Ophthalmo-acromelic syndrome

Description

Ophthalmo-acromelic syndrome is a condition that results in malformations of the eyes, hands, and feet. The features of this condition are present from birth. The eyes are often absent or severely underdeveloped (anophthalmia), or they may be abnormally small (microphthalmia). Usually both eyes are similarly affected in this condition, but if only one eye is small or missing, the other eye may have a defect such as a gap or split in its structures (coloboma).

The most common hand and foot malformation seen in ophthalmo-acromelic syndrome is missing fingers or toes (oligodactyly). Other frequent malformations include fingers or toes that are fused together (syndactyly) or extra fingers or toes (polydactyly). These skeletal malformations are often described as acromelic, meaning that they occur in the bones that are away from the center of the body. Additional skeletal abnormalities involving the long bones of the arms and legs or the spinal bones (vertebrae) can also occur. Affected individuals may have distinctive facial features, an opening in the lip (cleft lip) with or without an opening in the roof of the mouth (cleft palate), or intellectual disability.

Frequency

The prevalence of ophthalmo-acromelic syndrome is not known; approximately 35 cases have been reported in the medical literature.

Causes

Mutations in the *SMOC1* gene cause ophthalmo-acromelic syndrome. The *SMOC1* gene provides instructions for making a protein called secreted modular calcium-binding protein 1 (SMOC-1). This protein is found in basement membranes, which are thin, sheet-like structures that support cells in many tissues and help anchor cells to one another during embryonic development. The SMOC-1 protein attaches (binds) to many different proteins and is thought to regulate molecules called growth factors that stimulate the growth and development of tissues throughout the body. These growth factors play important roles in skeletal formation, normal shaping (patterning) of the limbs, as well as eye formation and development. The SMOC-1 protein also likely promotes the maturation (differentiation) of cells that build bones, called osteoblasts.

SMOC1 gene mutations often result in a nonfunctional SMOC-1 protein. The loss of SMOC-1 could disrupt growth factor signaling, which would impair the normal development of the skeleton, limbs, and eyes. These changes likely underlie the anophthalmia and skeletal malformations of ophthalmo-acromelic syndrome. It is unclear how *SMOC1* gene mutations lead to the other features of this condition.

Some people with ophthalmo-acromelic syndrome do not have an identified mutation in the *SMOC1* gene. The cause of the condition in these individuals is unknown.

Learn more about the gene associated with Ophthalmo-acromelic syndrome

- SMOC1

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Anophthalmia-syndactyly
- Anophthalmia-Waardenburg syndrome
- Anophthalmos with limb anomalies
- Anophthalmos-limb anomalies syndrome
- Microphthalmia with limb anomalies
- OAS
- Ophthalmoacromelic syndrome
- Syndactyly-anophthalmos syndrome
- Waardenburg anophthalmia syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Microphthalmia with limb anomalies (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0599973/)

Genetic and Rare Diseases Information Center

- Microphthalmia with limb anomalies (https://rarediseases.info.nih.gov/diseases/722/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- MICROPHTHALMIA WITH LIMB ANOMALIES; MLA (https://omim.org/entry/206920)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ophthalmo-acromelic+syndrome%5BTIAB%5D%29+OR+%28anophthalmia-syndactyly%5BTIAB%5D%29+OR+%28anophthalmos+with+limb+anomalies%5BTIAB%5D%29+OR+%28microphthalmia+with+limb+anomalies%5BTIAB%5D%29+OR+%28ophthalmoacromelic+syndrome%5BTIAB%5D%29+OR+%28waardenburg+anophthalmia+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

References

- Abouzeid H, Boisset G, Favez T, Youssef M, Marzouk I, Shakankiry N, Bayoumi N, Descombes P, Agosti C, Munier FL, Schorderet DF. Mutations in the SPARC-relatedmodular calcium-binding protein 1 gene, SMOC1, cause waardenburg anophthalmiasyndrome. Am J Hum Genet. 2011 Jan 7;88(1):92-8. doi: 10.1016/j.ajhg.2010.12.002.Epub 2010 Dec 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21194680) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3014360/)
- Gambhir PS, Gambhir SP, Bankar SM. Ophthalmoacromelic syndrome: two furthercases expanding the phenotype. Clin Dysmorphol. 2010 Apr;19(2):91-94. doi: 10.1097/MCD.0b013e328336a1a6. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20179580)
- Okada I, Hamanoue H, Terada K, Tohma T, Megarbane A, Chouery E, Abou-Ghoch J,Jalkh N, Cogulu O, Ozkinay F, Horie K, Takeda J, Furuichi T, Ikegawa S, NishiyamaK, Miyatake S, Nishimura A, Mizuguchi T, Niikawa N, Hirahara F, Kaname T,Yoshiura K, Tsurusaki Y, Doi H, Miyake N, Furukawa T, Matsumoto N, Saitsu H. SMOC1 is essential for ocular and limb development in humans and mice. Am J HumGenet. 2011 Jan 7;88(1):30-41. doi: 10.1016/j.ajhg.2010.11.012. Epub 2010 Dec 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21194678) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3014372/)
- Rainger J, van Beusekom E, Ramsay JK, McKie L, Al-Gazali L, Pallotta R,Saponari A, Branney P, Fisher M, Morrison H, Bicknell L, Gautier P, Perry P,Sokhi K, Sexton D, Bardakjian TM, Schneider AS, Elcioglu N, Ozkinay F, Koenig R,Megarbane A,

Semerci CN, Khan A, Zafar S, Hennekam R, Sousa SB, Ramos L,Garavelli L, Furga AS, Wischmeijer A, Jackson IJ, Gillessen-Kaesbach G, BrunnerHG, Wieczorek D, van Bokhoven H, Fitzpatrick DR. Loss of the BMP antagonist,SMOC-1, causes Ophthalmo-acromelic (Waardenburg Anophthalmia) syndrome in humansand mice. PLoS Genet. 2011 Jul;7(7):e1002114. doi: 10.1371/journal.pgen.1002114.Epub 2011 Jul 7. Erratum In: PLoS Genet. 2018 Dec 26;14(12):e1007866. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21750680) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131273/)

Last updated March 1, 2014