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Case Study: Progeria

Progeria is a rare genetic disorder that usually manifests itself during the first years of life and is defined by a set of symptoms that resemble premature aging. The name of the condition derives from the Greek word “pro” meaning something premature and word “geras” meaning old age. Children affected by progeria develop certain changes in facial appearance. Newborns with the condition appear normal with no diagnosable signs. However, within typically a year their speed of growth decelerates, and other symptoms come into force. This paper will describe and explain progeria with emphasis on research on its treatment.

The disorder was first observed and described by doctors Jonathan Hutchinson and Hastings Gilford in 1886 in England. The condition was named Hutchinson-Gilford Progeria Syndrome after the doctors who described it (Ghosh & Zhou 41-46). Since the extremely rare rate of occurrence and lack of scientific data there was no progress in understanding the nature of progeria since the majority of the 20th century. The first round of research on progeria began in the 1990s. The first major discovery regarding the etiology of progeria was made in 2003 when a mutation in genes that were associated with the condition was observed and reported (Eriksson et al. 293-298).

The occurrence of the condition is extremely rare; it is estimated that only 1 in 4 million is affected worldwide. There are approximately 350 children with progeria in the world at any time

(Ghosh & Zhou 41-46). No racial or sex disparity has been proved for progeria. The scientific literature holds the record for more than 130 cases of progeria since it was first described.

Progeria have not been reported to affect siblings or relatives of the affected individuals. The condition is an autosomal dominant with spontaneous point mutations occurring during embryonic development (Pollex & Hegele 375-381). One copy of the mutated gene LMNA is enough to cause progeria.

Symptoms

Progeria has several characteristic symptoms that are associated with the genetic etiology of the condition (Pollex & Hegele 375-381). Symptoms of progeria can be divided into several categories depending on the systems they affect:

Growth:

- Noticeably short stature that remains lifelong
- Low weight and failure to thrive
- Disproportionally large head when comparing to face
- High pitched voice

Globally diminished subcutaneous fat that results in following signs:

- Prominent veins that can be seen on most of the body
- Bluish discoloration of the skin or circumoral cyanosis (Gordon, Brown and Collins)
- In some cases, ear lobes can be absent

A range of symptoms pertaining to hair, skin, nails, and eyes:

- Variably pigmented and mostly dry skin
- Loss of eyebrows

- Fingernails and toenails are often dystrophic
- Nocturnal lagophthalmos that is an inability to close the eye completely

Symptoms related to skeletal system:

- Pear-shaped thorax
- Nasal bridge is narrow with nasal tip often being pointed (Gordon, Brown and Collins)
- Low bone density is characteristic of the condition
- Limbs are very thin

Symptoms related to cardiovascular and neuromuscular systems:

- Angina, myocardial infarction, and congestive heart failure
- Transient ischemic attacks and various types of strokes

The mutation in LMNA gene is associated with syndrome and the symptoms described above. The gene in question is responsible for production of protein lamin A which is essential for determining the shape of nucleus of cells (Broers 967-1008). The lamin A is also a component responsible for strength of nuclear envelope (Figure 1). Mutations in the gene that cause Hutchinson-Gilford progeria result in a build up of a mutated protein also called progerin (Eriksson et al. 293-298). Accumulation of progerin occurs naturally over the lifespan. However in children with progeria this process is significantly faster.

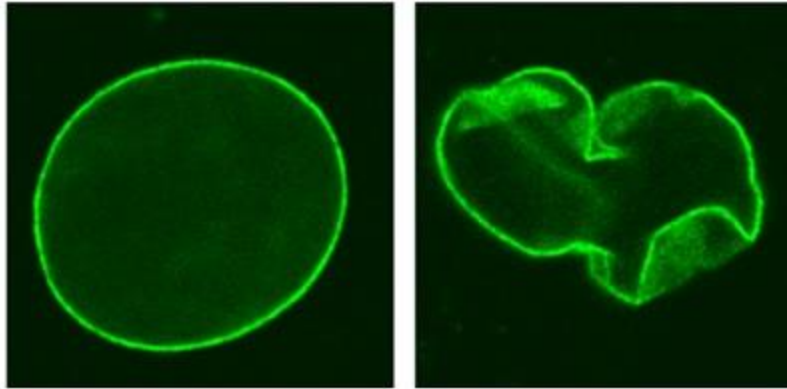


Figure 1. Normal cell nucleus opposing to Progeria cell's nucleus (Salameh)

Treatment

- Currently, there is no effective treatment for progeria capable of causing a remission. Treatment of manifestations is a primary type of care used to help the affected individuals.
- Dietary augmentations are often recommend to offset the abnormal lipid profile. Such medication as statin can be prescribed.
- Physical and occupational therapies are highly recommended to alleviate the low muscular index. Physical therapy is also the primary treatment for hip dislocation management.
- Patients suffering from congestive heart failure are prescribed with anti congestive therapy. In order to prevent possible secondary complications with cardiovascular system aspirin may be prescribed.
- Ocular lubrication may be necessary in the case of exposure keratopathy resulting from nocturnal lagophthalmos. Other symptomatic treatments may be required depending on manifesting symptoms.

Current Research

The Progeria Research Foundation is one of the leading organizations in studying the condition. In 2012 a breakthrough discovery was made when farnesyltransferase inhibitors were

proven to be useful in treating progeria. Farnesyltransferase inhibitors (FTI) are the compounds that were used in cancer treatments but can also lead to cell restoration. During the initial trials FTI-277 demonstrated its ability to restore localization of nucleolar antigen in cells with progeria (Mehta, Bridger & Kill 287-291). Additionally, recent study have identified the correlation between progerin and telomeres. Telomerase normally prevents detrimental effects of progerin while in patients with the syndrome telomeres are impaired resulting in proliferation of progerin-induced cellular defects (Chojnowski et al.).

Conclusion

Conclusively, progeria is a genetic disorder that results in build up of altered proteins leading to premature aging in children. It is a rare condition affecting only 1 in 4 million people. A range of symptoms caused by cellular ageing is present in affected individuals. Recent studies have delivered promising result for treatment of progeria.

Take-Home Messages:

Progeria is a genetic while usually non-inheritable disease that causes premature physiological aging.

Recent discoveries pave the way for potential treatment of progeria by elimination harmful effects of progerin. This discoveries can also lead to better understanding of causes of aging in general.

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