Abstract:
Branchio-oto-renal syndrome (Melnick-Fraser syndrome) is a rare autosomal dominant disorder characterized by syndromic association of branchial cysts or fistulae along with external, middle, inner ear malformations and renal anomalies. We are reporting an 8 yrs old male child born to second degree consanguinous parents who presented with oliguria, stunted growth and right anotia. Ultrasound abdomen revealed a cyst (2X1.5mm) in left renal area, right hydronephrosis. He was diagnosed as a case of Branchio-oto-renal syndrome (Melnick-Fraser syndrome) and his parents and sibling were normal.

Keyword: Branchio-Oto-Renal Syndrome, Anotia, Posterior Urethral Valve (PUV)

INTRODUCTION:
Branchio-oto-renal (BOR) syndrome refers to an autosomal dominant disorder occurring in approximately 1:40,000 new born infants. BOR syndrome is associated with major clinical findings of branchial cysts or fistulae, external ear malformation and/or preauricular sinus, various types of hearing loss and renal anomalies ranging from mild, asymptomatic hypoplasia or dysplasia to complete agenesis of kidney. Phenotypic presentation of BOR syndrome is extremely variable.

CASE DESCRIPTION
Eight years old male child presented to our paediatric medical department with history of breathlessness for four days, low grade fever for two days and not passed urine for 24 hours. On examination the child was irritable with effortless tachypnoea with no features of shock. Child developed seizure (uprolling eye balls) once during the stay and it was the first episode. There was previous history of breathlessness, fever and diminished urine output for which he was not evaluated. His height was 96 cms against 125 cms. This is 76.8% falling under short stature according to McLaren's classifications. His weight was 10kgs against 25.5kgs. This is 39% coming under grade IV malnutrition according to Indian academy of paediatrics classification. Upper to lower segment ratio was 1:1.
Head circumference was 47cms. Blood pressure measurement with mercury sphygmomanometer showed hypertension (140/90mm of Hg) in right arm in supine position. Clinical examination revealed right side anotia (figure 1) with mild hearing loss on left side and short stature (figure 2). There was no branchial cyst or fistula. Cardiovascular examination was normal. Abdominal examination showed no organomegaly. Central nervous system examination showed normal motor and sensory system. There were no meningeal signs.

Haemoglobin 9.1gms %, urea 106mg %, creatinine 3.5 mg%, sodium 118moll equiv. per liter. Ultrasonogram of abdomen and pelvis showed right hydronephrosis, cyst in left renal area with thickened (8 mm) and irregular bladder wall with no abnormality mentioned in urethra. Urine culture showed growth of klebsiella sensitive to cefotaxime. Micturating cysto urethrogram was done which showed irregular trabeculated bladder wall, dilated posterior urethra and no vesicoureteric reflux. Cystoscopy with vesicostomy was done under caudal analgesia. Cystoscopy revealed gritty and congested mucosa of anterior urethra, roomy valves of posterior urethra and normal ureteric orifice. Fulguration procedure was not completed due to bleeding. Hence cystostomy was planned after three months. Since there was anaemia, hypertension, elevated renal parameters, short stature and seizure, child was suspected to have chronic renal failure probably due to obstructive uropathy. He was treated with appropriate intravenous fluids, antibiotics and anticonvulsant drug. Presence of right anotia and right hydronephrosis with left renal cyst meets minimal criteria for the diagnosis of branchio-oto-renal syndrome for this child.

**DISCUSSION**

Branchiootorenal syndrome (BOR; OMIM 113650) is an autosomal dominant disorder caused by mutations in the EYA1 gene (OMIM 601653). BOR is characterized by hearing loss, branchial cleft fistulas or cysts, ear pits, renal dysplasia, and otologic manifestations ranging from mild hypoplasia to complete absence with reduced penetrance and variable expressivity [Melnick et al., 1975; Fraser et al., 1978]. Clinical diagnosis of BOR is based on the presence of (1) at least three major criteria including branchial anomalies, deafness, preauricular pits, and renal abnormalities, (2) two major criteria, and at least two minor criteria including external ear anomalies, middle ear anomalies, inner ear anomalies, preauricular tags, facial asymmetry, and palate abnormalities, or (3) one major criterion and an affected first-degree relative who meets the criteria for BOR syndrome [Chang et al., 2004]. Branchiooticsyndrome (BOS; OMIM 602588), a related disorder but without the renal anomalies, can also be caused by allelic defects in EYA1. The Branchio-oto-renal syndrome is an infrequent but well described entity that combines deafness, early onset renal failure together with branchial clefts & pre auricular pits. Among profoundly deaf children 2% are diagnosed to have BOR syndrome. EYA 1, the human homologue of the drosophilia eye absent gene plays an important role in the development of BOR syndrome. EYA 1 gene maps on 8q13.3 chromosome and expresses very early, between 4th & 6th weeks of human embryogenesis. Deafness relates to abnormalities in the three ossicles of the middle ear derived from the first and second branchial arches, while the branchial fistulae relates to second, third and fourth arches. EYA 1 gene is strongly expressed in the human embryonic kidney and in
BOR syndrome there is fault between the ureteric bud and metanephric mesenchymal mass as the ureteric bud branches into renal parenchyma, resulting in renal anomalies. Deafness is the most common presenting symptom reported in 90% of cases which can be conductive (30%) or sensorineural (20%) but is most often mixed (50%). Preauricular pits are present in 70% to 80% patients and sometimes can be the only external ear finding while 30% to 60% patients with BOR syndrome have external ear anomalies in the form of microtia to small lop or cupped ears with over folded superior helices. Middle ear anomalies include ossicular malformations (fusion, displacement, and underdevelopment), facial nerve dehiscence, absence of oval window and reduction in the size of middle ear cleft and inner ear anomalies include cochlear hypoplasia or dysplasia. Enlargement of the cochlear or vestibular aqueducts may be seen and there may be hypoplasia of the lateral semicircular canal. Structural kidney anomalies seen in 12% to 20% patients, includes unilateral renal agenesis with contralateral hypodysplasia or bilateral hypodysplasia that lead to end-stage renal disease (ESRD). Less common findings are preauricular tags (13%), lacrimal duct aplasia (11%), short palate (7%), retrognathia, euthyroid goitre and facial paralysis. BOR syndrome often may be confused with Alport’s syndrome, characterised by deafness, chronic renal failure, anterior lenticonus & other eye disorders. Anterior lenticonus, a conical protrusion of the central portion of lens in to the anterior chamber is pathognomonic for Alport’s syndrome. Retinal changes of perimacular flecks are also found in 35% cases of Alport’s syndrome. Other uncommon ocular lesions include recurrent corneal ulceration and corneal endothelial vesicles. Deafness in the Alport’s syndrome manifests at a later age.

REFERENCES:


