Cockayne Syndrome

Subjects: Genetics & Heredity
Contributor: Nicole Yin

Cockayne syndrome is a rare disorder characterized by an abnormally small head size (microcephaly), a failure to gain weight and grow at the expected rate (failure to thrive) leading to very short stature, and delayed development.

Keywords: genetic conditions

1. Introduction

The signs and symptoms of this condition are usually apparent from infancy, and they worsen over time. Most affected individuals have an increased sensitivity to sunlight (photosensitivity), and in some cases even a small amount of sun exposure can cause a sunburn or blistering of the skin. Other signs and symptoms often include hearing loss, vision loss, severe tooth decay, bone abnormalities, hands and feet that are cold all the time, and changes in the brain that can be seen on brain scans.

People with Cockayne syndrome have a serious reaction to an antibiotic medication called metronidazole. If affected individuals take this medication, it can cause life-threatening liver failure.

Cockayne syndrome is sometimes divided into types I, II, and III based on the severity and age of onset of symptoms. However, the differences between the types are not always clear-cut, and some researchers believe the signs and symptoms reflect a spectrum instead of distinct types. Cockayne syndrome type II is also known as cerebro-oculo-facio-skeletal (COFS) syndrome, and while some researchers consider it to be a separate but similar condition, others classify it as part of the Cockayne syndrome disease spectrum.

2. Frequency

Cockayne syndrome is estimated to occur in 2 to 3 per million newborns in the United States and Europe.

3. Causes

Cockayne syndrome can result from mutations in either the *ERCC6* gene (also known as *CSB*) or the *ERCC8* gene (also known as *CSA*). These genes provide instructions for making proteins that are involved in repairing damaged DNA. DNA can be damaged by ultraviolet (UV) rays from the sun and by toxic chemicals, radiation, and unstable molecules called free radicals. Cells are usually able to fix DNA damage before it causes problems. However, in people with Cockayne syndrome, DNA damage is not repaired normally. As errors build up in DNA, cells malfunction and eventually die. The faulty DNA repair underlies photosensitivity in affected individuals, and researchers suspect that it also contributes to the other features of Cockayne syndrome. It is unclear how *ERCC6* or *ERCC8* gene mutations cause all of the varied features of this condition.

3.1. The Genes Associated with Cockayne Syndrome

- ERCC6
- ERCC8

4. 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.

5. Other Names for This Condition

- CS
- dwarfism-retinal atrophy-deafness syndrome

References

1. Cleaver JE, Lam ET, Revet I. Disorders of nucleotide excision repair: thegenetic and molecular basis of heterogeneity. Nat Rev Genet. 2009Nov;10(11):756-68. doi: 10.1038/nrg2663.
2. Laugel V. Cockayne Syndrome. 2000 Dec 28 [updated 2019 Aug 29]. In: Adam MP,Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors.GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle;1993-2020. Available from http://www.ncbi.nlm.nih.gov/books/NBK1342/
3. Laugel V. Cockayne syndrome: the expanding clinical and mutational spectrum.Mech Ageing Dev. 2013 May-Jun;134(5-6):161-70. doi: 10.1016/j.mad.2013.02.006.
4. Nance MA, Berry SA. Cockayne syndrome: review of 140 cases. Am J Med Genet.1992 Jan 1;42(1):68-84. Review.
5. Weidenheim KM, Dickson DW, Rapin I. Neuropathology of Cockayne syndrome:Evidence for impaired development, premature aging, and neurodegeneration. MechAgeing Dev. 2009 Sep;130(9):619-36. doi: 10.1016/j.mad.2009.07.006.
6. Wilson BT, Stark Z, Sutton RE, Danda S, Ekbote AV, Elsayed SM, Gibson L,Goodship JA, Jackson AP, Keng WT, King MD, McCann E, Motojima T, Murray JE, OmataT, Pilz D, Pope K, Sugita K, White SM, Wilson IJ. The Cockayne Syndrome NaturalHistory (CoSyNH) study: clinical findings in 102 individuals and recommendations for care. Genet Med. 2016 May;18(5):483-93. doi: 10.1038/gim.2015.110.
7. Wilson BT, Strong A, O'Kelly S, Munkley J, Stark Z. Metronidazole Toxicity in Cockayne Syndrome: A Case Series. Pediatrics. 2015 Sep;136(3):e706-8. doi:10.1542/peds.2015-0531.