Crouzon syndrome with acanthosis nigricans

Crouzon syndrome with acanthosis nigricans is a disorder characterized by the premature joining of certain bones of the skull (craniosynostosis) during development and a skin condition called acanthosis nigricans.

The signs and symptoms of Crouzon syndrome with acanthosis nigricans overlap with those of a similar condition called Crouzon syndrome. Both conditions involve premature fusion of the skull bones, which affects the shape of the head and face. Other common features of both conditions include wide-set, bulging eyes due to shallow eye sockets; eyes that do not point in the same direction (strabismus); a small, beaked nose; and a flat or sunken appearance of the middle of the face (midface hypoplasia). Less common features that can occur in either disorder include an opening in the roof of the mouth (cleft palate), dental problems, or hearing loss. People with Crouzon syndrome or Crouzon syndrome with acanthosis nigricans usually have normal intelligence.

Crouzon syndrome with acanthosis nigricans is distinguished from Crouzon syndrome by several features, including skin abnormalities. Acanthosis nigricans is a skin condition characterized by thick, dark, velvety skin in body folds and creases, including the neck and underarms. People with Crouzon syndrome with acanthosis nigricans may also have other skin abnormalities; for example, scars in the thick, dark areas of skin are flat and pale. These scars are usually from surgical procedures that are commonly needed in affected individuals. Additionally, in some people with the condition, one or both nasal passages are narrowed (choanal stenosis) or completely blocked (choanal atresia), which can cause difficulty breathing. A buildup of fluid in the brain (hydrocephalus) can also occur. Nasal passage abnormalities and hydrocephalus are rare in Crouzon syndrome. Less common features of Crouzon syndrome with acanthosis nigricans include subtle changes in the bones of the spine (vertebrae), abnormalities of the finger bones, and noncancerous growths in the jaw called cementomas.

Frequency

Crouzon syndrome with acanthosis nigricans is rare; this condition occurs in about 1 person per million. For unknown reasons, it affects females more than twice as often as males.

Causes

A mutation in the \( FGFR3 \) gene causes Crouzon syndrome with acanthosis nigricans. This gene provides instructions for making a protein that is involved in the development and maintenance of bone and other tissues. The genetic change involved in this
disorder causes the FGFR3 protein to be overly active, which disrupts the normal growth of skull bones and affects skin pigmentation. These changes lead to the features of Crouzon syndrome with acanthosis nigricans.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In some cases, an affected person inherits the mutation from one affected parent. More commonly, this condition results from new (de novo) mutations in the gene. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

• CAN
• Crouzonodermoskeletal syndrome

Diagnosis & Management

Genetic Testing Information

• What is genetic testing? /primer/testing/genetictesting

Research Studies from ClinicalTrials.gov

• ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22Crouzonodermoskeletal+syndrome%22+OR+%22Craniofacial+Dysostosis%22+OR+%22Crouzon%27s+Disease%22+OR+%22Crouzons+Disease%22+OR+%22Craniosynostosis%22+OR+%22Crouzon+Disease%22

Other Diagnosis and Management Resources

• MedlinePlus Encyclopedia: Craniosynostosis https://medlineplus.gov/ency/article/001590.htm
Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Acanthosis Nigricans
  https://medlineplus.gov/ency/article/000852.htm

- Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm

- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html

- Health Topic: Skin Pigmentation Disorders
  https://medlineplus.gov/skinpigmentationdisorders.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Craniosynostosis
  Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Craniosynostosis-Information-Page

Educational Resources

- American Academy of Dermatology: Acanthosis Nigricans

- Center for Craniofacial Development and Disorders, Johns Hopkins Medicine: Craniosynostosis
  https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/pediatric_neurosurgery/conditions/craniosynostosis/

- KidsHealth from Nemours: Acanthosis Nigricans

- MalaCards: crouzon syndrome with acanthosis nigricans
  https://www.malacards.org/card/crouzon_syndrome_with_acanthosis_nigricans

- Orphanet: Crouzon syndrome-acanthosis nigricans syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=93262

- Seattle Children's Hospital and Regional Medical Center: Crouzon Syndrome
  https://www.seattlechildrens.org/conditions/chromosomal-genetic-conditions/crouzon-syndrome

- UC Davis Children's Hospital: Craniofacial Anomalies--Crouzon Syndrome
Patient Support and Advocacy Resources

- Children's Craniofacial Association
  https://ccakids.org/

- Resource List from the University of Kansas Medical Center: Facial Anomalies/ Craniofacial Conditions
  http://www.kumc.edu/gec/support/craniofa.html

Clinical Information from GeneReviews

- FGFR-Related Craniosynostosis Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1455

Scientific Articles on PubMed

- PubMed
  +syndrome%29+OR+%28crouzon+syndrome+with+acanthosis+nigricans
  %29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last
  +3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- CROUZON SYNDROME WITH ACANTHOSIS NIGRICANS
  http://omim.org/entry/612247

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17935505

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21536014 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110564/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23437153 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3577887/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10213050

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23571469
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301628

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11426459

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10696568

Reprinted from Genetics Home Reference:

Reviewed: March 2017
Published: May 14, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services