Case Series

Acrorenal ocular syndrome: Case series of a rare familial congenital syndrome

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ABSTRACT

Acrorenal ocular syndrome includes a spectrum of acral anomalies such as oligodactyly, ectrodactyly, syndactyly, brachydactyly, humerus/carpal hypoplasia, cutaneous syndactyly, and renal anomalies such as unilateral renal agenesis, unilateral hypoplasia, ectopia, horseshoe kidney, and vesico-ureteric reflex. The common ocular manifestations include Duane anomaly, coloboma, and ptosis.

Keywords: Renal anomaly, Acral anomaly, Familial syndrome

INTRODUCTION

Acrorenal syndrome is a spectrum of congenital disorders characterized by the cooccurrence of distal limb anomalies and renal defects that can be associated with other anomalies such as those of genitourinary tract (genital anomalies, ureteral hypoplasias, and vesicoureteral reflux), abdominal wall defects, intestinal atresias, and lung malformations. Familial cases have been reported which may have either autosomal recessive or dominant inheritance.

CASE SERIES

Case 1

The propositus is a 25-years-old male, who presented with congenital acral anomalies decreased appetite since a month, easy fatigability since a month, and increasing pedal edema since a month. He is born of a second-degree consanguineous marriage; term, normal vaginal delivery, cried normally after birth; there is no history of maternal diabetes/hypertension/abnormal drug intake. The developmental history is normal. He was apparently normal until the age of 19 years when he developed facial puffiness and bilateral pedal edema. These were gradually progressive but there was no history of decreased urine output, hematuria, fever, or recurrent UTI. Urine microscopy showed presence of albumin (+ + +), RBCs (6−8), and epithelial cells (1−2/hpf). Serum creatinine was 1.5 mg/dL, urea 35, BH 14.9, total count 13600, fasting glucose 112, serum cholesterol 221, and serum albumin 3.2 g.
The acral anomalies noted are oligodactyly, absent bilateral thumb, syndactyly and deformed, and fused carpal bones. Abdominal CT plain showed absent right kidney and normal position of the left kidney [Figure 1]. Further evaluation of the patient showed no cardiac abnormalities, no neurological abnormalities, no eye abnormalities, no spine abnormalities, and no lower limb deformities. CT brain plain and 2D echo were normal.

Case 2

He is the younger brother of Case 1, 19-year-old, and had no presenting complaints. The patient was found to have acral anomalies at birth, which included bilateral hypoplastic thumbs, oligodactyly, syndactyly, and deformed/fused carpal bones. On imaging, the patient was found to have left cross fused ectopia [Figure 2]. Serum urea and creatinine were normal. However, he also did not have any eye abnormalities, no facial deformities, no lower limb deformities, no cardiac abnormalities, and no neurological abnormalities.

On further inquiry, we found that the patient’s sister, who is younger to him also has acral abnormalities. Other than these three, three other people in the family, the propositus's father, paternal uncle and paternal aunt also had acral abnormalities, and all three have died. His father had two renal transplants and paternal uncle also had a renal transplant. Eye abnormalities could not be evaluated in other cases in the family except the propositus and his brother.

DISCUSSION

The incidence of renal and acral anomalies occurring together was first described by Dieter and Opitz in 1969.[2-4] The term acrorenal syndrome in such cooccurrences was first used by Curran and Curran in 1972.[3] The constellation of acral, renal, and eye anomalies represents a distinct autosomal dominant trait of variable expressivity in this syndrome.[3,5] Embryological fact is that development of all these organs is considered to be completed in the 6–8th week of embryogenesis.[6]

Difficulty in diagnosis often arise when not all features is present in an affected subject or within a family. The differential diagnosis of SALL4 (a gene product is a zinc finger protein which act as a transcription factor) related diseases includes Duane-radial ray syndrome (DRRS), (DRRS Okihiro syndrome), and SALL4-related Holt-Oram syndrome.[7] Other conditions such as Goldenhar syndrome, Wildervanck syndrome, Townes-Brocks syndrome, and Duane anomaly also possess certain constellation of findings similar to above SALL4-related diseases.[8]

Goldenhar syndrome differs from Okihiro syndrome and the acro-renal-ocular syndrome by the presence of hemifacial microsomia and epibulbar dermoid.[6] Goldenhar-like features including Duane anomaly can also be seen with Townes-Brocks syndrome. However, the later also feature renal anomaly, Sensorineural hearing loss, and thumb abnormalities.[8] In the acro-renal-ocular syndrome, renal abnormalities are frequent, but radial ray defects and/or ophthalmological findings may be
absent whereas, Wildervanck syndromes are characterized by the absence of limb abnormalities. Facial asymmetry and microtia have been reported frequently with Okihiro syndrome.[6]

The other syndromes that manifest with renal agenesis include Branchio-oto-renal syndrome (Melnick-Fraser syndrome), Renal coloboma syndrome (papillorenal syndrome), Alagille syndrome (arteriohepatic dysplasia), Winter syndrome, and CHARGE association.[1]

Branchio-oto-renal syndrome (Melnick-Fraser syndrome) is an autosomal dominant disease characterized by coexistence of deafness, branchial fistulae, pre-auricular pits, and renal anomalies, unilateral agenesis being more common.[1] Renal coloboma syndrome (papillorenal syndrome) is characterized by renal hypoplasia and agenesis, vesicoureteral reflux, and optic nerve coloboma. Almost all patients develop end-stage kidney disease.[8]

Alagille syndrome (arteriohepatic dysplasia) show marked arterionephrosclerosis with diffuse calcinosis, vertebral anomalies (butterfly vertebrae), peripheral pulmonary stenosis, mental and growth retardation, and neonatal cholestasis.[3] Winter syndrome is compiled by renal agenesis (unilateral/bilateral), middle-ear anomalies and internal genital malformations are noted in these patients.[1] CHARGE association includes duplicated upper pole of one kidney, coloboma, choanal atresia, cardiac, genital, and ear defects.[1]

**CONCLUSION**

To conclude, SALL 4-related diseases are rare and one should be aware of all the syndromes. In our case due to no availability of genetic testing in our center, the patient was referred to a higher center for genetic/chromosomal testing and for further treatment. Counseling the patients against consanguineous marriage is important to prevent genetic inheritance of the disease.

### TEACHING POINTS

1. It is important to be aware of these syndromes as they are very rare. It is also important to look for other abnormalities of a syndrome when suspected.
2. As they run in families of subsequent generation, genetic tree mapping to be done to assess the penetration and severity of the disease. It is also very important to create awareness about genetic counseling in consanguineous marriage.

### MCQ

1. All are SALL-4 associated syndromes except?
   a) DRRS
   b) Okihiro syndrome
   c) Acro-renal-ocular syndrome
   d) Renal coloboma
   Answer Key: d

2. All are manifestations of acro-renal ocular syndrome except?
   a) Oligodactyly
   b) Renal agenesis
   c) Ocular coloboma
   d) Retinal detachment
   e) Vesico-ureteric reflux
   Answer: d

3. What is the mode of inheritance of SALL-4 associated syndromes?
   a) Autosomal dominant
b) Autosomal recessive

c) X-linked recessive

d) X-linked dominant

Answer: a

Declaration of patient consent

The authors certify that they have obtained appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES


