Bilateral Femoral Dysgenesis Syndrome: A Case Report.

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This paper reports a child with the *Bilateral femoral dysgenesis—unusual facies syndrome* (BFD–UF). The child has, in addition to previously reported findings, a *ventricular septal defect* with valvar and infundibular pulmonic stenosis, *absence* of *the labia majora,* bilateral syndactyly of the second and third toes, bifid great right toe and a pilonidal sinus. The similarity to cases of *Caudal Regression Syndrome* (phocomelic diabetic embryopathy) is noted.

The syndrome of cleft palate, bilateral femoral hypoplasia, and unusual facies (BFD-UF) has been described in several previous reports (Daentl et al., 1975; Gorlin et al., 1976; Smith, 1976). The purpose of this paper is to present a patient with this syndrome who has the previously unreported findings of ventricular septal defect with valvar and infundibular pulmonic stenosis.

Description

CCFD #910 (date of birth—7/12/73) is a 2-1/2-year-old Puerto Rican female, the product of the first pregnancy of a thirty-year-old woman and a thirty-seven-year-old man. The parents are nonconsanguineous. The family history is not contributory. Gestation was complicated by maternal hospitalization and treatment during the first trimester with tricyclic antidepressants and other psychoactive drugs for emotional disorder. The delivery was by Caesarean section because of nonprogression of labor. There was no perinatal distress and the Apgar score was 9/10. Birth weight was 1.9 kg. Length was well below normal limits because of absent femurs. Examination at birth revealed cleft palate and femoral aplasia with equinovarus deformity of the feet. The infant was kept in the hospital for 3 1/2 months for chronic respiratory difficulty which persisted throughout her first year. A heart murmur was first heard within the first month of life. At nine months, an orthopedic procedure to lengthen the Achilles tendon was performed.

From one year of age onward, the child reached normal developmental milestones and began to ambulate using her hands. Speech intelligibility remained poor, although vocabulary was normal.

At twenty-two months, she was first admitted to the hospital for pneumonia. Physical examination at that time revealed a length of 60 cm. (3rd percentile), weight 6.15 kg. (3rd percentile), and head circumference 45 cm. (5th percentile). Other pertinent findings included low-set hypoplastic ears (Figure 1), flattened nasal bridge, frontal bossing, micrognathia, (Figure 2) and a wide U-shaped cleft of the soft palate (Figure 3). Chest was symmetrical. The heart was not enlarged. There was a parasternal heave and a thrill along the left sternal border. S1 was normal;

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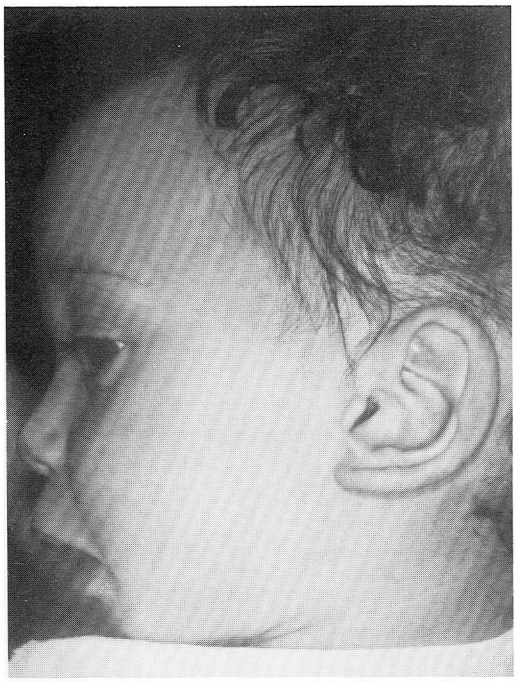

FIGURE 1. Lateral facial view showing malformed auricles, micrognathia and frontal bossing.

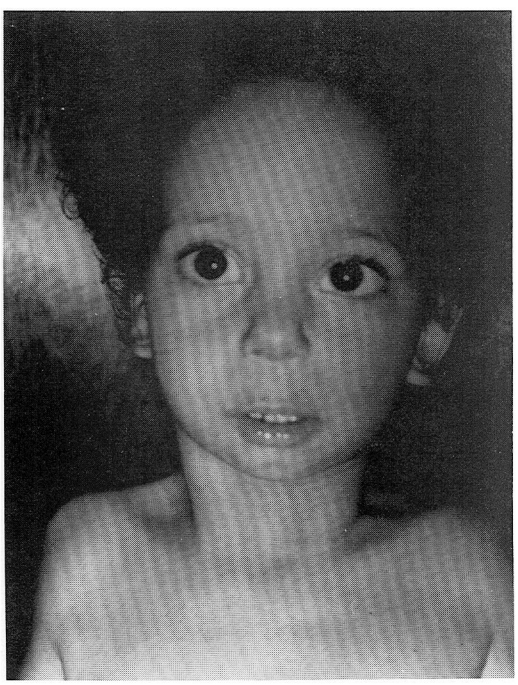

FIGURE 2. Frontal facial view showing shortened nose, long philtrum and micrognathia.

S2 was single. There was no click and no gallop. A Grade V/VI, harsh pansystolic murmur was heard. Liver and spleen were of normal size. There were no abnormal masses. The labia majora were absent (Figure 4).

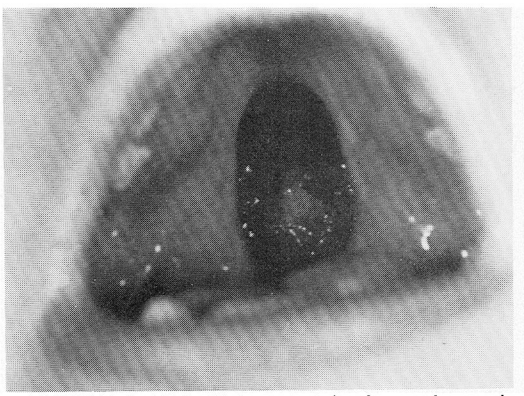

FIGURE 3. Wide U-shaped cleft of secondary palate.

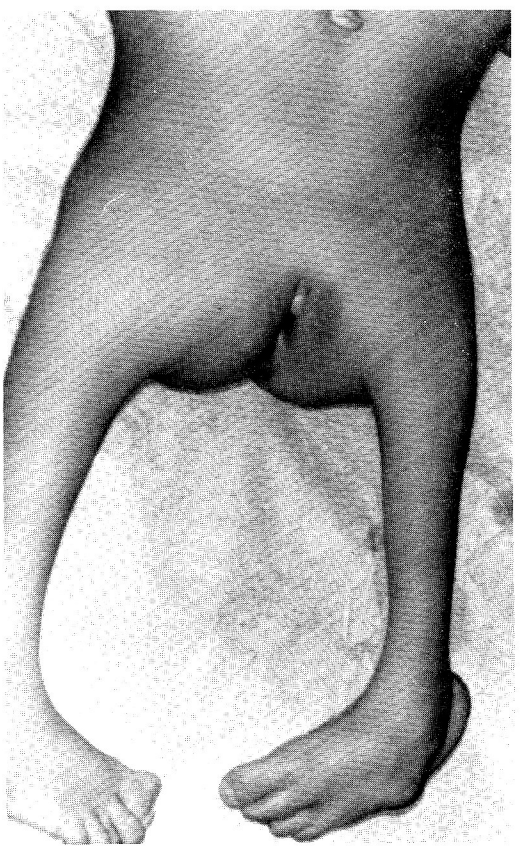

FIGURE 4. Lower torso showing hypoplastic external genitalia, shortened legs, residual varus deformity and polysyndactyly.

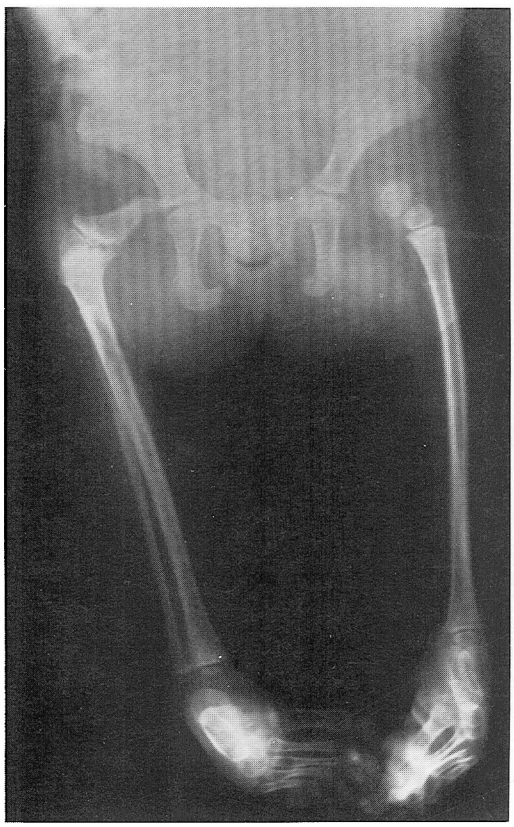

FIGURE 5. Radiograph of pelvis showing severely hypoplastic femurs, absent patellas and malformed feet bilaterally. Note normal orientation of tibia and fibula.

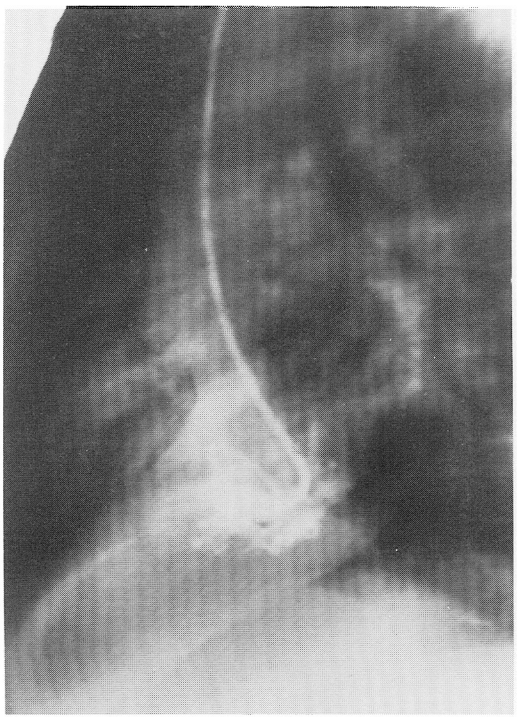

FIGURE 6. AP angiogram showing left to right ventricular level shunts, right aortic arch with mirror image branching.

Upper extremities were entirely normal with no limitation of motion. The spine showed accentuated lordosis. The coccyx was abnormally prominent with a deep dimple. Legs were shortened secondary to complete absence of the femoral shaft. No patella was identified. The tibia and fibula were in their normal orientation (Figure 5). The feet showed residual varus deformity and syndactyly of the second and third toe bilaterally and a bifid right great toe. Neurological examination revealed no deficit of sensation and no deficit of balance or coordination. Tendon reflexes of the lower extremities were difficult to elicit. Babinski response was plantar.

ECG revealed RVH and RAD. Chest x-ray showed mild cardiomegaly with predominantly right ventricular enlargement and pulmonary overcirculation. X-ray of the skull demonstrated micrognathia. The spine, pelvis, and lower extremities showed multiple abnormalities, including slight scoliosis and absent femoral heads and shafts with no acetabulae identified. Intravenous pyelogram revealed normal sized kidneys and normal collecting systems. Cardiac catheterization at age twenty-seven months demonstrated ventricular septal defect with systemic level right ventricular pressures with obstruction to flow in the outflow tract as well as at the pulmonary valve. There was minimal, if any, overriding of the aorta. The aortic arch was on the right with mirror image branching. There was minimal bidirectional shunting (Figure 6).

Discussion

We have reported a case of BFD-UF Syndrome with the previously unreported features of ventricular septal defect, absence of the labia majora, bilateral syndactyly of the second and third toes, bifid great right toe, and pilonidal sinus. It is important to note that, in no previous case, was the heart involved. The diagnosis of BFD-UF Syndrome is made on this overall pattern of anomalies,

not on any single feature. All abnormalities in this syndrome are individual and can occur as non-specific isolated defects. The Robin Complex has been described as a feature of seventeen known syndromes to date (Cohen, 1976; Gorlin et al., 1976; Hanson and Smith, 1975). It has been hypothesized repeatedly that a primary defect in mandibular growth prevents the tongue from descending into the mandible and, instead, causes it to mechanically impede the closing palatal shelves. This, therefore, explains the U-shape of the cleft. Ventricular septal defect can occur as an isolated anomaly. Femoral dysgenesis has been reported as an isolated anomaly as well (Bailey, 1970; Lenz et al., 1964; and Franz and O'Rahilly, 1961).

The grouping described in this patient is so distinctive that only one other pattern of malformation can be considered as part of the differential diagnosis and that is the previously mentioned syndrome of phocomelic diabetic embryopathy, sometimes referred to in the literature as Caudal Regression Syndrome (Passarge, 1966; Assemany, 1972; Lenz, 1964). However, even though in our case, there was no evidence of diabetes mellitus in the mother or in the family, it is noted that the case reported by Assemany et al., (1972) of an infant with phocomelic diabetic embryopathy bears a striking similarity to our patient.

All cases of BFD-UF syndrome to date have been sporadic and of unknown etiology. In the previously reported cases of Daentl et al., (1975) the fathers' ages were 25, 36, 27 and 22, respectively. In our case, the father was 37. The advanced paternal age in case #2 Daentl and our case suggests the possibility of a dominant mutation. In the case now reported, the mother was a frequent user of diazepam (Valium). It is of interest that, in the case of Assemany (1972), it is mentioned that the mother took Librium for "nerves." The etiology of this unique pattern of malformation and its relationship to maternal diabetes will require further study.

Reprints: Mrs. Rosalie Goldberg, Genetic Counselor, Center for Craniofacial Disorders, betes will require further study.

Addendum: Since this paper went to press, two further articles on the Bilateral Femoral Dysgenesis Syndrome by Eastman and Esobar (*Clin Genet*, 13: 72–76, 1978) and Gleiser et al (*Eur. J. Pediatr.*, 128: 1–5, 1978) have appeared. Clinical similarity to the Caudel Regression Syndrome was emphasized. Another pertinent reference is that of Holmes (*J. Pediat.*, 87: 668–669, 1975).

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