Case Report

High-Grade Vesicoureteral Reflux in Pfeiffer Syndrome

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INTRODUCTION

In 1964, Pfeiffer described an acrocephalosyndactyly syndrome consisting of bicoronal craniosynostosis, midface hypoplasia, broad thumbs, broad big toes, and partial and variable soft-tissue syndactyly of the hands and feet.[1] Autosomal dominant inheritance with complete penetrance is the main characteristic despite variable expressivity related to the presence or absence of syndactyly and its degree of severity. Based on the severity of the phenotype, Cohen proposed a classification of Pfeiffer syndrome into 3 clinical subtypes.[2] We report, a case of Pfeiffer syndrome type 2 with high-grade bilateral vesicoureteral reflux (VUR), and discuss the importance of surveillance for urogenital problems in patients with this syndrome.

CASE REPORT

A 4-month-old male infant was admitted to our hospital because of fever since 3 days earlier and generalized tonic-clonic seizure. He was a product of term normal vaginal delivery. He had 3 normal siblings. There was a history of abortion at the third month of gestation in the first maternal pregnancy. The parents had a normal phenotype and were not consanguineous. The mother was 34 years and the father was 36 years old.

The child had failure to thrive with a birth weight of 3.8 kg. His present weight was 4.5 kg. Developmental delay was also noticed. On physical examination, the patient had a cloverleaf skull, cleft palate, cleft lip, flat nasal bridge, broad toes, and low-set ears. Proptosis and some degree of strabismus were also noticed (Figure 1). On cardiac examination, a grade 2/6 systolic murmur was auscultated at the pulmonary area. Mild valvular pulmonary stenosis was documented by echocardiography.

Skull radiography showed acrocephaly and the prominence of temporal bones (cloverleaf skull). Computed tomography of the skull and brain showed bicoronal craniosynostosis and enlargement of lateral ventricles suggestive of moderate hydrocephalus. Electroencephalography showed paroxysmal discharge. According to the abovementioned findings, diagnosis of Pfeiffer syndrome was made clinically.

Ultrasonography of the urogenital

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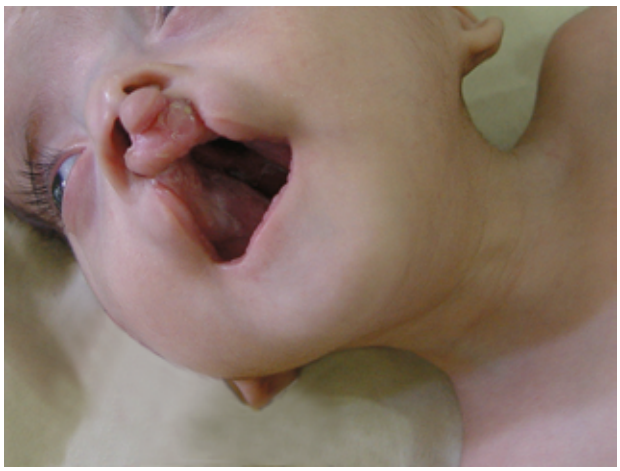

Figure 1. The patient had a cloverleaf skull, cleft palate, cleft lip, flat nasal bridge, low-set ears, proptosis, and some degree of strabismus.

system revealed intermittent dilatation in the pyelocaliceal system and also bilateral ureteral dilatation. The findings were suggestive of VUR. A grade 4 bilateral VUR was documented by voiding cystourethrography (Figure 2). Subsequently, dimercaptosuccinic acid renal scintigraphy showed bilateral cortical scars with moderate cortical loss in the right and severe cortical loss in the left side. Blood urea and serum creatinine were 32 mg/dL and 0.6 mg/dL, respectively. During the course of hospitalization, urinary tract infection was documented by an active urinalysis and a positive urine culture for pathogen microorganisms.

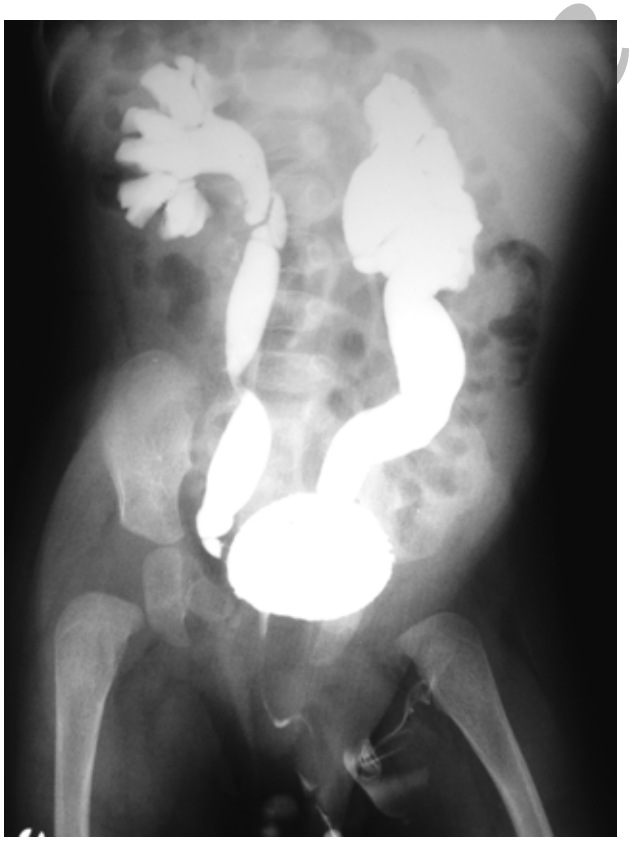

Figure 2. Voiding cystourethrography showed grade 4 bilateral vesicoureteral reflux.

DISCUSSION

The exact incidence of Pfeiffer syndrome is unknown, but is expected to be 1 in every 100 000 births in the western population. Approximately, 60 cases had been reported in the literature,[3] and it is even rarer in the Asian population, with few cases reported in Japan and Korea.[4,5]

Pfeiffer syndrome is known to be caused by mutations in exon IIIa or exon IIIc of the fibroblast growth factor receptor 1 or 2 gene.[6,7] Therefore, the disease is genetically heterogeneous. In Pfeiffer syndrome type 1, fresh mutations or autosomal dominance are the genetic disorders. In types 2 and 3, inheritance is sporadic. Pfeiffer syndrome type 1, which is named "classic," involves individuals with mild manifestations including brachycephaly, midface hypoplasia, and toe abnormalities. This type is associated with normal intelligence and generally good outcome. Pfeiffer syndrome type 2 consists of cloverleaf skull, extreme proptosis, finger and toe abnormalities, elbow ankylosis or synostosis, developmental delay, and neurologic complications. Type 3 of this syndrome is similar to type 2, but without a cloverleaf skull. It should be noted that clinical overlap between the three types may occur.[2] Our patient had clinical manifestations in favor of Pfeiffer syndrome type 2 in addition to high-grade bilateral VUR.

Cloverleaf skull is a characteristic feature of Pfeiffer syndrome type 2, which is often associated with hydrocephalus due to aqueductal stenosis. Patients with Pfeiffer syndrome type 2 may have variable degrees of abnormalities in their hands and feet, including elbow ankylosis, short broad thumbs, and big toes which are deviated away from other digits.[5,8,9] They may have other congenital anomalies of the upper airway, cleft palate, cleft lip, choanal atresia, fused vertebrae, imperforate anus, hydrocephalus,

and Arnold-Chiari malformation.[5] There have been occasional reports of hydronephrosis (without any obvious etiology) and pelvic kidney as abnormalities of the urogenital system accompanying Pfeiffer syndrome.[2,3] However, to our knowledge, the association of Pfeiffer syndrome and VUR has not been reported to date. This shows the importance of investigation for urogenital abnormalities not described yet such as VUR, especially when presenting with urinary tract infection.

CONFLICT OF INTEREST

None declared.

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