CASE REPORT

Apert Syndrome Presenting with Omphalocele

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Abstract:

Apert syndrome is a congenital acrocephalosyndactyly syndrome. It is mainly presented by craniosynostosis, syndactyly of the hands and feet and dysmorphic facial features. The condition has an autosomal dominant inheritance assigned to mutations in the Fibroblast Growth Factor Receptors (FGFR-2) gene. The reported case is a 9 months old boy with clinical suspicion of Apert syndrome as he had turricephaly, stubby hands with short fingers, omphalocele measuring 10 × 10 cm, bilateral undescended testes, Congenital Talipes Equinovarus (CTEV) and polydactyl and syndactyl of great and second toes. He was developmentally normal. The omphalocele was surgically repaired. Early diagnosis and intervention helps rehabilitation of patients with Apert syndrome and help them to lead a better life.

Keywords: Apert Syndrome, Acrocephalosyndactyly, Craniosynostosis, Omphalocele

Introduction:

Apert syndrome (acrocephalosyndactyly) is a congenital craniosynostosis syndrome. The estimated birth prevalence is 10 to 15.5 cases per 1,000,000 live births [1]. The condition was reported by Wheaton in 1894. In 1906, a French physician Eugene Apert summarized nine cases of this syndrome characterized by craniosynostosis, midface hypoplasia, and symmetric syndactyly of hands, and feet. The Apert syndrome has an autosomal dominant inheritance assigned to mutations in the Fibroblast Growth Factor Receptors (FGFR-2) gene which maps to chromosome 10q25-10q26 [2].

Apert syndrome has characteristic clinical features in which the coronal suture fuses prematurely (at less than 3 months), leading to a cone-shaped head known as acrocephaly with a high prominent forehead. The mid face is hypoplastic. Hypertelorism, down slanting palpebral fissures (anti mongoloid slant) and proptosis are the ocular anomalies. The nose is wide and short and the nasal bridge is depressed [3-5]. Anomalies of the skeleton as cervical vertebrae fusion usually at C5, C6, viscera (cardiac, respiratory, gastrointestinal, and genitourinary tract anomalies), skin (acne at adolescence) and impaired mental function due to central nervous system anomalies as corpus callosum agenesis, nonprogressive ventriculo-megaly, hydrocephalus and gyral abnormalities have been reported by previous studies [2, 5]. The most common type of syndactyly found in these patients is cutaneous and osseous syndactyly of fingers ("mitten glove") and toes varying from total fusion to partial fusion, involving variable number of digits. Diagnosis can be made clinically by recognizing the distinctive cranial, facial and limb findings and can be confirmed by molecular study (OMIM, omim.org/entry/101200) [6].

Case Report:

The reported case is of a 9 month old male child of a non consanguineous married healthy couple with maternal and paternal ages of 22 year and 28 year respectively who was brought with the complaints of abnormal shape of the head since birth, presence

of a protrusion on the abdomen since birth and abnormal feet. The couple had one previous healthy daughter with no significant family history. There were no prenatal ultrasounds done. The boy was born via normal vaginal delivery weighing 2.7 kg with uneventful birth. The child was developmentally normal and he did not present with any symptoms related to cardiac and respiratory system up to now. The child was brought to us for the management of the omphalocele. On gross examination, the child had turricephaly, epicanthal fold, depressed nasal bridge, low set ear, stubby hands with short fingers, omphalocele measuring 10 × 10 cm, bilateral undescended testes (cryptorchidism), Congenital Talipes Equinovarus (CTEV) and polydactyl and syndactyl of great and second toe.

The radiological evaluation of the head revealed altered contour of the calvaria with closed anterior fontanelle and fusion of saggital and metopic suture, flattened contour of bassiocciput, bipartite atlas, cerebral ventriculomegaly, with cerebral parenchyma normal, also radiological evaluation of abdomen revealed large ventral hernial defect with bowel loop and liver herniation.

Repair of the omphalocele and cryptorchidism via surgical intervention was decided which was performed successfully by reducing the contents of omphalocele and placing testis in scrotum both sides. For CTEV cast was applied.

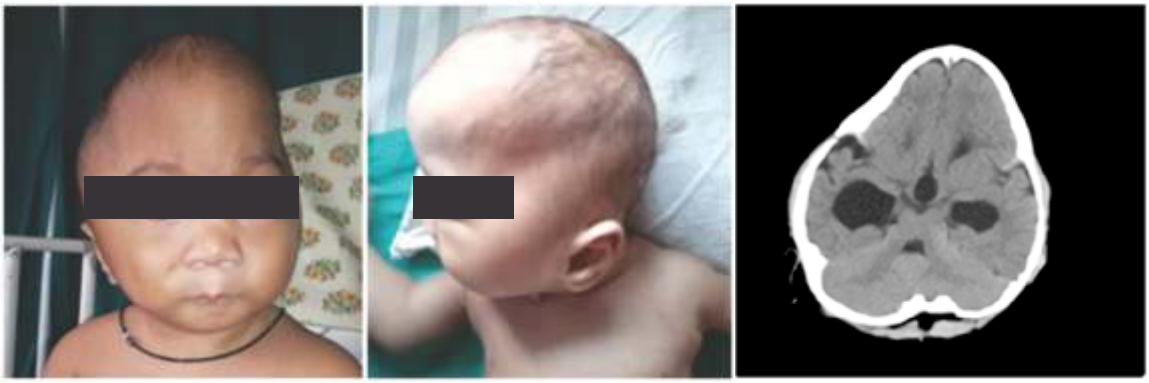

Fig. 1A: Anterior View showing Turricephaly, Epicanthal Fold, Depressed Nasal Bridge, Fig.1B: Lateral View showing Low Set Ear Fig. 1C: CT Scan Head showing Abnormal Head Shape or Turricephaly

Fig. 2: Showing Stubby Hands with Short Fingers

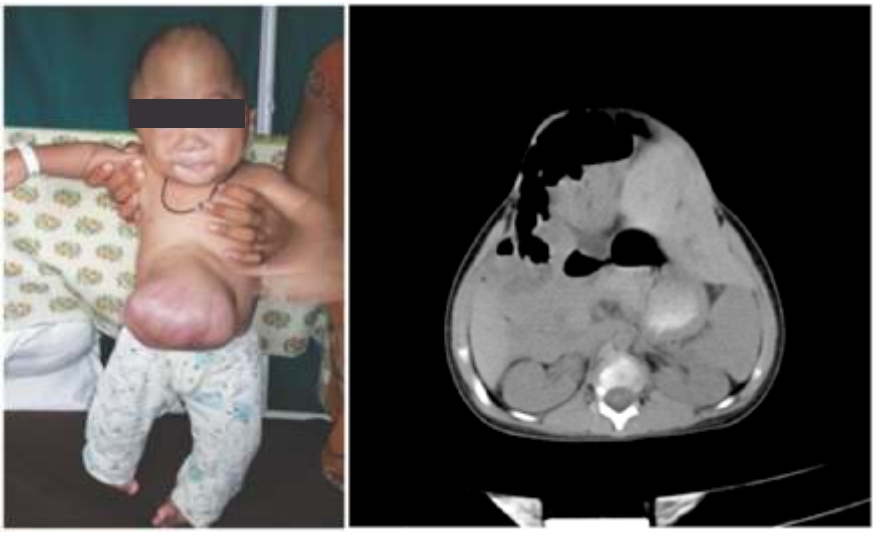

Fig. 3A: Anterior View and Fig. 3B: CT Scan Abdomen showing Ventral Hernia Defect s/o Omphalocele

Fig. 4A: Anterior View, Fig. 4B: Lateral View, Fig. 4C: X-ray AP View showing Bilateral CTEV with Polydactyly and Syndactyly

Discussion

In 1906, Apert described the triad consisting of craniosynostosis, syndactyly of the hands and feet, and dysmorphic facial features, characterizing the syndrome [3, 4]. Later, an autosomal dominant heritance was linked to the syndrome, with mutations in the Fibroblast Growth Factor Receptors (FGFR-2) gene, which maps to chromosome 10q26 [4].

Apert syndrome has considerable varied clinical presentation with distinctive craniofacial and limb features. The case described has craniosynostosis, syndactyly, polydactyly of feet and stubby hands with short fingers. The syndrome is clinically characterized by early fusion of the coronal suture and hypoplastic midface [3-5]. Ocular anomalies, short nose with depression of the nasal bridge as described by Apert [3, 4] were also present. The main limitation of the present report is the absence of genetic diagnosis. Genetic diagnosis for cases clinically diagnosed with syndromes is not routinely performed in our center because of unaffordability. However, clinical diagnosis of Apert syndrome could be made reliably in presence of craniosynostosis, midfacial hypoplasia, and

syndactyly of hands and feet. Differential diagnosis includes other genetic disorders associated with craniosynostosis are Crouzon syndrome, Pfeiffer syndrome, Chotzen syndrome and Carpenter syndrome. In Crouzon syndrome brachycephaly, ocular proptosis and hypertelorism is prominent. In Pfeiffer syndrome eyes are prominent and widely spaced. Chotzen syndrome is associated with facial asymmetry, ptosis of the eyelids, and a broad forehead with low hairline. In Carpenter syndrome, intellectual disability is common.

Till now this is the third reported case where Apert syndrome is associated with omphalocele. The first case reported by Herman and Siegel, 2010 [7] presented with a phenotype consistent with Apert syndrome and a giant omphalocele, the content of which was most of the liver. In that case, the mutation S252W was detected in the FGFR2 gene. The second case reported by Ercoli *et al*. 2014 [8] where he reported a newborn with craniosynostosis, syndactyly, omphalocele, cryptorchidism, oesophageal atresia and mega cistern megna. FGFR1 and FGFR2 are expressed during abdominal wall development in mice.

Conditional inactivation of both FGFR2 alleles and one FGFR1 allele resulted in omphalocele in approximately 38.7% of mutants (Nichol *et al*., 2011) [9]. However, there are mechanistic differences between the FGFR2 S252W mutation present in the first reported case and FGFR2 conditional mutagenesis, which is associated with omphalocele in mice. Apert syndrome occurs due to increased affinity of mutant receptors for specific FGF ligands which in turn causes activation of signaling when availability of ligand is limiting (Anderson et al., 1998) [10] whereas, the mechanism responsible of omphalocele in mice is the inactivation of FGFR2 receptors, not the increased ligand affinity (Nichol *et al*., 2011) [9]. The present case has bilateral undescended testes (cryptorchidism), which was also reported by Ercoli *et al*., 2014 [8].

Conclusion:

Apert syndrome is an autosomal dominant inheritance disorder which affects many parts of the body. The integral healthcare delivery should include a multidisciplinary approach provided by pediatricians along with neurosurgeons (for craniosynostosis), plastic surgeons (for syndactaly), pediatric surgeons (for omphalocele and cryptorchidism as in our case), ophthalmologists (for ocular defects), geneticists (counselling) and orthopedicians (for CTEV in our case) for the effective planning and treatment of such patients.

References

1. Cohen MM Jr, Kreiborg S, Lammer EJ, Cordero JF, Mastroiacovo P, Erickson JD, *et al*. Birth prevalence study of the Apert syndrome. *Am J Med Genet* 1992; 42 (5):655-59.
2. Saritha S, Sumangala GS, Kumar MP. Apert syndrome (Acrocephalosyndactyly): a case report. *Int J Res Med Sci* 2017; 1(1):36-40.
3. DeGiovanni CV, Jong C, Woollons A. What syndrome is this? Apert syndrome. *Pediatr Dermatol* 2007; 24 (2):186-8.
4. Freiman A, Tessler O, Barankin B. Apert syndrome. *Int J Dermatol* 2006; 45(11):1341-3.
5. Carneiro GV, Farias JG, Santos FA, Lamberti PL. Apert syndrome: review and report a case. *Braz J Otorhinolaryngol* 2008; 74 (4): 640.
6. OMIM (Online Mendelian Inheritance in Man). Johns Hopkins University, Baltimore, MD. MIM: 101200. Available at: http:// omim.org/entry/101200. Accessed June 6, 2014.

7. Herman TE, Siegel MJ. Apert syndrome with omphalocele. *J Perinatol* 2010; 30(10):695-7.
8. Ercoli G, Bidondo MP, Senra BC, Groisman B. Apert syndrome with omphalocele: a case report. *Birth Defects Res A Clin Mol Teratol* 2014; 100(9):726-9.
9. Nichol PF, Corliss RF, Tyrrell JD, Graham B, Reeder A, Saijoh Y. Conditional mutation of fibroblast growth factor receptors 1 and 2 results in an omphalocele in mice associated with disruptions in ventral body wall muscle formation. *J Pediatr Surg* 2011; 46(1):90-6.
10. Anderson J, Burns HD, Enriquez-Harris P, Wilkie AO, Heath JK. Apert syndrome mutations in fibroblast growth factor receptor 2 exhibit increased affinity for FGF ligand. *Hum Mol Genet* 1998; 7(9):1475-83.

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