OVERVIEW:

Progeria or HGPS is a premature aging disease that occurs in 1 in 8 million newborns. It was described by two English doctors, Jonathan Hutchinson and Hastings Gilford in 1886 and 1897 respectively. Progeria is derived from Greek and means prematurely old. It occurs only in children and has a 0% chance of survival with the average age of death being thirteen years, but ranging between 13-21 years (Progeria Research Foundation). Not to be confused with Werner’s Syndrome or Adult Progeria, HGPS symptoms first appear during infancy between 18-24 months (American Pregnancy Association). In February 2006 there were 42 children in 20 countries diagnosed with Progeria (Progeria Research Foundation).

Hutchinson-Gilford Progeria Syndrome
Helen Daifotis & Shaan Gurnani

INHERITANCE AND GENETICS:

Inheritance: HGPS is a sporadic autosomal dominant disorder. In history there have been two documented cases of twins with this disorder and only one pair of siblings. It is impossible for a child with Progeria to reproduce because these children were never infants to produce any children. This disease almost always occurs in individuals with no family history of the mutation. In rare cases, with frequency of 1 in 400 million births or 100 cases of HGPS, the syndrome may be passed down within a family (Progeria Research Foundation).

Genetic Sequence: This disease is the result of a mutation in the LMNA gene on chromosome 1. The LMNA gene provides the instructions used to produce the Lamin A protein, which is the structural scaffolding of the nucleus. Researchers have discovered that the abnormal Lamin A protein present in Progeria patients results in a nuclear unstable and leads to premature cell death and Progeria. However, it is not being cleared up as how these changes lead to the symptoms of HGPS. The abnormal Lamin A protein occurs when a cryptic splice site is activated and a section of 55 amino acids is spliced resulting in a truncated form called Progerin. Which disrupts the network that supports the nuclear envelope and acts as a dominant-negative Lamin A protein (Frontiers in Science). Normal Lamin A contains two “tags” that direct the protein to its proper place. One reduces translocation, without losing function. A second sequence acts as a retention tag that increases the resistance of Lamin A to degradation (Frontiers in Science). Researchers believe the splicing event is due to its “signal-on” feature to the normal portion of the protein, including the farnesyl group, causing Lamin A to become more stable and reducing its degradation (Progeria). However, the Progerin does not have the cleavage tag. Scientists speculate that this causes the malfunction of the nuclear maintenance and believe these defects could be prevented by blocking the farnesyltransferase pathway (Progeria).

Symptoms:

Children with Progeria suffer no mental side effects due to the illness because the LMNA is not expressed by the brain cells (Progeria Research Foundation). They do not need special education programs and may participate in the same activities as any other child. However, they may have some limitations because of their physical stature and joint stiffness.

SYMPTOMS, DIAGNOSIS, AND TREATMENT:

Symptoms: Children afflicted with Progeria are born with no noticeable abnormalities, but around 18 months the symptoms become noticeable. These may include: lack of growth, loss of body fat and hair, sunken eyes, protruding ears, joint stiffness, and premature deterioration of heart and other internal organs (Genetics Home Reference). Despite all this however, there are no mental side effects to the disease.

Diagnosis: Since the discovery of the HGPS gene on April 16, 2003, accurate testing for the LMNA mutation has been developed. This is done by testing a sample of the patient’s blood for the specific genetic variation that causes Progeria.

Treatment: Currently the only treatments available are used to lessen the strain of living with Progeria and are used on a patient-to-patient basis. The three options are physical and occupational therapy, nutritional supplements, and a low-dose aspirin treatment. In addition to this, a new drug called an FTI, farnesyltransferase inhibitor, is currently in the testing phase to become the first-ever drug treatment for children with Progeria. In lab tests FTIs have been able to reverse an abnormality in Progeria cells (Progeria Research Foundation). The FTI’s aim to block the farnesylation of progerin or “paralyze” it.

References:


References:


