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Minor dysmorphic features in a patient with papillorenal syndrome – A Case Report

Ferit Kulali[1], Ahmet Yagmur Bas[2], Fatma Iyigun Guzel[3], Husniye Yucel[4], Caner Kara[5], Cigdem Uner[6], Nihal Demirel[7]

1 Dr. Behcet Uz Child Disease and Pediatric Surgery Training and Research Hospital, Turkey; **2,3,5,7** Etlik Zubeyde Hanim Women's Health Teaching and Research Hospital, Turkey; **4 6** Dr. Sami Ulus Maternity and Children Research and Training Hospital, Turkey

Correspondence: Ferit Kulali. **Email**: fkulali@hotmail.com

Abstract

Papillorenal syndrome, also known as renal coloboma syndrome, is characterised by congenital optic disc anomalies and renal abnormality. The syndrome causes mutations in the PAX2 gene, which plays a critical role in embryogenesis. Other related anomalies are less commonly observed.

To our knowledge, ours is the first case reported in the literature in which Papillorenal syndrome accompanied various dysmorphic features.

Keywords: Renal coloboma syndrome; PAX2-related disorder; coloboma of optic nerve, multicystic dysplastic kidney; eye abnormalities

Introduction

Papillorenal syndrome, also known as renal coloboma syndrome, is characterised by congenital optic disc anomalies and renal abnormality.(1) Since the first case was reported by Rieger, more than 180 cases with Papillorenal syndrome have been reported worldwide.(2) This syndrome is inherited in an autosomal dominant pattern and is often associated with mutations in the PAX2

gene. The PAX2 gene is located on chromosome 10 that is expressed in primitive cells of the kidney, ureter, eye, ear and central nervous system.[3] A diagnosis of Papillorenal syndrome should be made in the presence of characteristic fundus findings and renal disease.[2] Other extrarenal manifestations such as Arnold-Chiari malformation, seizures, and joint laxity have been observed in less than 20% of Papillorenal syndrome patients.[4] We believe, we are reporting the first case of minor dysmorphic features accompanied with Papillorenal syndrome.

Case Report

A girl was born by Caesarean section at 35 weeks gestation, weighing 1,400 gm, with head circumference of 28.0 cm, to non-consanguineous parents. The case was seen at Etlik Zubeyde Hanim Women's Health Teaching and Research Hospital in June 2016. The mother was a 33-year-old gravida 2 para 2 and had received regular prenatal care throughout the pregnancy. Family history was unremarkable. A third-trimester ultrasound showed intrauterine growth retardation and multiple cortical cysts within the left kidney. Amniocentesis was performed for elevated maternal alpha-fetoprotein level and the karyotype was 46, XX.

There were no complications during delivery, and Apgar scores were 7 and 8 at one and five minutes, respectively. After birth, the infant was noted to have mild respiratory distress. She was started on oxygen supplementation and was transferred to the neonatal intensive care unit. Physical examination revealed respiratory rate of 66 breaths per minute, dysmorphic features including hypoplastic nails, clinodactyly of the second fingers and toes, equinovarus deformity in left foot, together with hypotonia. Laboratory tests were within normal limits. Chest radiography and cranial ultrasound were normal. Abdominal ultrasound scan showed left multicystic dysplastic kidney and right hydronephrosis grade 1 (Fig. 1). Echocardiogram revealed patent foramen ovale.

Ophthalmological examination showed “morning glory” of right optic disc (Fig. 2). On the basis of the ophthalmological findings along with abdominal ultrasound scan, Papillorenal syndrome was diagnosed. Renal function and urine test results, blood pressure measurements, and auditory tests (auditory evoked potentials, otoacoustic emissions) were within normal limits.All family members were examined for ocular and renal findings but there were no signs of kidney or eye disease. She was discharged from the hospital on postnatal day 33. The patient was given antibiotic prophylaxis for prevention of urinary tract infection and was regularly followed by a multidisciplinary team including a neonatologist, a paediatric nephrologist, an audiologist, a paediatric genetic specialist and a paediatric ophthalmologist. Physical, neurological and developmental assessments were performed for 18 months but no complications were noticed in the patient. The parents were concerned about the long-term prognosis of Papillorenal syndrome including the risk of development of end stage renal disease and visual outcome.

Discussion

Papillorenal syndrome is characterised by congenital optic disc anomalies and renal abnormality. We suspected that PAPRS due to ocular and renal findings. The characteristic optic disc anomalies are optic nerve dysplasia, optic disc coloboma and morning glory anomaly (a congenital cavity of the peripapillary fundus, expansion of the optic disc). The most common renal findings are renal hypoplasia, renal hypodysplasia, vesicoureteric reflux, oligomeganephronia, horseshoe kidney and multicystic dysplastic kidney[1]. In our patient, there are both the morning glory anomaly and multicystic dysplastic kidney. Diagnosis of the Papillorenal syndrome is typically made on the basis of clinical findings. It has been reported that the majority of published cases have mutations in PAX2[1]. In our patient, chromosomal analysis revealed 46,XX with deletion of chromosome 10 (q25.2q26.3). Although Sanger sequence analysis is important

because there is a relationship between the presence of PAX2 gene mutations and the risk of development of end-stage renal disease, we could not perform the analysis for PAX2 gene due to expense issues. In some publications, optic disc appearance is considered a more reliable finding than PAX-2 gene mutation for diagnosis[5]. The diagnosis of Papillorenal syndrome is made in the presence of chromosomal 10 (q25.2q26.3) deletion, morning glory anomaly and multicystic dysplastic kidney.

Papillorenal syndrome can also be associated with other anomalies as Arnold-Chiari malformation, seizures of unknown cause, sensorineural hearing loss, and joint laxity.[4] To our knowledge, skeletal abnormalities associated with Papillorenal syndrome have not yet been described. We report various skeletal abnormalities including hypoplastic nails, clinodactyly, equinovarus deformity, and hypotonia. Diagnosis of Papillorenal syndrome was made by Hoefeleet al[4] and the same mutations on chromosome 10q were also reported. Although our patient had hypoplastic nails, clinodactyly, equinovarus deformity, and hypotonia, their patient had only pes calcaneous. These results indicate that the mutations probably cause dysmorphic features in patients with Papillorenal syndrome. Minor dysmorphic features may occur due to deletions in chromosome 10q.

The differential diagnosis of Papillorenal syndrome should include CHARGE syndrome, branchio-oto-renal syndrome and Joubert syndrome.[2] Comprehensive evaluation is essential, particularly before development of complications to assess disease extent and severity. No accurate and reliable prognostic data for Papillorenal syndrome is available due to rarity of the syndrome. While it increases the risk of retinal detachment in patients with optic nerve dysplasia (coloboma), patients with mutations in PAX2 have an increased risk of developing end-stage renal disease. Visual acuity ranges from normal to light perception only. Impaired visual acuity have been reported in approximately 75% of Papillorenal syndrome patients.[2] Renal disease can occur at any age

from birth to 79 years and usually is progressive.[2] Early identification of patients with Papillorenal syndrome is important because future complications such as blindness, end-stage renal disease and hearing loss can be followed through.

Conclusion

Papillorenal syndrome, also known as renal coloboma syndrome, is a rare clinical, radiologic and ophthalmological condition. Papillorenal syndrome should be considered in the presence of the combination of renal and ocular anomalies. The patient with papillorenal syndrome should be monitored closely due to high-frequency sensorineural hearing loss as well as ocular and renal anomalies.

In conclusion, we have presented one patient with a classic clinical presentation of Papillorenal syndrome having skeletal abnormalities not previously described.

Informed Consent: Written informed consent was obtained from the parent who participated in this study.

Disclaimer: None to declared.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Figure 1: Left multicystic dysplastic kidney

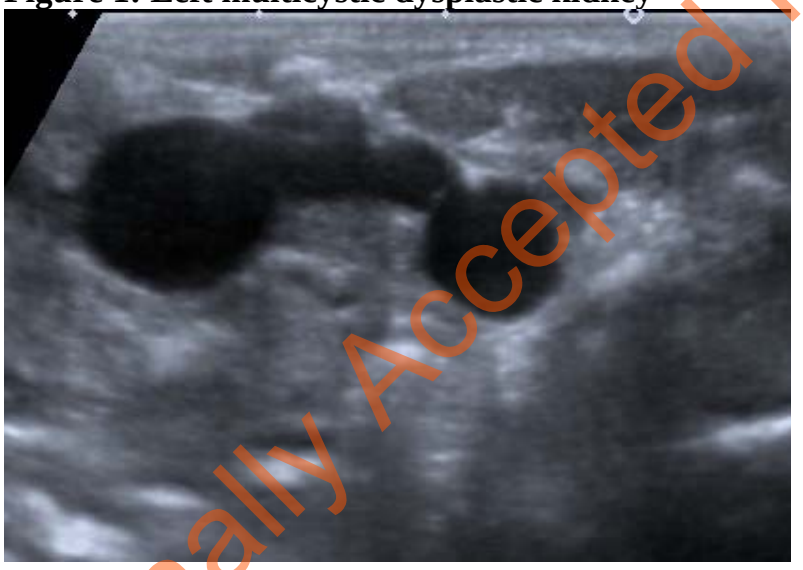

Figure 2: Fundus photograph showing morning glory anomaly