Shprintzen-Goldberg Craniosynostosis Syndrome

Alternative Names
SGS
Craniosynostosis with Arachnodactyly and Abdominal Hernias
Marfanoid Disorder with Craniosynostosis, Type 1
Marfanoid Craniosynostosis Syndrome

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
182212

Mode of Inheritance
Isolated cases

Gene Map Locus
15q21.1

Description
Shprintzen-Goldberg Craniosynostosis Syndrome (SGCS) is an extremely rare connective tissue disorder that is usually characterized by a marfanoid habitus, with craniofacial, skeletal and cardiovascular abnormalities, and learning disabilities. The most frequently described craniofacial abnormalities in SGCS include dolichocephaly (abnormal head shape), a high, prominent forehead, ocular proptosis (bulging eyes), hypertelorism (wide spaced eyes), down slanting eyes, maxillary hypoplasia (small jaw), high narrow palate, and low-set ears. The main skeletal findings in SGCS are: arachnodactyly (long, thin fingers), flat feet, "bird" chest deformity, scoliosis (curvature of the spine), and loose joints. Less than 50 cases have been reported to date worldwide.

Molecular Genetics
Shprintzen-Goldberg Craniosynostosis Syndrome is caused by genetic mutations in fibrillin-1 gene (FBN1) that contributes to the formation of connective tissue. Many researchers think that these mutations only predispose a person to develop SGCS, and other factors are required in addition to mutations to develop the disease. The other factors may be other genetic mutations, environmental influences, or a combination of these, but they are not well-understood at this time. Although the mutations in FBN1 appear to be sporadic in nature, only one mutation is necessary to be predisposed to the disease (autosomal dominant). Sporadic genetic mutations in the sperm occur (in any gene, not just FBN1) at a higher rate in older men (over 45 years). There is one case report of a child with SGCS whose father was 49 years old. The father of another child with SGCS reportedly had chemotherapy and radiation treatment prior to conception of the child.

Epidemiology in the Arab World

Bahrain
Greally et al. (1998) presented four patients with Shprintzen-Goldberg syndrome. Clinical and radiologic findings were used to confirm the diagnosis and differentiate it from the related Furlong syndrome. Greally et al. (1998) indicated that radiologic investigations appear to be more specific, since an abnormality of the first and second cervical vertebra, hydrocephalus, dilatation of the lateral ventricles, and a Chiari-I malformation of the brain were found only in the patients with Shprintzen-Goldberg syndrome.

Lebanon
Megarbane and Hokayem (1998) described a 16 and half-year-old boy with craniosynostosis and marfanoid habitus. He was the first child of healthy non-consanguineous parents. His psychomotor development was delayed from the beginning. At the age of six months, he was treated for a right inguinal hernia and...
omphalocele. Physical examination, echocardiography, and total body skeletal radiography were performed to allow a clear case differentiation. He displayed the following features: normal intelligence, muscular hypotrophy, hypoplasia, ptosis of the eyelids, microretrognathism, long thorax, thin limbs, camptodactyly and clinodactyly, kyphoscoliosis, cubitus and hallux valgus, flat foot with long toes, enlarged aortic root, biconvex vertebrae, and enlarged diaphyses. Chromosomes were normal (46, XY). According to the findings, the patient had features of two types of craniosynostosis with marfanoid habitus; type I (Shprintzen-Goldberg Craniosynostosis Syndrome) and type II (Furlong Syndrome). Due to the absence of consanguinity in healthy parents of the Lebanese patient and of the two previously studied male patients, Megarbane and Hokayem (1998) suggested autosomal dominant inheritance. However, X-linked recessive inheritance could not be excluded.

Morocco
Brooks et al. (1999) studied four patients of a large consanguineous Moroccan family with Shprintzen-Goldberg syndrome (SGS). The patients were related to two sibships. The index patient was the daughter of a consanguineous couple. She presented short segment Hirschsprung disease (HSCR) since birth. At two weeks of age, she showed telecanthus, a prominent nasal bridge, and tapering fingers. Involuntary movements of the head started from three months of age. When she was nine months, a brain MRI scan showed slight general brain atrophy with delayed myelinization. At two years, she displayed the SGS dysmorphism, progressive microcephaly, palpebral fissures, a flat occiput, short philtrum, and large ears. Her development was retarded at 26 months which was equivalent to a chronological age of 14 months. The other sibship had two affected males and one affected female who had normal karyotypes. One of the affected boys had a broad nasal bridge, low set ears, a short neck, and long segment HSCR and he died from complications of sepsis at the age of three weeks. His sister was born having a lesion of the brachial plexus. A barium enema was suggestive of HSCR in her case. A biopsy was obtained from the girl and it showed absence of ganglion cells and increased acetylcholinesterase staining in nerve fibers. Her brain CT at five years displayed hypoplastic septum pellucidum. When she was five years, she was evaluated to have high arched eyebrows, dense curled eyelashes, a broad nasal bridge, blue sclera, large cornea, mild thoracic scoliosis, and a broad hallux. She had mental retardation and severe hearing loss, related to therapy resistant middle ear infections. Progressive scoliosis and proximal muscle weakness were noted at her ten years. The other affected boy was noticed to have developmental delay at eight months. He had dense eyebrows with mild synophrys, a broad nasal bridge, low set ears, large cornea with blue sclera, and hypotonia. At his 13 months, telecanthus, palpebral fissures, a high arched palate, short thumbs, overlapped toes, and corneal hypoesthesia, and recurrent corneal infections were observed. He had no HSCR. Gel electrophoresis of all exons of the endothelin receptor type B (EDNRB) gene was performed to the index patient and other 12 family members and it showed the presence of a non homozygous EDNRB variant (Ser305Asn substitution) in the index patient and five family members. Therefore, Brooks et al. (1999) proposed that the Ser305Asn substitution could not explain the SGS phenotype because it presented not only in two affected individuals, but also in four healthy members.

References

Contributors
Ghazi O. Tadmouri: 12.8.2006
Abeer Fareed: 18.6.2006