Familial Occurrence of Trisomy 16-18

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The purpose of this paper is to report 2 cases of multiple congenital anomalies associated with trisomy in the group 16-18, most probably trisomy 16, in two sisters aged 37 and 31 years.

Case Reports

Case 1. A female patient, P.U., aged 37 years was admitted to the Department of Neurology with complaints of muscular weakness of the upper and lower extremities, impaired walking, and pains in the knees. The symptoms had started 6 years earlier and had gradually progressed. At the age 26 she was operated on for bilateral cataracts. She had difficulties in learning at school and finished only the fourth form. Menstruation, which started in the 22nd year, was slight,

irregular, of a day's duration, and ceased at the age of 37 years.

Both parents had died many years ago. Photographs of the father show him to have been of very short stature, and an anomaly, i.e. drooping eyelids, is clearly evident. She had two sisters, one of whom died in infancy of congenital heart disease, and the other is Case 2.

On *physical examination* the following changes were found. She was short, her height being only 153 cm., and she was of stocky build. The cranium was small; the facial part was strongly developed but the jaw was recessed. Her face was pale with coffee-coloured stains on the forehead. There was a slight paresis of upward movement of the eye and ptosis of the upper lids with subsequent narrowing of the eye-slits forcing the patient to tilt her head backwards (Fig. 1). There was no mechanical myotonia of the tongue. The sternum showed shortening of the manubrium, the sternal parts of the clavicles were distinctly felt and had an increased range of movements, so the patient could easily hunch her shoulders (Fig. 2). The sterno-mastoid muscles were not palpable. In the upper extremities

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FIG. 1. Case 1. The face of the patient showing under-developed cranium, drooping eyelids, and stains on the forehead.

FIG. 2. Case 1. The hypermobility of the shoulders is shown.

FIG. 3. Lymphoedema and tapering of the fingers with hyperconvex nails.

FIG. 4. The hand of Case 1. A retroflexible thumb and absence of the proximal transverse crease are evident.

lymphoedema was present on the back of the hands and fingers (Fig. 3); muscle wasting was not obvious. There was a retroflexible thumb in the left hand. All the fingers tapered towards the tips which were narrowed, the finger-nails showed lateral hyperconvexity, especially on the first, fourth, and fifth digits. In the right hand the fifth finger was shortened and curved medially. On the left palm there was a complete absence of one of the principal flexion creases—the proximal transverse crease (Fig. 4)—while on the right palm this crease was only rudimentary. The thenar crease and the distal transverse crease were normal. On the fingertips, including the thumb, low arches were found in 4 digits of the left hand and 3 digits of the right hand, the remaining fingertips having ulnar loop pattern (Fig. 5). The flexion of the fingers was limited and there was a marked weakness of the small muscles of both hands. A slight tremor of the upper extremities was noticed when the arms were extended. There was no myotonia of the grip or mechanical myotonia of the thenar and hypothenar muscle groups.

The lower extremities were thick with lymphoedema involving the calves and feet. Muscle wasting was not evident. In the hip joints the abduction, flexion, and rotation were considerably limited. Both feet were flat. There was severe weakness of all muscle groups in the lower extremities. The knee and Achilles tendon reflexes were absent. Walking and standing were difficult for the patient even when supported.

No changes were found in the internal organs, including the heart and kidneys. An umbilical hernia was present.

Although the nasal mucosa was normal the patient had no sense of smell and was unable to distinguish

the simplest scents. The blast olfactometer examination showed a complete anosmia to 'O' substances and marked hypo-osmia to 'O' + 'T' substances. The taste, as judged by the nerve VII and IX sensitivity, was symmetric and normal. The ophthalmological examination

FIG. 5. Print of the thumb showing a low arch pattern.

FIG. 6. Drawing of the laminograms of the sternum reveals a gross shortening and broadening of the manubrium with articular facets of the clavicles on its upper end.

revealed secondary cataracts but no changes were found in the fundus.

The electromyographic examination of the first interosseal muscles of the hands showed a moderate myotonic reaction. The electroencephalogram revealed a generalized dysrhythmia, more pronounced in the deep leads. The Wechsler test gave a result of 1:1 : 66, confirming the diagnosis of mental debility as established during the psychiatric examination.

The blood and urine examinations, including chromatography of free amino acids, showed no abnormalities. CSF analysis was normal. The basal metabolic rate was -19%, the serum cholesterol level was 205 mg./100 ml., and the ^{131}I uptake of the thyroid amounted to 43%.

The urinary excretion of 17-ketosteroids was 8.6 mg. and of 17-ketogenic steroids 6.5 mg. per day. The chromatin pattern in buccal mucosa smears was positive, but no cells containing 2 or 3 Barr bodies were found. The vaginal smears revealed effect of oestrogen deficiency. At laparotomy the uterus, tubes, and ovaries were of normal shape and nearly normal size. The histological examination of the ovary specimen showed a complete absence of follicles with the presence of multiple corpora albicantia, findings that indicate fibrosis of the ovary.

Radiological Examination. Lateral skull radiographs showed a posterior protruding of the occiput and the frontal bones and fossa cranii anterior were of reduced size. The sternal radiographs, including laminograms, revealed a broadening and marked shortening of the manubrium with articular facets of the sterno-clavicular joints on its upper end (Fig. 6). The hand showed a decrease in bone density, positive metacarpal sign, and shortening of the middle phalanx of the fifth finger. In the hip joints the femoral heads were flattened and the iliac angles were reduced.

Chromosome studies on several peripheral blood cultures were made using the phaseoline technique. In all, 87 cells in metaphase were counted; in 72 of them 47 chromosomes were found, and in the remaining cells the chromosome number was 46. In cells with 47 chromosomes the extra chromosome resembled those of the 16-18 group but a precise identification to which pair 16, 17, or 18 the extra chromosome belonged was not possible (Fig. 7).

Case 2. The sister of the described patient, aged 31, was of very short stature 140 cm. and of stocky build (Fig. 8 and 9). She was mentally retarded to a severe degree and was a permanent inmate of a mental asylum. Her complaints were muscular weakness, progressing in time, and easy fatigability. On physical examination multiple congenital anomalies were found as listed in the Table. The chromosome analysis of peripheral blood revealed a modal number of 47 chromosomes with the extra chromosome in the group 16-18.

Discussion

These two patients belong most probably to the trisomy 16 syndrome. Although the chromosomal studies did not permit an exact differentiation as to which pair in the E group the extra chromosome belonged, the fact that both patients survived more than 30 years strongly favours the diagnosis of trisomy 16. According to published reports all patients with trisomy 17-18 die in early childhood, between the ages of 2 and 9.

Trisomy of autosome 16 was only recently briefly described by Lewis, Hyman, MacTaggart, and Poulding in 1963, in a 59-year-old woman with multiple congenital anomalies.

Our patients have many features in common with both trisomy D and trisomy E as listed in the Table; however, other cardinal signs of these syndromes are not present. In addition, some of the signs are similar to those found in patients with Turner's syndrome.

The familial occurrence deserves mention; the presence of trisomy syndrome was fully confirmed in the two above-described sisters, and there is a strong suspicion that the same syndrome was present in a third sib, a female child, who died in infancy of congenital heart disease. The short

FIG. 7. Karyotype of peripheral blood revealing 47 chromosomes, the extra chromosome being in the group 16-18.

FIG. 8. Case 2. Short stature and stocky build with lymphoedema of the legs and hands.

FIG. 9. Case 2 showing drooping eyelids, stains on the forehead, and low-set ears.

TABLE

Anomalies	Case 1	Case 2	Trisomy 13-15	Trisomy 17-18	Turner's Syndrome
Eye defects (cataracts)	+	+	+	+	+
Blepharoptosis	+	+	+	+	+
Congenital heart disease	+	+	+	+	+
Scalp defects	+	+	+	+	+
Abnormal palm creases	+	+	+	+	+
Distal phalanges narrowed	+	+	+	+	+
Nail hyperconvexity	+	+	+	+	+
Nerve olfactory changes	+	+	+	+	+
Mental retardation	+	+	+	+	+
Low arches on fingertips	+	+	+	+	+
Sternum defects	+	+	+	+	+
Hypermobility of shoulders	+	+	+	+	+
Hip changes	+	+	+	+	+
Protruding occiput	+	+	+	+	+
Small jaw	+	+	+	+	+
Muscle defects	+	+	+	+	+
Lymphoedema	+	+	+	+	+
Thick legs	+	+	+	+	+
Pes equinovarus	+	+	+	+	+
Dorsiflexion of big toe	+	+	+	+	+
Positive metacarpal sign	+	+	+	+	+
Gonadal dysfunction	+	+	P	P	+
Osteoporosis	+	+	P	P	+
EEG abnormality	+	+	P	P	+
Umbilical hernia	+	+	+	+	+

+ present, - absent, P probable.

stature and drooping eyelids in the father suggest a possibility that he also had a partial trisomy syndrome.

Summary

Two adult sisters with the signs and symptoms of both D trisomy and E trisomy are described. Chromosome studies in both cases revealed a modal number of 47 chromosomes with the extra chromosome in the group 16-18.

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