Case Report

A Variant BORS in a 20 Weeks Foetus – A Case Report

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Abstract:

A still born male foetus of 20weeks gestation was brought to the Department of Anatomy from one of the private nursing homes in Vizianagaram as a part of routine research work in the department. Foetal autopsy revealed bilateral cleft lip with cleft palate, anotia (absence of ear pinna), absence of external acoustic meatus and auricular tags on the right side, where as left pinna and acoustic meatus were normal. Study also revealed anomalies in the right middle ear and internal ear. Orientation of thoracic and abdominal viscera was normal. There were two large cysts in the abdominal cavity in place of kidneys. Both ureters were dilated. Branchial arch anomalies, ear anomalies and renal anomalies constitute Melnick-Fraser syndrome, otherwise called as Branchio-oto-renal syndrome.

Key Words: Cleft lip, Cleft palate, BORS, Cystic kidneys.

Introduction:

Branchio-oto-renal (BOR) syndrome is a rare genetic disorder characterized by the auricular malformations, hearing loss, branchial arch anomalies and renal anomalies. It was first recognized by Melnick et al in 1975 and further delineated by Fraser et al (1978). Branchio-oto-renal syndrome is also known as Melnick-Fraser syndrome. Approximately 90% of individuals diagnosed with BORS have an autosomal dominant inheritance and have an affected parent, where as 10% of cases are caused by de novo- mutation syndrome (Soriano, 2003; Chang et al, 2004). The diagnosis of BOR spectrum disorders is diagnosed on clinical criteria. The prevalence of BORS ranges from 1:700000 (Fraser et al, 1978) to 1:40000 (Fraser et al, 1980). The syndrome occurs in about 2% of profoundly deaf children (Jones, 1988).

Case report:

A still born unclaimed male foetus was brought to the Department of Anatomy of Maharaj Institute of Medical Sciences, Vizianagram. On enquiry, the antenatal period of the mother was uneventful as per the hospital records available. The foetus was embalmed and fixed in 10% formalin. The age of the foetus was calculated by measuring crown rump length, and on its basis, the gestational period was calculated to be approximately 20 weeks.

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On external examination, both upper limbs and lower limbs were normal without any anomaly. The anal and urethral openings were normal. There was bilateral cleft lip with cleft palate (Fig I). There was absence of ear pinna and external acoustic meatus on the right side, where as left pinna and external acoustic meatus were normal (Fig II). On opening the thorax, lungs and heart were found to be normal. There was no malformation of the diaphragm.

A large cyst of irregular shape occupied the entire abdomen except left hypochondriac and epigastric region, which was occupied by coils of the small intestine. Sub-hepatic vermiform appendix was noted. Another, large irregular cyst was found in the left hypochondriac region (Fig 1). On gross examination, both kidneys were absent. Both the ureters were dilated and connected to above mentioned cysts and to the urinary bladder. The liver, stomach, pancreas and spleen were normal. Both right and left testes were

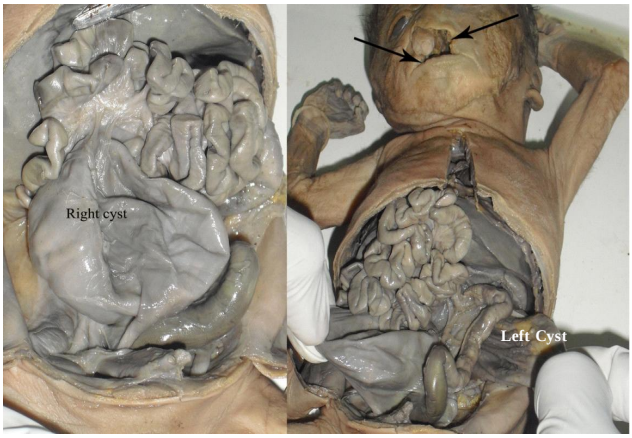

Fig I: Showing bilateral cleft lip with cleft palate and bilateral cysts occupying entire abdomen.

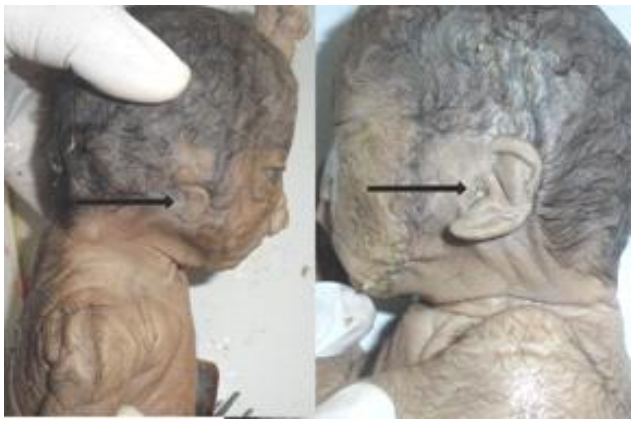

Fig II: Showing anotia and pre auricular tags on the right side and normal left pinna and external acoustic meatus.

still intra-abdominal overlying the right and left cysts (Fig. I). On histological examination, both the cysts revealed the following findings.

Right Cyst:

Capsule was well defined without any septa. Nephrogenic zone was not evident. Cortico- medullary differentiation was not appreciated. Very few glomeruli per field were noticed. Deeper glomeruli were large. Proximal convoluted and distal convoluted tubules were not well differentiated, as there was no differentiation of tubules, hence no pyramid formation was observed (Fig. IV a).

Left cyst:

Capsule was well defined without any septa. Thin nephrogenic zone was evident. Cortico- medullary differentiation was not appreciated. Relatively more number of glomeruli were noticed when compared with right cystic kidney. Proximal and distal convoluted tubules were appreciated. Presence of collecting ducts was evident, but without pyramid formation (Fig.IV b).

On opening the cranial cavity, the cerebral hemispheres were found to be normal. After removal of the cerebral hemispheres, tegmen tympani of petrous part of the temporal bone was removed on both the sides. There was hypoplasia of middle ear ossicles with complete aplasia of the internal ear (cochlea and vestibular apparatus were absent) on the right side, where as middle ear cavity of the left side showed three normal ossicles with normally developed semicircular canals and cochlea (Fig. III). The external auditory meatus on the right side was completely stenosed and was normal on the left side. No other anomaly of the 2nd branchial arch, such as cysts and fistulae were found on either side.

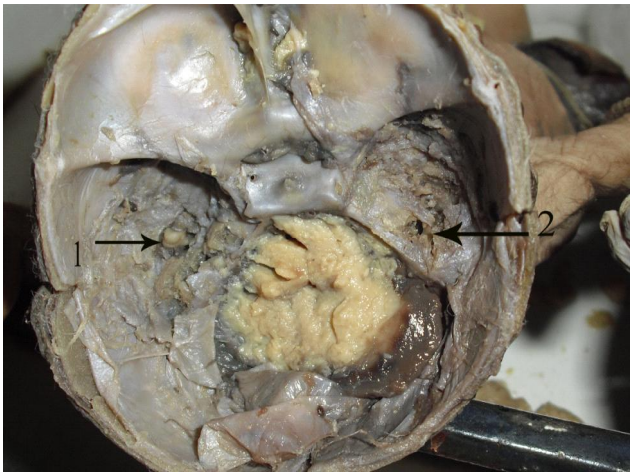

Fig. III: Showing normal middle ear ossicles on left side 1 & hypoplasia of ossicles on right side 2.

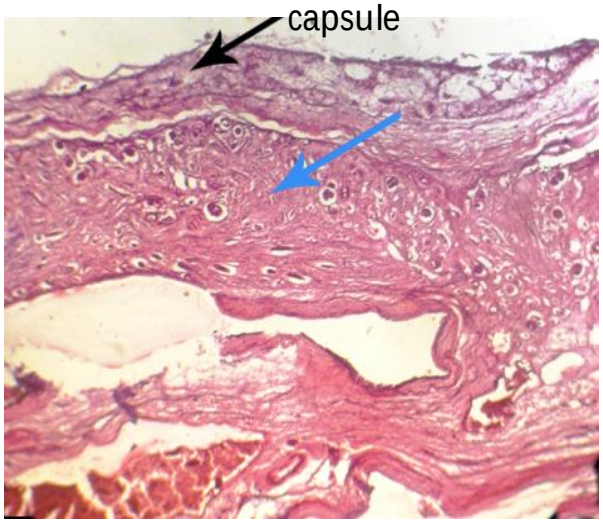

Fig. IV a: Showing no evidence of cortico medullary differentiation and Less number of glomeruli per field in right cystic kideny (H & E, 10x).

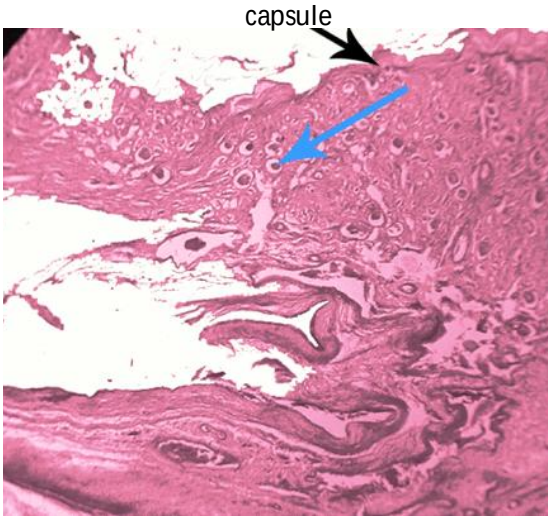

Fig. IV b: Showing evident naphrogenic zone and more number of glomeruli per field in left cystic kidney (H & E, 10x)..

Discussion:

Melnik-Fraser syndrome or Branchio-oto-renal dysplasia is characterised by external ear malformation, cervical fistulae, mixed hearing loss and renal anomalies, which is inherited in an autosomal dominant manner (90 % cases) and has variable clinical expression. Branchio-oto- renal syndrome gene was mapped to chromosome region 8q13.3 and its sequence was identified as the human homologue of the Drosophila eyes absent (EYA1) gene; other genes associated with mutation are SIX1 and SIX5 gene.

Stratakis et al (1998) studied Branchio -oculo-facial (BOF) syndrome with deafness, ear pits and associated conditions & BOR. They found that, though both the conditions are phenotypically similar but they differ genetically.

Kumar et al (1998) investigated Branchio-otic (BO) syndrome in a large family to determine whether BOR and BO syndromes were allelic to each other. On genetic linkage analysis, they found no evidence that BO syndrome is allelic to the BOR gene at 8q13. However, Clarke et al (2006) found that dominant mutations in the human homologue of the Drosophila eyes absent gene (EYA1) are frequently the cause of both BOR and BO syndrome. They studied the South African family of Afrikaner descent with effected individual presenting with pre-auricular abnormalities and either having hearing loss or bilateral absence of kidney. On genetic analysis of the pedigree they detected a novel EYA1 heterozygous nonsense mutation in effected family members but not in unaffected family members on a random DNA panel.

Jones (1988) reported ear deformities in 77 to 89% of cases, branchial fistulae and renal dysplasias in 63% cases each. Whereas, Chang et al (2004) observed 67% renal anomalies in a study of 21 affected individuals. Middle ear abnormalities include malformation, malposition, dislocation or fixation of ossicles. Internal ear abnormalities include agenesis of cochlea, and hypoplasia of semicircular canals (Kemperman et al, 2002).

The mechanism of development of dysplastic kidneys is not always clear and may be variable. It is generally accepted that renal dysplasia can be the result of very early in-utero urinary tract obstruction, whether it is at the level of urethra, bladder or ureter. The most severe dysplasia is the result of early obstruction with abnormal disappearance of nephrogenic blastema and subsequent arrest of nephrogenesis (Benacerraf et al, 1990). The present case is a variant of Melnick-Fraser syndrome, since mortality of foetus took place in the midterm, which could most probably be due to complete renal dysplasia. Zhang et al (2004) grouped this as due to EYA 1 mutation that is activating with resultant severe phenotype anomalies as presented. If a prenatal diagnosis is made a canaloplasty can be done to overcome hearing defect in some of the individuals affected. The BOR syndrome appears to belong to a larger group of hereditary ear dysplasia-renal adysplasia syndromes that must be carefully ruled out in all patients with familial branchial arch malformations as well as in the parents and siblings of infants with "Potter facies" in the presence of auricular malformation and renal adysplasia (Melnik et al, 1978).

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