Caspersson, T., resolution cannot translocation No. Mrs Anna two fingers 1, 3, and 5 of both hands, radial loops on both index fingers, and whorls on the fourth fingers.

The father’s palms showed six ulnar loops on fingers 1, 3, and 5 of both hands, radial loops on both index fingers, and whorls on the fourth fingers.


The mother had whorls on all 10 fingers.


Male Pseudohermaphroditism in a Child with Down’s Syndrome*

Summary. A case of male pseudohermaphroditism in a child with Down’s syndrome is reported. The patient had infantile testis, ambiguous genitalia, and no apparent internal female genitalia indicating a failure of either gonadal function or end-organ response.

Down’s syndrome, the most common of the chromosomal abnormalities, has been reported in association with a number of seemingly unrelated sex chromosome aneuploidies, of which the most frequent is the double aneuploid 48,XXY,+G (Hamerton, 1971). Although there has been one report of a female with Down’s syndrome and congenital adrenal hyperplasia (Srivuthana et al, 1971) we are unaware of any published cases of Down’s syndrome associated with male pseudohermaphroditism. We will describe such a child.

Case Report

The proposita is the first child of 25-year-old parents. She was born at term by a spontaneous vaginal delivery after a four-hour labour and weighed 3115 g. The

can Journal of Human Genetics, 24, 189-213.


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Received 12 February 1973.

This work was supported by grants from the National Foundation—March of Dimes; The Maternal and Children Health Service (USPHS), the National Institute of General Medical Sciences (GM-19, 527), and the John A. Hartford Foundation.

The opinions expressed herein are those of the authors and do not necessarily reflect those of the United States Air Force or the Department of Defense.

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mother had severe nausea and took anti-emetics from the first to fifth month of pregnancy but was not seen by a physician. She has a history of goitre and intermittently took varying dosages of a United States Pharmacopeia thyroid preparation throughout the pregnancy. No other drugs were ingested and there were no prenatal infections or other complications. There was no family history of congenital malformations or mental retardation, and the patient’s parents were not related.

The patient was cyanotic at birth and required a 40% oxygen environment. Her early course was complicated by cardiomegaly for which she was treated with digitalis, and pneumonia which responded to antibiotic therapy. She did well, the digitalis was discontinued and no primary cardiac defect was identified. A number of stigmata of Down’s syndrome were noted, and a chromosome study at that time was reported as 47,XX,+G.

In addition to the typical somatic stigmata of Down’s syndrome she had bilateral talipes equinovarus (Fig. 1) and several abnormalities of the genitalia. These included bilateral soft movable 1 x 1 cm inguinal masses, an enlarged phallic-like structure, and rugated fused labioscrotal folds (Fig. 2).

Developmental milestones were markedly retarded. From 3 to 17 months of age the patient had grand mal seizures and was treated with phenobarbital. The seizures were controlled but recurred when the mother discontinued the medication and therapy was reinstated.

At 24 months of age she was hospitalized for evaluation of her ambiguous genitalia. Laboratory studies included a normal complete blood count, urinalysis, serum electrolytes, thyroid function tests, uric acid, calcium, and phosphorus. Blood urea nitrogen was 20 mg% and an electrocardiogram revealed minimal right ventricular hypertrophy. A 24-hour urine collection contained 1.0 mg 17-hydroxycorticosteroids, 0.9 mg 17-ketogenic steroids, 1.7 mg 17-ketosteroids, and less than 0.1 mg pregnanetriol. These urine values are all within normal limits for that age.

While hospitalized cystoscopy, vaginoscopy, and biopsy of the inguinal masses were performed. She was found to have a normal bladder without ureteral reflux and a short blind vaginal pouch with no demonstrable cervix. No uterus or adnexae could be palpated. The urethral orifice was at the base of the enlarged clitoris. Bilateral inguinal exploration revealed vas deferens and gonads that on frozen section showed immature testicular tissue. Ligation of the cords and bilateral orchiectomy were performed.

Difficulty in correlating the karyotype and the surgical findings led to referral of the patient to the University of California Medical Center for genetic evaluation.

Review of the surgical specimen slides showed an immature testis, the tubules of which consisted mostly of Sertoli cells with widely scattered germ cells (Figs. 3a and b). Rete testis, epididymis, and ductus deferens were also present.

Analysis of both cultured peripheral lymphocytes and skin fibroblasts revealed 47 chromosomes. Giemsa-banding studies (using the modified method of Sumner, Evans, and Buckland, 1971) delineated the karyotype as 47,XY,+21. Review of pictures of the earlier karyotype that had reported the sex chromosomes as XX indicated that they had been misinterpreted. Peripheral
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lymphocyte cultures showed a 46,XX karyotype on the patient's mother; the father was unavailable for testing.

Discussion

Male pseudohermaphroditism covers a group of genetically and clinically heterogeneous diseases. A few entities such as testicular feminization syndrome and XY gonadal dysgenesis have been well delineated. A number of others have been described but are not entirely nosologically distinct. Attempts have also been made to classify male pseudohermaphroditism as resulting from either faulty testicular androgenic function or end-organ insensitivity to androgens. However, this is complicated by a number of cases in which both entities seem to be normal (Saez, Frédérich, and Bertrand, 1971).

Our patient had an infantile testis, ambiguous genitalia, and no apparent internal female genitalia. The normal urine steroid studies indicate that this was not secondary to an adrenal malfunction. The lack of internal female genitalia suggests the testicular secretion of Müllerian-inhibiting substance in utero was normal. We cannot state whether this patient's condition resulted from a gonadal or end-organ failure. The end-organ responsiveness could be determined by giving the patient testosterone and observing for its metabolic functioning (e.g., nitrogen retention, sebum secretion, etc) but this has not been done due to parental wishes. Direct evidence of gonadal incompetence is impossible to obtain after castration.

The fact that the present case was born partially masculinized suggests further virilization would have occurred at puberty if the testis had been left in situ. The clinical problem (i.e., Down's syndrome plus inadequate male external genitalia) and the parents' concept of their child as a daughter indicated that this patient is best reared as a female. To attempt multiple hypospadiac repairs seemed unwarranted. Appropriate psychological support for
this decision was provided to the parents throughout many visits.

Patients with Down's syndrome may have cryptorchidism or a small penis but other genital developmental abnormalities are uncommon (Hamerton, 1971). Only one case of pseudohermaphroditism in a patient with Down's syndrome has been reported previously and that was a female with congenital adrenal hyperplasia (Srivuthana, et al, 1971). There is some evidence, however, that the association of sex chromosome abnormalities and Down's syndrome is higher than would be statistically expected (Taylor and Moores, 1967). The lack of reported cases with the association of the two abnormal states seen in our patient suggests their simultaneous occurrence is coincidental. In view of the large series of patients with Down's syndrome reported we feel that if a common mechanism for these abnormalities existed more cases of their co-existence would have been reported.

Two and a half years after the birth of the patient, her mother became pregnant by her second husband. Fifteen weeks after her last menstrual period an amniocentesis was performed because of her increased risk of bearing another child with Down's syndrome. The karyotype on the amniotic fluid cells was 46,XY. The possibility of this fetus being affected if the mother was the carrier of an X-linked form of male pseudohermaphroditism was discussed with the parents. A normal male infant was delivered at term.

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Möbius Syndrome with Poland's Anomaly*

Summary. A five-year-old boy with Möbius syndrome, Poland's anomaly, and dextrocardia is described. These malformations have not been previously reported. The propositus had ipsilateral absence of the sternal portion of the pectoralis major muscle associated with acromelia, syndactyly, brachydactyly of the index, middle, ring, and fifth finger, as well as radiological evidence of hypoplasia of the index middle and ring fingers, associated with syndactyly and absent middle phalanges.

Möbius syndrome associated with Poland's anomaly, as represented by the case reported here, has not been previously described. The first report of congenital bilateral facial paralysis was made by von Graefe in 1880. In 1888, Möbius emphasized the nuclear agenesia of the cranial nerves. Some of the most comprehensive reviews of this rare disorder were made by Henderson in 1939, Danis in 1945, Gorlin and Pindborg in 1964 as well as others (Hellström, 1949; Richards, 1953; Evans, 1955).

Alfred Poland in 1841, dissected the body of a criminal with unilateral symbrachydactyly associated with ipsilateral (same side) aplasia of the sternal head of the pectoralis major muscle. In 1900, Fürst provided a detailed analysis of the type of hand malformation, the associated muscle defects and insight into the aetiology.

Case Report

This 5-year-old boy was first seen at the Orthopaedic Hospital, Los Angeles, California in May 1971, because of multiple congenital abnormalities involving the eye, facial muscles, jaw, teeth, palate, sternum, chest, and hand. The mother's pregnancy was apparently normal. She gained approximately 15-9 kg in weight from an initial weight of 66-7 kg. The father and mother were unrelated, and were both 30 years of age at the time of the patient's birth. The birthweight was 4-0 kg. The baby breathed and cried spontaneously. No diagnosis of any syndrome was made. He had two operations on his eye muscles for strabismus, at age 1 and 3 years. There was no family history of neurological or somatic disorders.

Received 27 November 1972.

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