Published on *My46* (https://www.my46.org) 01/23/2022

My46 Trait Profile

Freeman-Sheldon syndrome

Other Names: Distal Arthrogryposis type 2A

Arthrogryposis is the presence of congenital (i.e., present at birth) contractures (i.e., the inability to fully move a joint) of two or more different body areas (e.g., hands, shoulders, ankles, hips). Freeman-Sheldon syndrome (FSS) is a rare condition characterized by contractures of the hands and feet. It is caused by mutations in the MYH3 gene that encodes a protein called embryonic myosin.

Characteristics of Freeman-Sheldon syndrome

Arthrogryposis is the presence of congenital (i.e., present at birth) contractures (i.e., the inability to fully move the area around a joint) of two or more different body areas (e.g., hands, shoulders, ankles, hips). Distal arthrogryposis type 2A or Freeman-Sheldon syndrome (FSS) is a condition in which individuals usually have contractures of the fingers and toes (i.e., camptodactyly) and foot contractures (clubfoot or vertical talus) that are noticeable at birth. The contracted facial muscles seen in FSS result in a small, tight, pinched mouth, "H-shaped" dimpling of the chin, and deep creases around the mouth. Because of the characteristic facial appearance, this condition has also been described as "whistling face syndrome." Other features commonly seen in FSS include abnormal curving of the spine (scoliosis), problems aligning the eyes (strabismus), hearing loss, crowding of the teeth, and feeding difficulties in the newborn period. Intelligence is usually normal in individuals with FSS.

Diagnosis/Testing

Most individuals with FSS have a change or mutation in a gene called MYH3 that makes a myosin protein. Myosin, along with other proteins, are responsible for helping skeletal muscles contract. Mutations in the MYH3 gene are thought to interfere with muscle development and the ability of muscle fibers to contract and relax.

Management/Surveillance

Management of FSS often includes physical, occupational, and speech therapies, as well as nutritional intervention. Most individuals with FSS need surgical operations or casting procedures to correct the contractures of the hands and/or feet or scoliosis.

Individuals with FSS have been reported to have an increased risk of malignant hyperthermia – a severe reaction to certain medications used during surgery. If exposed to these medications, individuals with malignant hyperthermia susceptibility may experience muscle rigidity, breakdown of muscle fibers, a rapid heart rate, high fever, and death, if not treated quickly. It is important for individuals with FSS to notify their doctors of this increased risk for malignant hyperthermia so that certain medications can be avoided during any surgical procedure.

Mode of inheritance

FSS is inherited in an autosomal dominant pattern. This means inheriting one MYH3 mutation is enough for an individual to be affected and show signs of FSS. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Risk to family members

The risk to family members depends on whether or not the individual with FSS has a parent affected with FSS. If a parent also has FSS, the risk of having a child with FSS is 50% with each pregnancy. If a parent does not have FSS, the risk of other siblings being affected is very low.

Special considerations

None

Resources

Freeman-Sheldon Research Group, Inc.
http://www.fsrgroup.org/
Genetics Home Reference: Freeman-Sheldon syndrome
http://ghr.nlm.nih.gov/condition/freeman-sheldon-syndrome

References

Stevenson, D. et al. (2006)."Clinical Characteristics and Natural History of Freeman-Sheldon Syndrome." Pediatrics 117(3): 754-762.
Toydemir, R. et al. (2006)."Mutations in embryonic myosin heavy chain (MYH3) cause Freeman-Sheldon syndrome and Sheldon-Hall syndrome." Nature Genetics 38: 561-565.

Created: 12/2012 **Created by:** Seema Jamal, MSc, LCGC
Updated: mm/yyyy **Edited by:** Michael Bamshad, MD