

49,XXXXY Chromosomal Anomaly in a Neonate*

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Since the first description of a patient with the 49/XXXXY chromosomal anomaly by Fraccaro, Kaijser, and Lindsten in 1960 individuals with this form of X chromosome polysomy have been recognized with significant frequency. In 1966 a comprehensive review of 33 patients appeared (Zaleski *et al*) and recently a total of 61 cases have been cited (Shapiro, 1970).

This report concerns a newborn infant with the disorder and provides information about the clinical presentation of the syndrome in the very young.

Case Report

A 3-day-old infant was transferred to the Massachusetts General Hospital because of feeding difficulties. He was born of a healthy, Rh negative mother and Rh positive father, 24 and 28 years old respectively, who had been parents of a normal boy 13 months previously. Neither parent had been exposed to known teratogens and the family history was unremarkable. Spontaneous vaginal delivery terminated an uncomplicated gestation of 36 weeks duration. At birth the patient's weight was 2580 g, and his Apgar score was 8. The infant was Rh + and the Coombs test on cord blood was positive. On the first day of life, respiratory distress and choking spells were noted in association with feedings. These were so persistent and distressing as to suggest tracheo-oesophageal fistula to the referring paediatrician.

Physical examination. At the time of entry the infant's weight was 2000 g, length 46 cm and head circumference 32 cm. He was slightly jaundiced but showed no respiratory distress. His face was full, there were no epicanthal folds, the chin was small and the base of the nose moderately depressed (Fig. 1). The neck was short with lax skin, but without true webbing. The chest was symmetrical with a mild pectus deformity and wide set nipples. A transient heart murmur was noted. The penis was normal and both testes were palpated in a

normal scrotum. All joints were normal except for hyperextensibility at the first metacarpophalangeal joint bilaterally. Each hand showed shortening and clinodactyly of the fifth finger and a simian crease. Marked hypotonia was reflected in his posture, head lag, and poor Moro response (Fig. 2).

When feedings were attempted he developed cyanosis, laboured respirations, and bradycardia; the latter appeared to be mediated by an overactive vagal reflex since the lowering of heart rate was abolished by atrophine. Choking and aspiration continued, however, required that the infant be fed by gavage. Because no improvement had occurred by the second week of life, a gastrostomy was performed. This resulted in the cessation of weight loss and at one month of age the infant was discharged to the care of his parents. When seen at age 5 months, he was taking oral feedings well, but his development was slow and hypotonia persisted.

Radiology. Radiology of the chest, pelvis, and bones of the upper extremities were normal; there was no evidence of radioulnar synostosis. A contrast study of the oesophagus and upper gastrointestinal tract showed no tracheo-oesophageal fistula, diaphragmatic hiatus hernia, or other anomaly predisposing to vomiting.

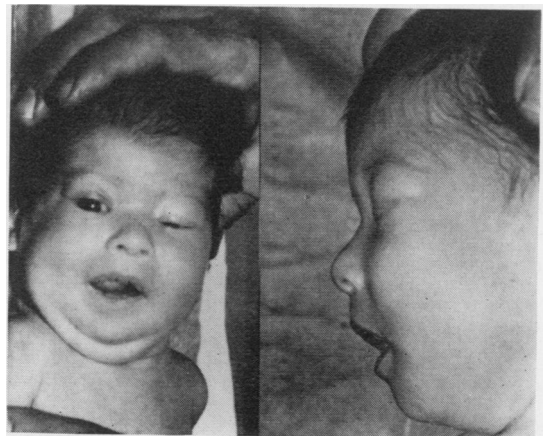


FIG. 1. Patient at age 1 week. Note the full face, small chin, and short neck.

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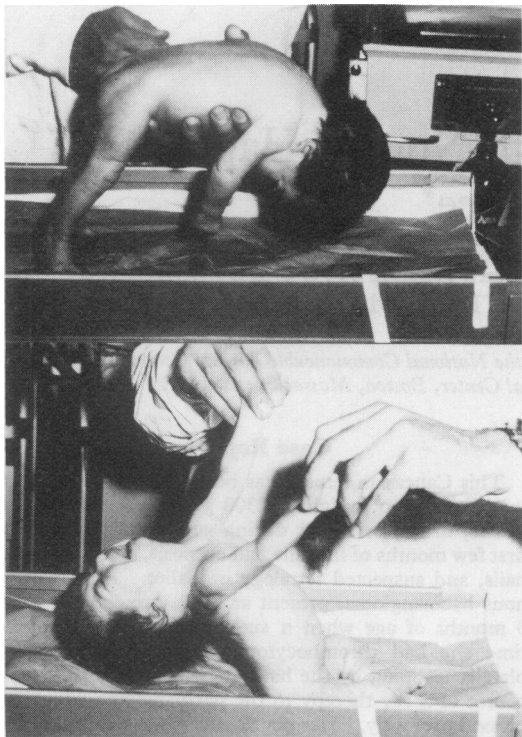


FIG. 2. Patient at age 1 week demonstrating profound hypotonia.

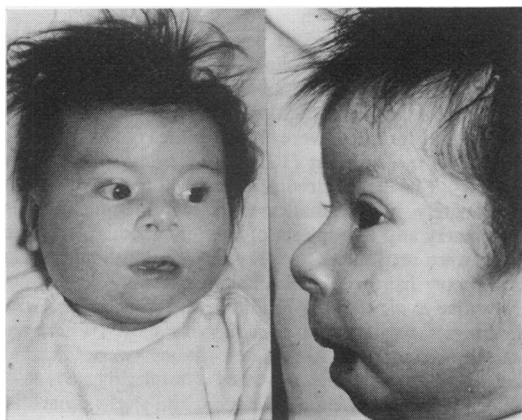


FIG. 3. Bitan's patient (Bitan *et al*, 1969). Front view age 2 months and profile age 1 month. Note the full face, small chin, and moderately depressed base of the nose.

Cytogenetics. All studies were initiated on or before the fifth day of life. In a peripheral blood smear, several polymorphonuclear leucocytes were found with a single 'drumstick' and one with two 'drumsticks'. A buccal smear showed 28% of the cells to have one Barr body, 13% to have two, and 3% to have three Barr

bodies. A 49,XXXXY karyotype was demonstrated from chromosome preparations of venous blood and fibroblasts cultured from a skin biopsy; there was no evidence of mosaicism. The 3 extra chromosomes were shown to be X chromosomes by late labelling with tritiated thymidine.

Family studies. The mother and father had normal chromosomal complements. X_g^a blood grouping studies showed that the patient was X_g^a -positive, as was his mother, while the father was X_g^a -negative.

Discussion and Conclusions

An infant with the 49,XXXXY chromosomal anomaly is described. A chromosomal disorder, including Down's syndrome, was suggested by the presence of multiple, nonspecific, minor, congenital anomalies including short neck, simian creases, and clinodactyly, in association with feeding difficulties, low birth weight for gestational age, and profound muscular hypotonia. There was no cryptorchidism, hypospadias, or elbow abnormalities. This patient contrasts markedly to most previously reported patients with regard to the timing and manner of diagnosis. Most patients have been recognized much later in life by chromosome screening studies in institutions for the mentally deficient; in a small number the diagnosis was specifically suggested by the combination of hypogonadism, cryptorchidism, severe mental retardation and radioulnar synostosis. The only previously reported newborn (Bitan, Schaffer, and Bach, 1969) had a normal neurological examination but clinodactyly and radioulnar synostoses were present. The similarity of the facial appearance of these 2 newborn patients can be appreciated in the pictures (Figs. 1, 2, and 3).

Diagnosis in this infant, in the absence of any 'typical' features may afford not only a better understanding of the natural history of this syndrome but also suggest that this entity should be entertained by the clinician when he is confronted by a floppy baby.

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