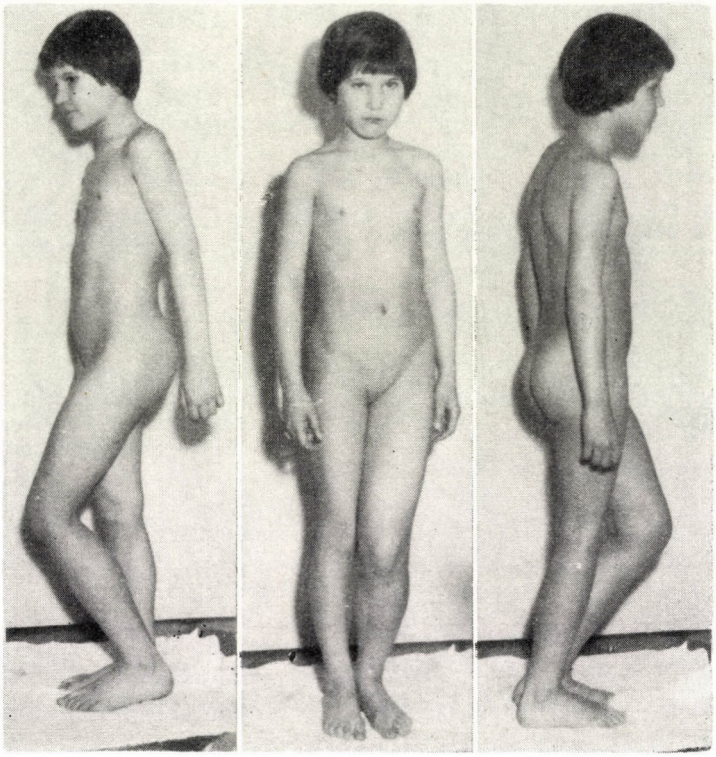
These findings have made us to perform a chromosomal study in a case of hemihypertrophy observed since infancy.

Report of a Case

Sz. I., a girl now 10 6/12 years old has been under our continuous observation for 10 years. On the paternal side there had been several twin-births. The mother around the time of conception had had influenza and at the end of pregnancy albuminuria and oedema. Labour had been induced artifically and delivery had been protracted. The patient's birth weight was 4400 g. It was noted immediately that the left extremities were thicker than the right ones. A significant difference in the length of the extremities had become apparent a few months later. At the first admission the patient was 8 months old, weighed 9100 g and measured 72 cm in length. Psychomotor development corresponded to age. A difference was evident between the two sides of the body. The asymmetry involved the entire body: Skull, face, ears, tongue, trunk, extremities were more developed on the left than on the right side, the spinal column showed convex scoliosis toward the left side. The difference between the two sides increased in caudal direction, the skull was the least and the lower extremities the most asymmetric (Figs 1a, b, c, and Fig. 2). Ephelides were present on the entire left side but none on the right one.

Follow-up examinations during 10 years showed the difference in length to increase in both the upper and lower extremities. Measurements of extremities and some bones are shown in Table I.

Chromosomal analysis was performed by the method of Moorhead et al., as modified by Schuler [16]. Two leucocyte cultures were studied in an interval of one month, examining a total of 35 cells.



a *b* *c*

FIG. 1. Sz. I. 10 6/12 year old girl. Hemihypertrophy
a and *c:* Note flexion of left knee with the heels joined, owing to 8 cm difference in length between the two lower extremities
b: Hypertrophy of the left side of the face and the wider left eye are clearly seen. Note difference in length and circumference of lower extremities. Circumference of the left thigh surpasses with 5.2 cm that of the right one; circumference of the lower leg surpasses with 5 cm that of the right one

20 karyotypes were made. The number of chromosomes was 46 in each cell. In most cells of both cultures, one member of the 3rd chromosome pair was longer than the other one (Fig. 3).

DISCUSSION

According to the accepted classifications [14, 17], the reported case is one of true and total congenital hemihypertrophy, since the differences involved not only the soft tissues but also the length and thickness of the bones. Other conditions leading to hypertrophy and differences in extremital length (Klippel—Trenaunay—Weber's syndrome, Recklinghausen's neurofibromatosis, Albright's polyostotic fibrous dysplasia, congenital lymphoedema, etc.) could be excluded.

In more than half of the reported cases the hemihypertrophy was associated with other manifestations, particularly with anomalies of the vessels and pigment disorders. Except the ephelides on the left side of the trunk,

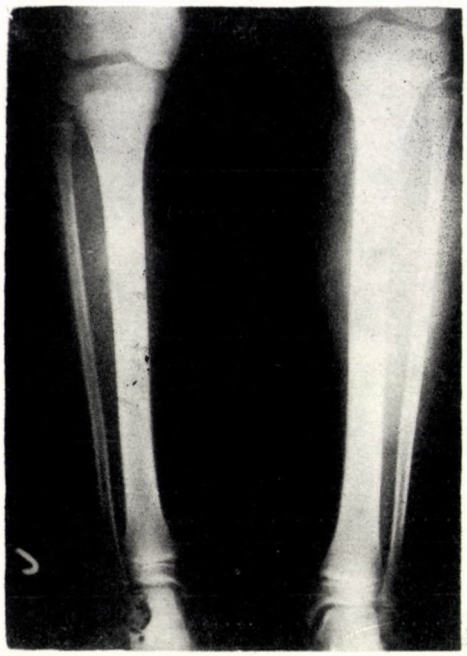


FIG. 2. Difference in length and thickness of bones. The left femur is 2.6 cm longer, the tibia 2.7 cm longer, the fibula 2.7 cm longer than the corresponding bones on the right side

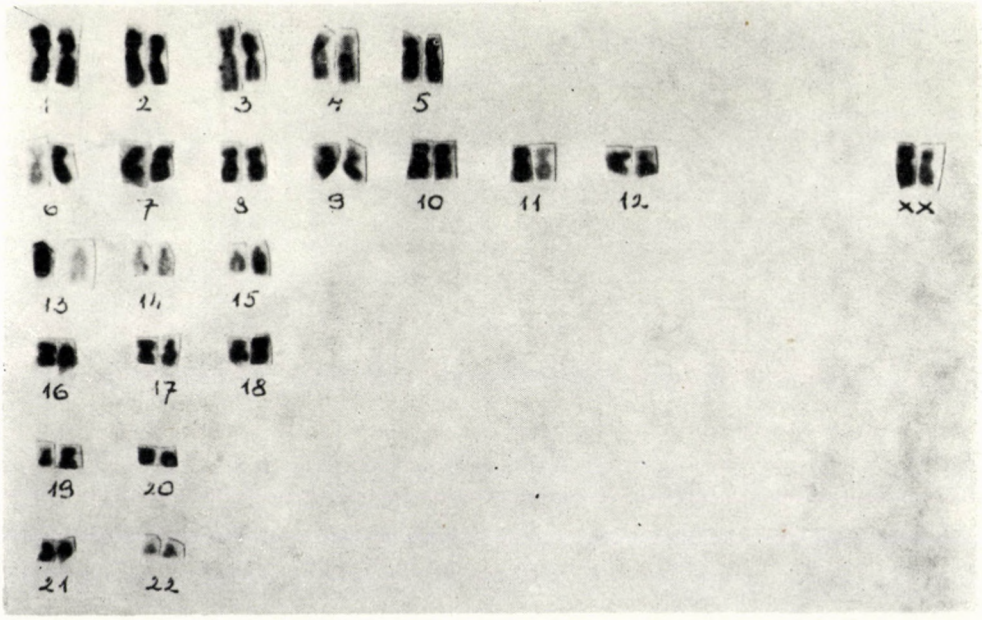


FIG. 3. One member of the 3rd chromosome pair is longer than the other one (Leucocyte culture; Unna's blue staining; magnification, ×4000)

TABLE I

Differences in length (in cm) of the extremities in a case of true hemihypertrophy

		July 1954	May 1955	March 1956	January 1958	May 1964
Length of upper extremity		0.25	—	0.3	1.0	—
Circumference of upper extremity	upper arm	0.5			0.5	—
	forearm	0.5			1.0	—
Length of lower extremity		2.5	3.5	4.3	4.0	8.0
Circumference of lower extremity	thigh	5.0	5.0	5.0	4.0	5.2
	lower leg	4.0	3.5	4.0	3.5	5.0
Length of sole		0.5		1.1	1.0	2.5
Radiological measurements						
Length of humerus					0.5	—
Length of radius					0.2	—
Length of ulna					—	—
Length of femur		1.0			2.0	2.6
Length of tibia		1.0			2.0	2.7
Length of fibula		0.9			2.0	2.7
Length of os ilei		0.5			1.0	
Width of os ilei		1.5			1.0	
2nd metacarpal					0.4	—

no additional anomaly was present in our case.

In contrast to the data in the literature, in our case the degree of hemihypertrophy was increasing during the 10 years of observation.

As to the hereditary nature of hemihypertrophy, there are few data in the literature. Only three authors have reported on the occurrence of a similar disorder in the family (grandparents, parents, siblings) of the patients [9, 12, 13]. As regards chromosome examinations, in a case of SILVER's syndrome (hemihypertrophy, short stature and increased gonadotropin secretion) a normal chromosome structure has been observed [15]. In 4 patients with hemihypertrophy, WIEDEMANN et al. [18] found

no chromosome aberration in cultures of peripheral blood. In a patient with hemihypertrophy, mental retardation, dolicho-oxycephaly, partial syndactylism, pigmented spots and cryptorchidism, FERRIER et al. [3] observed in the cells of the skin and fascia lata a mosaicism composed of diploid and triploid cells with 46, and 69 chromosomes, respectively, and acrocentric chromosomes with unusually large satellites. They could find no changes in the cells of peripheral blood.

As mentioned, in our case beside a normal number of chromosomes an enlargement of one member of the 3rd chromosome pair was observed. To exclude that a transformation had taken place *in vitro*, during culturing or preparation, a new culture was set up after the examination of the first 10 karyotypes. The anomaly having been present in the cells of the second culture, an alteration *in vitro* is not probable

Enlargement of one of the chromosomes is assumed to be due to translocation. In this case, however, if the chromosome number and the shape of the other chromosomes are normal, the translocated chromosome is either a surplus one or a chromosome fragment. BRAY and JOSEPHINE [1] observed in a case of multiple malformations (retardation in growth with malformation of the heart, kidneys and bones) an irregular enlargement of one member of the 4th chromosome pair, which they thought to be due to partial 13-trisomy + translocation. A similar observation has been reported by GAGNON et al. [4] who ascribed the malformations to 18-trisomy and translocation. An abnormally long chromosome has been observed in WALDENSTRÖM's macroglobulinaemia, but this long chromosome was a surplus 47th one [7].

The most probable explanation of the chromosome anomaly observed in our case is the presence of partial trisomy and translocation. Although a certain variability in size is known to occur in the two members of the chromosome pairs, the difference revealed in our case seems to surpass the limits of physiologic variability [2, 10]. Further examinations will show whether a relationship really exists between the observed chromosome anomaly and hemihypertrophy.

SUMMARY

In a female patient 10 6/12 years of age hemihypertrophy with predominance of the left side has been observed. During 10 years the asymmetry was gradually increasing. Chromosome examination revealed a normal chromosome number but a different shape of one member of the 3rd chromosome pair.

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