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BRANCHIO-OTO-RENAL SYNDROME: A CASE REPORT & REVIEW OF LITERATURE

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ABSTRACT:
Background: Branchio-oto-renal (BOR) syndrome is a rare autosomal dominant disorder characterized by syndromic association of branchial arch anomalies, otologic malformations and renal anomalies. Very few articles on this syndrome have been published in journals related to Otorhinolaryngology.
Case Report: A 18 years old male patient, presented with a right sided intermittently discharging neck sinus at the junction of middle 1/3rd and lower 1/3rd of anterior border of sternocleidomastoid muscle along with bilateral pinna deformity and preauricular sinus. Fistulogram revealed a fistulous tract communicating with the right tonsillar bed. NCCT temporal bone showed marked hypoplasia of bilateral external auditory canal, dysplastic middle ear ossicles and microtia. NCCT KUB showed a hypoplastic right kidney and malrotated left kidney although his renal function test were within normal limits. In the presence of 3 major symptoms, branchial fistula, bilateral middle ear malformations and renal structure abnormality this case was clinically diagnosed as branchio-oto-renal syndrome. The patient was treated for his active symptoms hence his fistulous tract was excised after initial medical management.
Conclusion: The BOR syndrome is an infrequent but a well described entity that combines branchial arch anomalies, otologic malformations and renal anomalies. The BOR syndrome should be included in the differential diagnosis of deafness and chronic renal failure in childhood and adolescence.
Key words: Branchio-Oto-Renal Syndrome, fistula, branchial, renal malrotation, preauricular sinus, renal hypoplasia.

INTRODUCTION:

Branchio-oto-renal (BOR) syndrome is a rare autosomal dominant disorder with prevalence of approximately 1 in 40,000 new born infants and in about 2% of children with profound deafness[1,2]. Branchio-oto-renal (BOR) syndrome was first described by Melnick et al[3] in 1975 followed by Fraser et al[4], thus giving the name Melnick-Fraser syndrome.
It is characterized by branchial arch anomalies (branchial clefts, fistula, cysts), hearing impairment (malformation of auricle with preauricular sinuses, conductive, sensorineural, or mixed hearing impairment), and renal malformations (urinary tract malformation, renal hypoplasia or agenesis, renal hypoplasia, renal cysts)[5]. Patients usually present with hearing impairment and discharging branchial fistula. Such patients should be further investigated for BOR syndrome and thus control its progress.
Phenotypic presentation of BOR syndrome is extremely variable[6]. The combination of deafness with chronic renal failure may be confused with the Alport syndrome. Anterior lenticonus, a conical protrusion of the central portion of lens in to the anterior chamber is pathognomonic for Alport's syndrome. Moreover deafness in the Alport's syndrome manifests at a later age[7,12].

CASE REPORT:

An 18 years old male patient presented to the Otorhinolaryngology out-patient department with the chief complaints of right sided intermittently discharging neck sinus since birth.

He was born of non-consanguineous marriage and there was no history of hearing deficits, renal disease and similar discharging sinuses in the parents or in his only sibling. His birth history was insignificant.

On examination the patient was noted to have a discharging fistulous tract over right side of the neck at the junction of middle 1/3rd and lower 1/3rd on the anterior border of sternocleidomastoid muscle. The patient also had bilateral pinna deformity along with bilateral preauricular sinus.

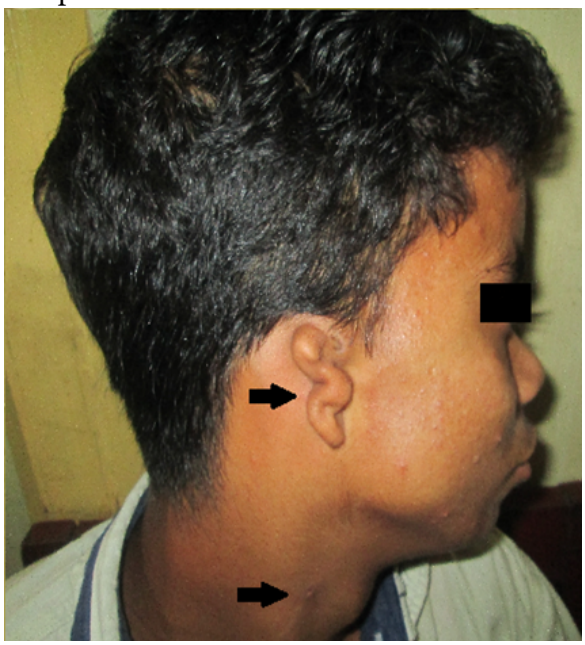

Fig 1: showing pinna deformity and discharging sinus over right side of neck

Fig 2: Showng bilateral pinna deformity

Facial nerve examination was within normal limits on both side and audiological assessment revealed bilateral severe mixed sensorineural hearing loss.

On investigating further, following were noted:

Fistulogram shows fluid contrast through fistulous tract communicating with the right tonsillar bed.

Fig 3: fistulogram

NCCT temporal bone shows marked hypoplasia of bilateral external auditory canal, dysplastic middle ear ossicles and bilateral microtia. Scans also revealed opacification of middle ear cavity on both side.

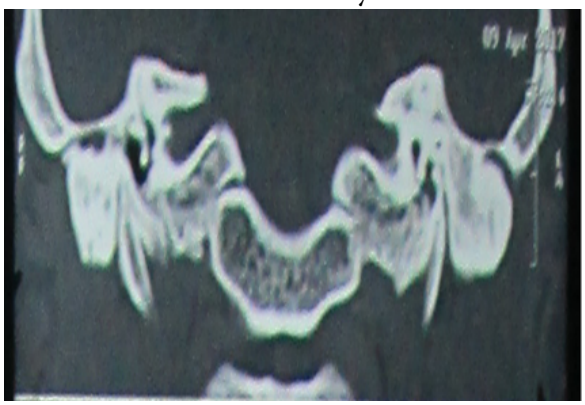

Fig 4: NCCT Temporal Bone

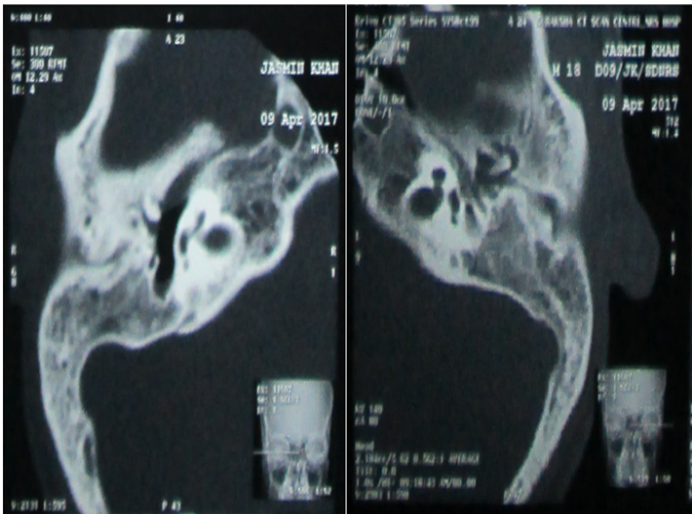

Fig 5 Right side Fig 6 Left side

Although the patient had no complaints related to renal function, but on the basis of suspicion for BOR syndrome a NCCT KUB was requested and it revealed a small right kidney and malrotation of left kidney.

He was then referred to a nephrologist for his renal anomaly and subsequent regular follow up.

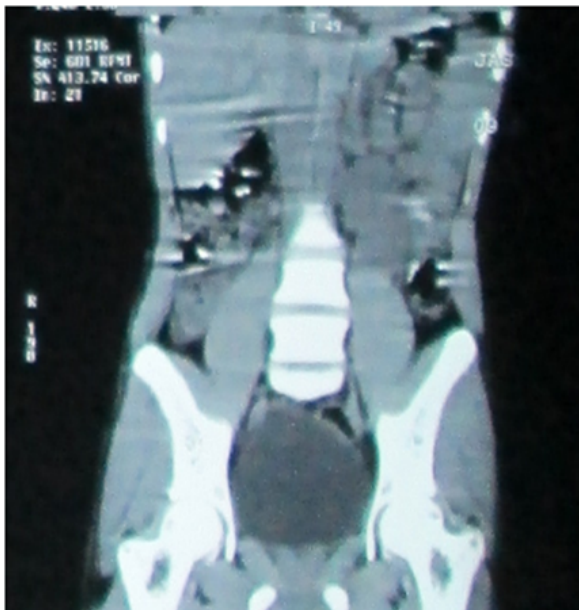

Fig 7 CT Abdomen

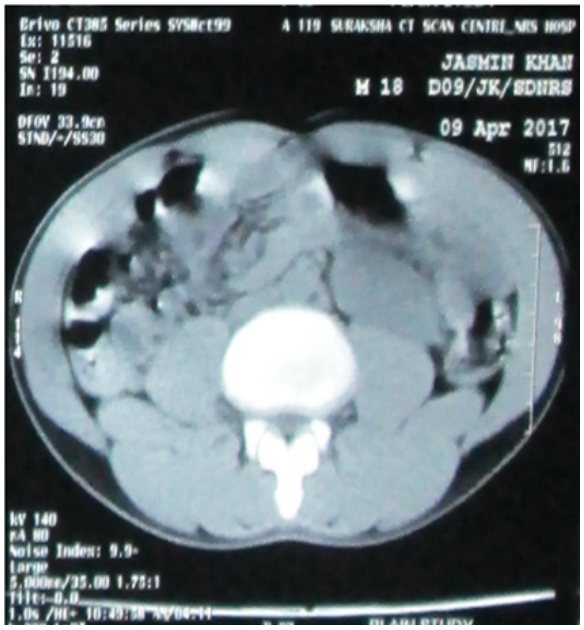

Fig 8: CT Abdomen

As a part of his management work up the patient was treated only for its active symptoms.

Hence the patient underwent complete excision of the fistulous tract after initial stabilization and medical management. He was advised hearing aids, regular hearing assessment, and periodic renal function monitoring.

In the light of 3 major symptoms, branchial fistula, bilateral middle ear malformations and renal structure abnormality this case was clinically diagnosed as Branchio-oto-renal syndrome.

DISCUSSION:

The BOR syndrome is a rare but well defined constellation of branchial arch anomalies (branchial fistulas, branchial cysts), external ear malformations with hearing loss and renal hypoplasia and dysplasia. It has an autosomal dominant transmission pattern with variable clinical expression[6]

Chang et al. developed the diagnostic criteria of BOR syndrome in 2004[8,9]. These include major criteria such as second branchial arch anomalies, hearing loss, preauricular pits, auricular deformity and renal anomalies, and minor criteria such as external auditory canal anomalies, middle ear anomalies, inner ear anomalies, preauricular tags and other symptoms such as facial asymmetry and palate abnormalities.

In patients with a family history, any single major criterion is sufficient for diagnosis of BOR syndrome. Without any family history, three major criteria or two major and two minor criteria are needed to make a confident diagnosis.

EYA1 (8q13.3), the human homologue of the Drosophila eyes absent gene, is the most frequent causative gene for BOR syndrome[10]. It expresses very early, between 4th & 6th weeks of human embryogenesis[11]. 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. EYA1 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 [12]. Mutations in SIX1 (14q23.1) and SIX5 (19q13.32) have been reported less frequently[13]. SIX1 interacts with EYA1 in the development of various organs[14]. SIX5 has a high degree of homology to SIX1 and directly interacts with EYA1 [15].

Clinical features are highly variable. The most common presenting symptom is deafness (90%) which can be sensorineural or conductive but is mostly mixed (50%)[16]. Pre-auricular pits can be the presenting features in over 70% of the cases and sometimes can be the only external ear finding as seen in our patient, while around 50% of patients have external ear anomalies in the form of microtia to small lop or cupped ears with over folded superior helices[17] · Middle ear anomalies include ossicular malformations and inner ear anomalies include cochlear hypoplasia or dysplasia[18]. Renal anomalies include renal dysplasia and agenesis which can lead to end-stage renal disease[19].

CONCLUSION:

BOR syndrome is a rare but well described clinical entity. It combines branchial anomalies with otologic and renal malformations. Most individuals with BOR syndrome do not have a life-threatening condition, and, in many families, it is not uncommon for the disease to go undiagnosed until the birth of a child with severe

manifestations of the BOR phenotype. This is unfortunate, as recognition of the hallmark features of BOR syndrome could ensure that affected persons receive appropriate medical information and care. Integral elements of medical care include audiologic, otologic, head & neck, urologic, and genetic evaluation. Patients with BOR syndrome who receive adequate treatment can lead normal, productive lives. It is therefore essential to provide early diagnosis including the relevant genetic tests, although further studies are needed to unearth the molecular mechanisms and undiscovered causative genes responsible for BOR syndrome.

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