Dyskeratosis congenita, RTEL1-related

What is dyskeratosis congenita, RTEL1-related?

Dyskeratosis congenita is an inherited disease of telomere dysfunction, with variable severity and age at onset even within families. Dyskeratosis congenita is characterized by bone marrow failure, cancer predisposition, pulmonary fibrosis, and the diagnostic triad of dysplastic nails, abnormal skin pigmentation, and oral leukoplakia. Individuals with dyskeratosis congenita, RTEL1 related, have a defect in the production of a protein called the regulator of telomerase elongation helicase 1. This protein has roles in regulating telomere length, in DNA replication and repair, and in maintaining the stability of the DNA in cells. In its severe form, dyskeratosis congenita is known as Hoyeraal Hreidarsson syndrome.

What are the symptoms of dyskeratosis congenita, RTEL1-related, and what treatment is available?

Signs and symptoms of dyskeratosis congenita, RTEL1-related, may include:

- Dysplastic (poorly formed) nails
- Abnormal skin coloration
- Oral leukoplakia (white patches inside the mouth)
- Bone marrow failure
- Pulmonary fibrosis (lung scarring)
- Liver disease
- Narrowing of the esophageal, urethral, or lacrimal (tear) ducts
- Developmental delay
- Premature graying
- Cancer, including squamous cell carcinoma of the tongue and acute myeloid leukemia
- Thrombocytopenia (low platelet count)
- Osteoporosis (fragile bones)

Signs and symptoms of Hoyeraal Hreidarsson syndrome also include intrauterine growth restriction, microcephaly, cerebellar hypoplasia, moderate to severe intellectual disability, growth and developmental delays, severe immunodeficiency, enteropathy, and pancytopenia.

There is no cure for dyskeratosis congenita, RTEL1-related. Treatment is supportive. Eighty to 90 percent of patients with dyskeratosis congenita develop bone marrow failure by the age of 30, making it the leading cause of death for these patients.

How is dyskeratosis congenita, RTEL1-related, inherited?

Dyskeratosis congenita is caused by mutations in at least eleven genes. Inheritance of dyskeratosis congenita caused by mutations in the RTEL1 gene can be autosomal recessive or autosomal dominant depending on telomere length. An individual with one RTEL1 gene mutation is a carrier. Some healthy carriers of an RTEL1 mutation may have bone marrow or pulmonary manifestations later in life. An individual who inherits two RTEL1 mutations, one from each parent, is expected to be affected with dyskeratosis congenita, RTEL1-related. As the mutated gene is passed from generation to generation the telomere length may become progressively shorter. A child who inherits one RTEL1 mutation and also inherits shortened telomeres may be affected with dyskeratosis congenita, RTEL1-related.

If both members of a couple are carriers of a mutation in the RTEL1 gene, the risk of having an affected child is at least 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing. If just one parent is a carrier of an RTEL1 mutation, the risk of having an affected child is 50% if the child inherits the mutation and also inherits shortened telomeres.
Who is at risk for dyskeratosis congenita, RTEL1-related?

Dyskeratosis congenita is a rare condition that can occur in individuals of all races and ethnicities. Mutations in RTEL1 may be seen more commonly in the Ashkenazi Jewish population with a carrier frequency of 1 in 86.\(^6\)

Having a relative who is a carrier or who is affected can increase an individual’s risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?


Dyskeratosis Congenita Outreach: [https://www.dcoutreach.org/](https://www.dcoutreach.org/)

References