



Apert Syndrome

Alternative Names

Acrocephalosyndactyly, Type I
ACS1
ACS I
Apert-Crouzon Disease
Acrocephalosyndactyly, Type II
ACS II
VOGT Cephalodactyly
Apert-Like Polydactyly Syndrome

Record Category

Disease phenotype

WHO-ICD

Congenital malformations, deformations and chromosomal abnormalities > Other congenital malformations

Incidence per 100,000 Live Births

2-5

OMIM Number

101200

Mode of Inheritance

Autosomal dominant

Gene Map Locus

10q26

Description

Craniosynostosis syndromes are human skeletal diseases that include Apert syndrome, Crouzon syndrome, Crouzon syndrome with Acanthosis Nigricans, coronal craniosynostosis, Pfeiffer syndrome, Jackson-Weiss syndrome, Antley-Bixler syndrome, and Beare-Stevenson cutis gyrate. Craniosynostosis syndromes share phenotypes that include premature closure of some cranial sutures, but have distinct facial features, limb abnormalities, and, in some cases, central nervous system malformations.

Apert syndrome is one of the most severe craniosynostosis syndromes and is associated with severe syndactyly of the hands and feet and with central nervous system malformations. All affected individuals have progressive calcification and fusion of bones of hands and feet and cervical spine. Apart from risk of developing raised intracranial tension and optic atrophy, patients with Apert syndrome are prone for other congenital anomalies, including megalencephaly, corpus callosal defect and limbic system. Others include overriding of aorta, septal defects; hydronephrosis, cryptorchidism, polycystic or hydronephrotic kidney, bicornuate uterus; tracheal stenosis, pulmonary hypoplasia, pyloric stenosis, and oesophageal atresia. Although, Apert syndrome is a sporadic condition, autosomal dominant inheritance may occur. Incidence of Apert syndrome is 15 per 1,000,000 births and it accounts for about 4.5% of all cases of craniosynostosis.

Molecular Genetics

Craniosynostosis syndromes are autosomal dominant diseases that result from various mutations in fibroblast growth factor receptor genes (FGFRs). FGFRs are transmembrane receptor tyrosine kinase proteins that contain an extracellular ligand-binding domain, a single transmembrane domain, and an intracellular tyrosine kinase domain. Apert syndrome is caused by one of the two missense mutations of the FGFR2 gene, which maps to chromosome 10q 25 – 10q 26, involving an amino acid substitution, S252W or P253R, in the linker region between the second and third extracellular Ig domains. S252W results from a C755G missense mutation and is more common than P253R caused by C758G in Apert syndrome patients, and each mutation shows differential effects on the phenotype of syndactyly and cleft palate in this syndrome. Apert mutation in the FGFR2 gene serves as a gain-of-function mutation by decreasing the dissociation rate of FGFs from FGFR2 as well as by evoking the ligand-dependent receptor activation. In addition to the retained ligand dependence for the



receptor activation, the loss of ligand specificity of FGFR2 is also elicited by Apert mutations.

Epidemiology in the Arab World

Lebanon

Sacy et al. (1998) reported the case of a newborn with Apert syndrome. She was born to non-consanguineous parents following a complicated pregnancy marked by gestational diabetes. Physical examination indicated a dysmorphic aspect. Brachycephaly in the cranium, hypertelorism of the skin, and cutaneous syndactyly of the upper members and ears were among the features observed. Neurological examination was not marked with any significant abnormality. At 48 hours, episodes of cyanose were observed especially when the mouth was closed because of incapacity to breath from the noses. A surgery was conducted to establish the nasal tubes. A day later, she was readmitted because of a high fever and hypotonia. Upon examination, she presented an extended fontanelle, hypotension, and abundant yellowish nasal secretions. Echography of the fontanelle showed an interventricular hemorrhage. She died 24 hours later because of cardiac arrest.

Morocco

Dihaj et al. (2005) reported the case of a two-month-old baby that was referred for respiratory distress occurring within the framework of a polymalformative syndrome. The parents were first cousins with no family history of a congenital malformation. The examination of the baby showed brachycephaly, bilateral exorbitism, syndactyly of the hands and feet and an anal fistula. Echocardiographic examination showed a cardiovascular malformation (interventricular communication), the whole suggestive of Apert syndrome. The child was admitted in intensive care during five days. He died following a respiratory infection.

Saudi Arabia

Al-Qattan and Al-Husain (1996) reported a 1-month-old male who was born with features characteristic of Apert's syndrome. The skull was brachycephalic with frontal bossing and a recessed supraorbital ridge. There were midfacial hypoplasia with bulging eyes, antimongoloid slant of the palpebral fissures, bilateral choanal atresia, and high arched palate. Simple (cutaneous) syndactyly of the index, middle and ring

fingers with separate nails and paronychia folds as well as clinodactyly of the index fingers were also observed. The feet showed simple syndactyly of toes with short deviated big toes. Hand radiographs revealed that the syndactyly was limited to soft tissues. In 2001, Al-Qattan used split-thickness skin grafts to correct Apert syndactyly in eight patients whose average age at first surgery was 6 months. Separation of all digits was accomplished before the age of 2 years. Al-Qattan (2001) utilized a dorsal rectangular flap and interposing triangular digital flaps to create the web space and partially cover the skin defects in the fingers. The remaining digital defects were covered with thin split-thickness skin grafts which took fully in all cases. At final follow-up (1-6 years), the areas covered by skin grafts have reduced in size significantly because of skin graft contraction. However, this did not result joint contracture or digital deviation.

References

- Al-Qattan MM, al-Husain MA. Classification of hand anomalies in Apert's syndrome. *Hand Surg [Br]*. 1996; 21(2):266-8. PMID: 8732416
- Al-Qattan MM. The use of split thickness skin grafts in the correction of Apert's syndactyly. *J Hand Surg [Br]*. 2001; 26(1):8-10. PMID: 11162005
- Dihaj S, Abada A, Baha Ali T, Benhaddou M, Rais L, Hamdani M, Amraoui A, Zaghoul K. Syndrome d'Apert: à propos d'une observation. *Bull Soc Belge Ophthalmol*. 2005; (295):5-10. PMID: 15849982
- Sacy R, Gebran S, Slaba C, Matar M, Haddad J, Kamel R. A propos d'un cas de syndrome d'Apert. *Rev Med Libanaise*. 1998; 10:110-5.

Related CTGA Records

Syndactyly, Type I

External Links

- <http://ghr.nlm.nih.gov/condition=apertsyndrome>
<http://www.ccakids.org/Syndrome/Apert.PDF>
<http://www.emedicine.com/ped/topic122.htm>
http://www.orpha.net/static/GB/apert_syndrome.html

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