

# New Clinical Signs at Fraccaro Syndrome (49, XXXXY)-Bilateral Club Foot: A Case Report

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Fraccaro syndrome: 49, XXXXY is rare chromosomal pattern and these patients have mental retardation, small penis, cryptorchidism and skeletal anomalies. We reported a six month-old boy who has hypotonia, microcephaly, hypertelorism, depressed nasal bridge, epicanthal folds, high arched palate, down set ears, micrognathia and patent ductus arteriosus. Among the skeletal anomalies, except ulnar radial distal dislocation and kyphoscoliosis, at first discovered bilateral club foot. Karyotype was found as 49, XXXXY and this cytogenetic analysis was help to establish clinical diagnosis Fraccaro syndrome. *Ann Med Sci* 2002;11:62-65

**Key words:** Fraccaro syndrome, club foot.

One of the Klinefelter's variant 49, XXXXY arises from sequential nondisjunction in meiosis. This karyotype has been reported in more than 100 patients after the first reported patient by Fraccaro and colleagues in 1960<sup>1</sup>. In addition to mental retardation, skeletal anomalies, hypoplastic external genitalia. These patients have also phenotypic similarities consisting of strabismus, microcephaly, epicanthal folds, hypertelorism, cleft palate. One of the anomalies is congenital heart disease<sup>2</sup>. The case we report is the first case with bilateral club foot in Fraccaro syndrome.

## Case Report

The six month-old boy who had recurrent fever, cough, enteritis and developmental delay was brought to the Pediatric Endocrinology and Metabolism Department. He has been examined because of bilateral club foot in the Orthopedics Department and also because of patent ductus arteriosus in the Pediatric Cardiology. Patient has been taking digoxin and captopril. He has been hospitalized four times before pneumonia and gastroenteritis.

Child was born prematurely (2040 gr 35 week) and had perinatal asphyxia. He was also the 4<sup>th</sup> living child of the couple. The parents had

consanguinity. His father was 43 years old and his mother was 35 years old. Child's mother had preeclampsia during pregnancy. His three sisters were healthy, but the first male child died when he was 18 months old due to meningitis.

Patient's physical findings were as follows: The weight 3500 g (< 5p for age) length 56 cm (< 5p for age) and head circumference 37 cm (< 5p for age), fever 36,5 °C, pulse 140/min. He was conscious and interested in the environment. He had hypotonia, microcephaly, dry sparse hair, depressed nasal bridge, hypertelorism, epicanthal folds, down-set ears, high arched palate and micrognathia. The size of his anterior fontanel was about 3x4 cm. The rachitic was noted at the costochondral junctions. A grade of 3/6 machinery murmur was heard in the 2<sup>nd</sup> left intercostal space. The liver was found 3 cm below the costal margin and spleen was 3 cm. At right hand ulnar radial distal dislocation and bilateral club foot deformities were seen. His testes were descended bilaterally and the penis was normal. (Table 1) (Figure 1)

Laboratory studies were as follows: Anemia was determined and his routine blood chemistries were normal. Computerized tomography of the brain demonstrated that he had cavum septum pellucidum variation. Ultrasonography of the abdomen was unremarkable. Metabolic screening of the urine was negative and amino acid chromatographies of the blood and urine were normal. Chromosome analysis was made and

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karyotype was found as 49, XXXXY. When beginning pulmonary incompetence last remedy

made tracheostomy. Patient died at the age of nine-month old.



A



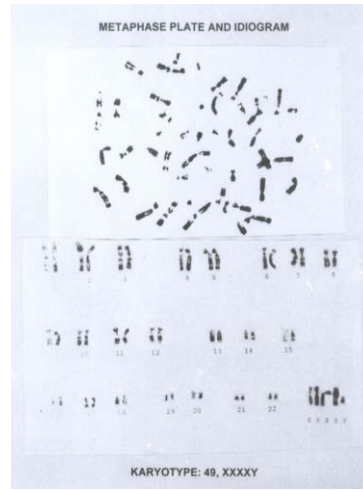
B



C



D



E

**Figure 1.** A-Facial appearance, B-Outward appearance, C- X-ray Club foot, D-X-ray ulnoradial distal dislocation, E-Idiogram

Table 1. Phenotypic Feature of Patient with Fraccaro Syndrome

| Phenotypic features in the literature | Features of our patient              |
|---------------------------------------|--------------------------------------|
| Mental retardation                    | Growth retardation<br>+              |
| Facial features                       |                                      |
| Mongoloid slant                       | Antimongoloid                        |
| Microcephaly                          | +                                    |
| Epicanthal folds                      | +                                    |
| Strabismus                            | +                                    |
| Hypertelorism                         | +                                    |
| Down-set ears                         | +                                    |
| Large malformed ears                  | +                                    |
| Depressed nasal bridge                | +                                    |
| Flat upturned nose                    | +                                    |
| Large open mouth                      | +                                    |
| Short neck                            | +                                    |
| Genital anomalies                     |                                      |
| Hypoplastic scrotum                   | -                                    |
| Cryptorchidism                        | -                                    |
| Small penis                           | -                                    |
| Small testicles                       | -                                    |
| Decreased of pubic hair               | -                                    |
| Congenital heart disease              | + (Patent ductus arteriosus)         |
| Skeletal anomalies                    | + (Club foot)                        |
| Computerized brain tomography finding | + (Cavum septum pellucidi variation) |

## Discussion

Rare form of the Klinefelter's syndrome 49, XXXXY was firstly reported by Fraccaro and colleagues in 1960. This variant has been described on more than 100 patients since then<sup>1</sup>. The disorder originates from sequential non-disjunction in meiosis. Affected patients are severely mentally retarded and many of them have large ears, a short neck. A mild mongoloid slant, epicanthus, hypertelorism, strabismus, a flat upturned nose, a large open mouth, sometimes cleft palate<sup>2,3</sup>. Moreover, patients with 49, XXXXY may have congenital heart disease<sup>4</sup>. Testes are small and frequently undescended, scrotum is hypoplastic and penis is small. External genitalia might be ambiguous if there were hypospadias, bifid scrotum, hypoplastic phallus and cryptorchidism<sup>5</sup>. We can be suspicious about Down syndrome if they have simian line, short incurved terminal fifth phalanges and hypotonia. Our patient had depressed nasal bridge, flat upturned nose, hypertelorism, epicanthal folds, high arched palate, down-set ears and he was microcephalic and hypotonic. Apart from the described, he had micrognathia, antimongoloid

eyes, and the growth delay was observed. His osseous bone was retarded. Testes were descended and penis was normal. Patent ductus arteriosus was noted (Table I).

The most frequent reported radiograph abnormalities on the 49, XXXXY patients are radioulnar synostosis or dislocation, bowed radius and ulna, elongated radius, abnormal ossification centers in hands, pseudoepiphyses, epiphyseal dysgenesis, scoliosis, kyphosis, fusion of vertebral arches, costa anomalies, coxa valga and retarded osseous age<sup>4,5,6</sup>. Sijmons et al<sup>7</sup> reported a 12 year old mentally retarded boy who presented at birth with bilaterally knee dislocation and also dislocation of right hip and general joint laxity. Karyotype on this patient was 49, XXXXY<sup>8</sup>. Our patient had ulnoradial distal dislocation and club foot deformities. According to our knowledge, club foot deformity has not been described in the literature before.

Tumba et al. reported two patients with 49, XXXXY with their cerebral computed tomographies showing enlargement of the lateral ventricles and also one of them had the formation of pneumatic cavities in the parietal bones<sup>9</sup>. Our patient had cavum septum pellucidi varia-

tion on cerebral computerized tomography. This variation was evaluated normally in terms of the patient's age.

In conclusion, our case with 49, XXXXY had findings similar to the ones previously reported in literature. Moreover, this is the first report of Fraccaro syndrome with bilateral club foot, a new sign for this disease.

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