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Review Article

PROGERIA: RARE CONDITION THAT CAUSES RAPID AGEING

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Abstract: Though Progeria is rare found only one in one million people, it is a serious disease, even today we do not have any treatment for it. Only mutation of one gene, the Lamin gene, makes all the difference. The newborns with the disorder appear to be healthy at birth but usually start to show signs of premature aging during their first one to two years of life; their growth rate slows and they don't gain. Children with the condition have typical intelligence. However, their rapid aging causes distinct physical characteristics by which they can easily identified. They do die early, the average age of death is 14.5 years, generally by stroke or heart attack.

Keywords: Progeria, Early aging

INTRODUCTION

Aging is unavoidable and natural phenomenon of life, defined as the total outcome of interactions genetic, environmental and lifestyle factors at a given time [1]. Nevertheless, it can be regulated by influencing cellular processes. While there is no known intervention that can stop or reverse aging in humans. Nevertheless, there are some epigenetic, factors such as exercise balanced diet, maintain healthy weight, no smoking, can regulate and promote healthy aging [2,3] More so, even in the same individual body systems and organs age at different rates. One person is a cardio-ager, another is a metabolic ager, another is an immune ager," as shown by changes over time in nearly 100 key molecules that play a role in those systems. "There is quite a bit of difference in how individuals experience aging on a molecular level [4,5].

The insulin/IGF-1 and TOR pathways are two evolutionarily conserved pathways that play critical roles in the regulation of cell proliferation, survival, and energy metabolism . Studies have demonstrated that insulin/IGF-1 and TOR pathways also play important roles in regulating aging and longevity [6].

Progeria:

There are some very rare genetic conditions that can cause to show signs of aging in childhood and early puberty. Though the newborns with the disorder appear to be healthy at birth but usually start to signs of premature aging during their first one to two years of life. Their growth rate slows and they don't gain weight as expected. Children with the condition have typical intelligence. However, their rapid aging causes distinct physical characteristics as shown by Lamis et al. [7].

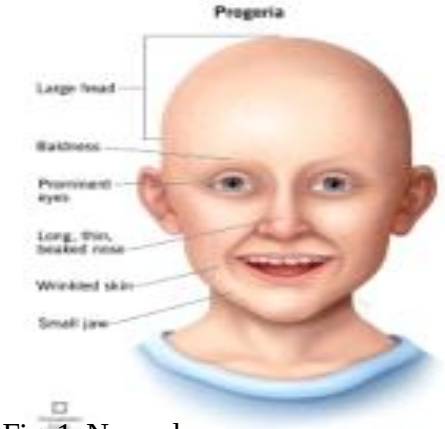

Fig. 1: Normal person

Lamis et al. [7].

Fig. 2: Progeria patients.

Change in morphological features in Progeria patients are evident in figures 1 and 2.

- Hair loss (baldness).
- Prominent eyes which they can't close all the way
- Aged look, wrinkled skin.
- Thin, spotted wrinkled skin
- A thin, beaked nose.
- Small face compared to head size, bigger head
- Loss of fat under the skin.
- A small lower jaw
- A thin nose with a "beaked" tip
- Ears that stick out
- Veins are visible
- Slow and abnormal tooth growth
- A high-pitched voice
- Loss of body muscle
- Loss of and eyebrows

Causes and Risk Factors:

LMNA gene mutations: These above mentioned symptoms are of the disease progeria. Werner syndrome affects 1 in 1 million people. It causes wrinkled skin, graying hair, and balding to develop between 13 and 30 years old. Hutchinson-Gilford syndrome is an even rarer condition, affecting 1 in 8 million babies. Children with this syndrome don't grow as quickly as others in their age group. They also experience thin limbs and baldness. The average life expectancy for children living with Hutchinson-Gilford syndrome is 13 years [8].The disease affects people of both the sexes and races equally. About 1 in every 4 million babies is born with it worldwide. And the average age of death is 14.5 years, although some adults with progeria will live into their early 20s. A drug called lonafarnib has been shown to slow down the progression of the disease. As children with progeria get older, they get diseases, normally, expect to see in people age 50 and older, including bone loss, hardening of the arteries, and heart disease. Children with progeria usually die of heart attacks or strokes. Progeria doesn't affect a child's intelligence or brain development. A child with the condition isn't any more likely to get infections than other kids, either [9].

Mutation in the LMNA gene causes progeria [10]. A single mistake in a certain gene causes it to make an abnormal protein. When cells use this protein, called progerin, they break down more easily. This leads kids with progeria to age quickly; here cellular senescence is a route by which cells exit prematurely from the natural course of cellular aging. Death most often occurs as a result of complications of severe atherosclerosis. This is the same heart disease that affects millions of typically aging adults but at a much younger age. Atherosclerosis occurs when plaque builds up within the walls of arteries. This makes them less elastic and therefore, stiffer. Complications can lead to heart attack or stroke.
The gene makes a protein that holds together the center of a cell. With progeria, the body makes an abnormal form of lamin A called progerin, which leads to rapid aging a protein aceous meshwork that

underlies the inner nuclear membrane and is essential for proper nuclear architecture. Alterations in lamin A and C that disrupt the integrity of the nuclear lamina affect a whole repertoire of nuclear functions, causing cellular decline [11-13]. Lamins are major components of the nucleoskeleton in the cell nucleus. Lamins interact with a wide range of nuclear proteins and are involved in numerous nuclear and cellular functions. Within the nucleus, they play roles in chromatin organization and gene regulation, nuclear shape, size, and mechanics, and the organization and anchorage of nuclear pore complexes. Lamin A/C-deficient cells have a normal response to ionizing radiation but are sensitive to agents that cause inter-strand cross links (ICLs) or replication stress. In response to treatment with ICL agents (cis-platin, campthotecin, mitomycin), lamin A/C-deficient cells displayed normal y-H2AX foci formation but a higher frequency of cells with delayed y-H2AX removal, decreased recruitment of the FANCD2 repair factor and a higher frequency of chromosome aberrations. They polymerize and depolymerize during the cell cycle, resulting in deformation and reformation of the nuclear envelope. Researchers haven't found any risk factors for progeria. It isn't inherited or passed down in families [8].

Kids with progeria are more likely to get dehydrated, so they need to drink plenty of water, especially when they're sick or it's hot. Small meals more often can help them eat enough, too. Cushioned shoes or inserts can ease discomfort and encourage the child to play and stay active. Use a broad-spectrum sunscreen with an SPF of at least 15. Reapply it every 2 hours, or more if the child is sweating or swimming.

Complications:

Children with progeria usually develop a condition called atherosclerosis, which hardens and slows blood flow from blood vessels that carry nutrients and oxygen to your body. Most children with progeria die of heart attacks and strokes related to athero-sclerosis.

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