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Short Communication

Cochlear implantation in branchio-oto-renal syndrome – A surgical challenge

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Abstract

Branchio-oto-renal syndrome (Melnick-Fraser Syndrome) is a rare Autosomal Dominant disorder characterized by the syndromic association of branchial cysts or fistulae along with external, middle & inner malformations and renal anomalies. Incomplete penetrance and variable expressivity are common with the phenotypic variation ranging from mild to severe forms & consisting of various eye, ear, oral and craniofacial abnormalities. Mutations in the EYA1 gene on chromosomal site 8q13.3 are identified as the primary cause of BOR syndrome. We present a 3year old child with BOR syndrome, who came to us with bilateral low set, malformed ears & profound cochlear hearing loss along with bilateral branchial fistulae & unilateral renal agenesis. This child underwent successful cochlear implantation recently. The clinical presentation, pre-operative investigations, intra-operative findings & post-op habilitation status are presented with special highlights on the unique facial nerve course along with middle and inner ear anomalies which posed a surgical challenge during cochlear implantation.

Keywords Branchio-oto-renal syndrome · Renal EYA1 gene · facial nerve anomaly

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Introduction

Branchio-oto-renal syndrome (BOR or Melnick-Fraser syndrome) refers to an autosomal dominant disorder occurring in approximately 1:40,000 births, which is associated with major clinical findings of branchial cysts or fistulae, external ear malformation and/or preauricular pits, various types of hearing loss and renal anomalies ranging from mild, asymptomatic hypoplasia or dysplasia to complete agenesis of kidney [1, 2]. The group of branchial, otic and renal anomalies observed in BOR syndrome is extremely variable. In a series of 45 individuals, reported by Chen et al [3], hearing loss was observed in 93%, preauricular pits in 82%, "lop-ear" deformity in 36%, branchial fistulae or cysts in 50% and renal anomalies in 67% of cases. Less common findings included preauricular tags (13%), lacrimal duct aplasia (11%) and short palate (7%). BOR syndrome occurs in about 2% of profoundly deaf children [4].

Renal malformations are common and can be unilateral or bilateral and occur in any combination. BOR gene expression is extremely variable from one family to another.

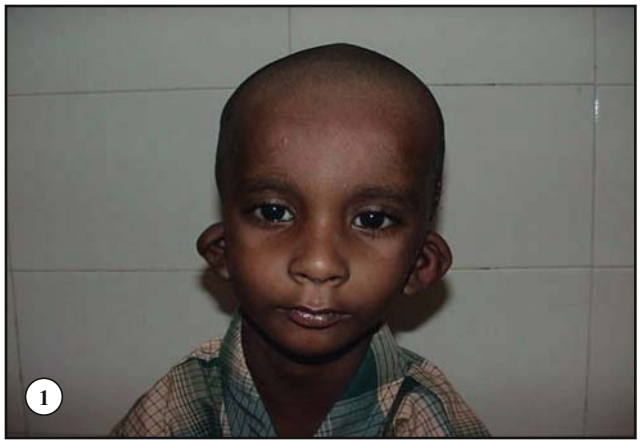

Fig. 1 Low set lop ears

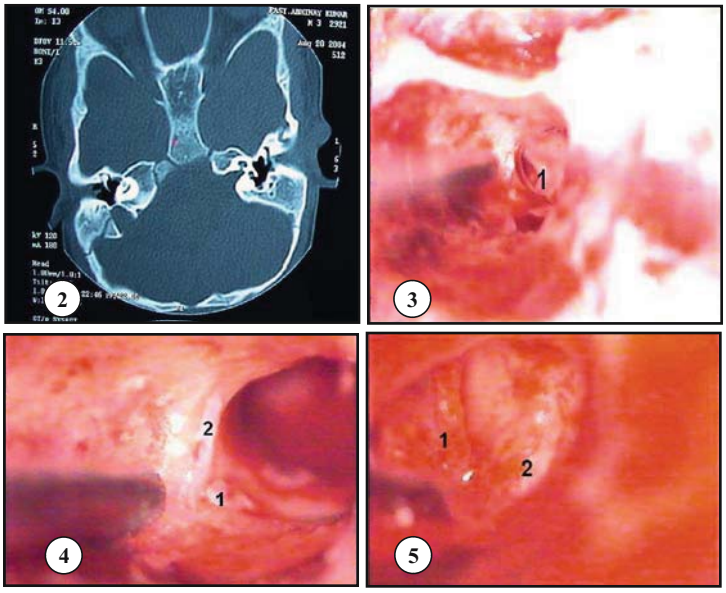

Fig. 2 HRCT temporal bone showing bilateral mondini deformity with vestibular dysplasia

Fig. 3 Wide aditus with malformed, exposed incudo-stapedial joint

Fig. 4 Dehiscent facial nerve (vertical segment) at chorda tympani origin.

Fig. 5 Monopodal stapes with exposed facial nerve (2nd genu) seen through a wide aditus.

When there are two or more affected family members, the presence of two findings is sufficient to establish the diagnosis, but in individuals with no other affected family members, the diagnosis is established by the presence of at least three findings. The BOR gene was mapped to 8q13.3 chromosomal site by linkage analysis [5, 6] and it was soon cloned and found to yield sequences homologous to the drosophila "eyes absent" (EYA) gene. The EYA1 gene, the human homologue of the drosophila "eyes absent" gene and three other related genes (EYA2, EYA3 and EYA4) play an important role in development of BOR syndrome. The EYA1 gene is expressed very early, between the 4th and 6th weeks of human embryogenesis [7]. Deafness relates to abnormalities in the three ossicles of the middle ear derived from the first and second branchial arches, while the branchial fistulae relate to abnormalities of the second, third and fourth arches [8].

Case report

A 3 year old male child, born of non-consanguinous parentage, presented to our clinic with history of bilateral profound congenital hearing loss detected at the age of 10 months. There was no family history of deafness. The child was given body-worn hearing aids to both ears at the age of 1 yr, with very little benefit and had poor speech development. He had an unremarkable pre-natal history except for oligohydramnios & breech presentation. The child was delivered by caesarian section at full term & Apgar score at birth was good. All neonatal & infantile milestones were normal. Bilateral branchial fistulae excision was done at 3 months of age. On further work-up at 9 months of age by the paediatrician, the right kidney could not be visualised by trans-abdominal ultrasonography. Subsequent DTPA scan revealed a dysmorphic, small sized and poor functioning right kidney. A grade II vesico-ureteral reflux on both sides was documented by micturating cysto-urethrogram. The relative renal functions were 92% on left & 8% on right side.

The child had low set, cup-shaped ears with a left pre-auricular sinus. On audiological work-up, in both ears, BERA waves could not be identified even at 99dbHL, DPOAE emissions were absent & ASSR thresholds could not be observed. Radiological assessment with HRCT scan of temporal bone & MRI of inner ear showed severe dysplasia of vestibule, dilated semicircular canals and malformed ossicles on both sides. Genetic work up with Karyotyping showed normal cyto-genetic study. IgM antibodies were positive on TORCH screening while complete blood work up was normal.

This child was taken up for left ear cochlear implantation at 3 years of age. The unique intra-operative findings encountered posed a surgical challenge, since the child had a contracted mastoid antrum with low-lying dura and a wide aditus-ad-antrum. Through this large aditus a malformed incus with absent short process and a rudimentary lenticular process was noted. A monopodal stapes with only the posterior crus were also seen. The malleus appeared fixed to the incus & the incudo-stapedial joint and footplate of stapes were also fixed. The course of the facial nerve was much more posterior than usual and its vertical course was visualized within the mastoid antrum. The facial canal was dehiscent near the origin of chorda tympani in the floor of the large aditus. The dome of lateral semicircular canal was not prominent. The cochlea appeared rotated cranially, the promontory appeared flat and the basal turn was at higher

level than normal. Hence the cochleostomy was sited more antero-superior to the round window niche than the usual site.

A Nucleus 24 channel straight array was inserted and 19 electrodes could be negotiated into the cochlea. Intra-operative neural response telemetry was normal. Post operatively the facial nerve function was normal. The child had an uneventful post-operative period & the post aural sutures were removed on the tenth post-operative day. Switch-on of the device was done 3 weeks after surgery & initial mapping responses were good. Child is undergoing intensive auditory verbal habilitation & is presently showing good improvement with closed-set speech recognition.

Discussion

The branchio-oto-renal (BOR) syndrome is an infrequent but well-described entity that combines early-onset renal failure and deafness together with branchial clefts & pre-auricular pits [9, 10]. The BOR syndrome is an autosomal dominant condition, characterized by conductive, sensorineural or mixed hearing loss of early onset, pre-auricular pits, cervical branchial clefts and renal anomalies which may progress to chronic renal failure in up to 40% of affected members. This syndrome is caused by genetic mutations in the EYA1 gene that maps on chromosome 8q13.3 [7, 9, 10]. In the embryonic human kidney the EYA1 gene is expressed strongly and in BOR syndrome there is an inductive fault between the ureteric bud and the metanephric mesenchymal mass as the ureteric bud branches into the renal parenchyma, resulting in renal anomalies.

Approximately 60% of cases have branchial cysts or fistulas, usually found on the external lower third of the neck, at the median border of the sternocleidomastoid muscle and 30% to 60% of patients with BOR have ear anomalies that range from severe microtia to small, lop or cupped ears with over-folded superior helices similar to TBS ears [11] Pre-auricular pits are present in 70% to 80% and sometimes can be the only external ear finding. There is a correlation between progressive, fluctuant sensorineural hearing loss with caloric hypofunction and the presence of an enlarged vestibular aqueduct in the BOR syndrome [11]. At least 75% have conductive, sensorineural, or mixed hearing loss, and 12% to 20% have structural kidney anomalies [12]. The most important renal abnormalities that lead to end-stage renal disease (ESRD) include unilateral renal agenesis with contralateral hypodysplasia or bilateral hypodysplasia characterized classically on ultrasound by decreased renal volume and size, loss of normal cortico-medullary differentiation and hyper-echogenicity of the renal cortex [13].

Many studies, have noted a significant association between renal anomalies and various ear anomalies. Ear pits and tags which are the most common minor ear malformation, occur with a frequency of 5 to 6 per 1000 live births. In the pediatric population, structural renal anomalies occur in 1 to 3 per 100 live births. A recent study [14] of 32,589 consecutive live births, still births, and abortions over 10 years in the Mainz Congenital Birth Defect Monitoring System noted a 1.2% prevalence of renal anomalies. External ear anomalies of all types, including deformations from fetal constraint, were found in 19.0% of all newborns, compared with 23.8% in newborns with renal malformations, showing a slightly significant increased risk (odds ratio: 1.3) for renal anomalies in children with ear anomalies. After patients with syndromic diagnoses were excluded, there continued to be a strong association between auricular pits or cup ears and specific renal anomalies. Kohelet and Arbel [15] noted that among 70 consecutive children who had isolated preauricular tags and were examined by renal ultrasonography, 6 (8.6%) had urinary tract abnormalities (5 with hydronephrosis, 1 with horseshoe kidney). Thus BOR syndrome needs to be included as an important differential diagnosis for deafness with chronic renal failure in childhood and adolescence. Due to the combination of deafness with chronic renal failure, it may often be confused with Alport's syndrome wherein deafness manifests at a later age.

Various ossicular chain defects & vestibular anomalies found by temporal bone imaging in cases of BOR syndrome have been widely discussed in recent literature [16, 17, 18] Propst EJ et al [18] described the most common characteristics of BOR on temporal bone imaging to be, 1) hypoplastic apical turn of the cochlea, 2) facial nerve deviated to the medial side of the cochlea, 3) funnel-shaped internal auditory canal, and 4) patulous eustachian tube.

The child we present in our case report, has all features of BOR syndrome such as low set lop ears, left pre-auricular sinus, ossicular chain & inner ear anomalies, along with bilateral branchial fistulae and unilateral renal agenesis. The unique intra-operative findings which we encountered were a cranially rotated cochlea, a wide aditus & an anomalous, dehiscent facial nerve (running a more posterior course than usual in its vertical segment within the mastoid antrum). A similar case has been reported in recent literature by Glastonbury et al [19] who described a 40-year-old woman with branchio-oto-renal syndrome and bilateral congenital hearing loss, whose HRCT scan showed bilateral anomalous facial nerve course along with severe cochleo-vestibular dysplasia. In the right ear, two distinct symmetric mastoid segments of the facial nerve exited via separate stylomastoid foramina, while in the left ear bifid mastoid segments of the facial nerve were seen with the smaller, medial segment exiting into the lateral wall of the jugular foramen and the labyrinthine portion of the nerve showed a loop-like anterior course, separate upto the internal auditory canal. Another case report by Graham GE et al [20] describes a 14 month old girl with BOR syndrome having congenital cholesteatoma co-existent with facial nerve anomaly (bifid course).

Summary

What we know from literature

- Branchio-oto-renal syndrome (Melnick-Fraser Syndrome) is a rare autosomal dominant disorder characterized by the syndromic association of branchial cysts or fistulae along with external, middle & inner ear malformations and renal anomalies.
- Incomplete penetrance and variable expressivity are common with the phenotypic variation ranging from mild to severe forms.
- Major clinical findings in the ear include low set or lop ears, pre-auricular sinus or tags, ossicular & inner ear malformations with various types and degrees of hearing loss.

What we found unique to our case

- Anomalous, dehiscent facial nerve course with vertical segment lying posteriorly in the mastoid antrum.
- Wide aditus with monopodal stapes, rudimentary incus with no short process & fixed ossicular chain.
- Cranially rotated cochlea with a flattened promontory & dome of lateral semicircular canal.

Conclusion

- This case of BOR syndrome, with an anomalous facial nerve course and a rotated cochlea has practical implications during cochlear implant surgery.
- This case also highlights the vital need to evaluate the renal function of children presenting with pre-auricular pits &/or branchial sinus along with congenital hearing loss.

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