ABOUT PROGERIA AND THE CONSULTATION OF THE DISEASE

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Annotation: Facing challenges of the progeria which is the cause of the vanishing timing and happiness from the children, leading them to the quick adulthood in a blink of the eyes.

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Progeria is a specific type of progeroid syndrome, also known as **Hutchinson–Gilford syndrome**. A single gene mutation is responsible for progeria. The gene, known as lamin A (LMNA), makes a protein necessary for holding the nucleus of the cell together. When this gene gets mutated, an abnormal form of lamin A protein called progerin is produced. Progeroid syndromes are a group of diseases that causes individuals to age faster than usual, leading to them appearing older than they actually are. Patients born with progeria typically live to an age of mid-teens to early twenties.

Severe cardiovascular complications usually develop by puberty, resulting in death.

Children with progeria usually develop the first symptoms during their first few months of life. The earliest symptoms may include a failure to thrive and a localized scleroderma-like skin condition. As a child ages past infancy, additional conditions become apparent, usually around 18–24 months. Limited growth, full-body alopecia (hair loss), and a distinctive appearance (a small face with a shallow, recessed jaw and a pinched nose) are all characteristics of progeria. Signs and symptoms of this progressive disease tend to become more marked as the child ages. Later, the condition causes wrinkled skin, kidney failure, loss of eyesight, atherosclerosis, and other cardiovascular problems. Scleroderma predominates, hardening and thickening of the skin of the trunk and extremities. People diagnosed with this disorder usually have small, fragile bodies, like older people. The head is usually large in relation to the body, with a narrow, wrinkled face and a beak-like nose. Protruding veins on the scalp (become more visible with alopecia), as well as bulging eyes, are noticeable. Musculoskeletal degeneration causes loss of fat and muscle, joint stiffness, hip dislocations, and other symptoms not usually present in the elderly. People usually retain typical mental and motor functions.

Developmental disorders of the skeleton. In people with this syndrome, the clavicles remain underdeveloped, the ribs become thinner, the bone tissue in the phalanges of the fingers is destroyed, osteoporosis occurs - the bones become less dense and more fragile. The neck of the femur is often deformed, osteoarthritis of the hip joints occurs (a disease in which cartilage and bone tissue is destroyed), and the mobility of the elbow and knee joints decreases.

Diseases of the skin and hair. In almost 80% of cases, with progeria, the skin changes - some areas thicken, pigment spots appear. The subcutaneous fatty tissue becomes noticeably thinner, the skin becomes dry and wrinkled. Hair, eyelashes and eyebrows fall out, nails do not develop normally, become brittle and bulging - this phenomenon is called "watch glass syndrome".

Neurological symptoms. Children with Progeria suffer from headaches, seizures, and muscle weakness due to reduced blood flow to the brain.

Endocrine symptoms. Patients with progeria do not reach puberty, their genitals remain underdeveloped. Approximately half of children have insulin resistance. With this pathology, the cells of the body begin to react worse to the hormone insulin, which leads to metabolic disorders.

Other symptoms. In addition, progeria patients erupt teeth late. They may be partially absent, and those that grow are usually crowded and twisted. These children are often diagnosed with hearing loss due to changes in the cartilage of the outer and inner ear, as well as nocturnal lagophthalmos (sleep with open eyes), which leads to dry eye syndrome and clouding of the cornea.

Progeria is caused by a sporadic mutation in the LMNA gene, which encodes a protein (lamin A) that provides molecular support to the cell nuclei. The protein defect leads to instability of the nucleus during cell division and early death of all cells in the body.

The mean age at death is 14.6 years; the cause, as a rule, is diseases of the coronary arteries and cerebral vessels. Insulin resistance and atherosclerosis may develop. It should be noted that other problems associated with normal aging (e.g., increased risk of cancer, degenerative arthritis) are absent.

Symptoms and signs of progeria develop over 2 years and include: Stunted growth (e.g., short stature, late teething) Craniofacial abnormalities (e.g., craniofacial disproportion, micrognathia, hooked nose, macrocephaly, large fontanel)

Physical changes with aging (e.g., wrinkling of the skin, baldness, decreased range of motion in the joints, thick skin that resembles scleroderma)

The diagnosis of progeria is usually obvious from the outside, but must be distinguished from segmental progeria (e.g., acrogeria, metageria) and other causes of growth retardation.

Lonafarnib is an oral medication that prevents the accumulation of defective progerin or a progerin-like protein. Small studies show that it increases life expectancy by up to 2.5 years.

Premature aging is a feature of other rare progeroid syndromes.

Werner's syndrome is premature aging after puberty with thinning hair and the development of conditions characteristic of old age (e.g., cataracts, diabetes mellitus, osteoporosis, atherosclerosis).

Rothmund-Thomson syndrome is characterized by premature aging with increased susceptibility to cancer. Both are caused by a gene mutation resulting in a defect in the RecQ DNA helicase, which is normally involved in DNA repair.

Cockayne syndrome is an autosomal recessive disorder caused by a mutation in the ERCC8 gene, which plays an important role in DNA excision repair. Clinical symptoms include severe growth failure, cachexia, retinopathy, hypertension, renal failure, skin photosensitivity, and mental retardation.

Neonatal progeroid syndrome (Wiedemann-Rauthenstrauch syndrome) is a recessive inherited syndrome of aging leading to death before the age of 2 years.

According to the research, Hutchinson-Gilford syndrome or progeria (senile nanism) is an extremely rare genetic disease of children with clinical features of premature aging. The frequency of the disease is 1 in 8 million newborns. HPGS is caused by mutations that weaken the structure of the cell nucleus, making normal cell division difficult. The histone mark H4K20me3 is involved and caused by de novo mutations that occur in a gene that encodes lamin A. Lamin A is made but is not processed properly. This poor processing creates an abnormal nuclear morphology and disorganized heterochromatin. Patients also do not have appropriate DNA repair, and they also have increased genomic instability. As there is no known cure, few people with progeria exceed 13 years of age. At least 90 percent of patients die from complications of atherosclerosis, such as heart attack or stroke.

Mental development is not adversely aoncefact, intelligence tends to be average to above average. With respect to the features of aging that progeria appears to manifest, the development of symptoms is comparable to aging at a rate eight-to-ten-time Concerningormal. With respect to those that progeria does not exhibit, patients show no neurodegeneration or cancer predisposition. They also do not develop conditions that are commonly asofated with the accumulation of damage, such as cataracts (caused by UV exposure) and osteoarthritis.

Progeria in Greek means "premature aging", but this is not a completely correct understanding of the disease. In the natural process of aging, age-related changes to a greater or lesser extent affect all organs and systems of the body. And in people with progeria, the immune system, liver, gastrointestinal tract, lungs, and kidneys continue to function normally. They do not have neoplasms more often than their peers, there are no cataracts, diabetes, senile personality changes. And in terms of intellectual development, they often even overtake their peers. For example, Sampson Gordon Burns, the most famous teenager with progeria, for several years drew public attention to this disease, acted as a motivational speaker. After graduation, Sam went to college to study genetics and cytology. He died at the age of 17 from the effects of the disease, and now his work is continued by the Progeria Research Foundation, which was founded by Sam's parents and aunt.

Sometimes Hutchinson-Gilford syndrome is called childhood progeria to distinguish it from another disease called Werner syndrome, which in some sources is referred to as "adult progeria". Werner's syndrome occurs in adolescence and is also manifested by senile diseases. But it is caused by a defect in another gene that is responsible for the production of the WRN protein. The mutation is inherited in an autosomal recessive way, that is, the disease manifests itself in those who received defective genes from both parents.

The disease is extremely rare, it is detected in one in 4 million newborns. According to the Progeria Foundation as of December 2022, there are 140 children and adolescents with Hutchinson-Gilford syndrome in the world.

Although there may not be any successful treatments for progeria itself, there are treatments for the problems it causes, such as arthritic, respiratory, and cardiovascular problems. People with progeria have normal reproductive development, and there are known cases of women with progeria who delivered healthy offspring.

To correct the deficit of weight and height, children are prescribed a special diet and growth hormones. They need frequent and regular visits to the dentist to prevent caries and periodontitis. To reduce pain and increase joint mobility, patients are prescribed

physiotherapy and kinesiotherapy, if necessary, they select orthoses, special devices to facilitate movement: walkers, canes, wheelchairs. Deficiency of the hormone leptin, which occurs due to a lack of adipose tissue, is compensated by subcutaneous administration of metreleptin. Patients need to undergo regular preventive examinations: ECG, echocardiogram, ultrasound of the carotid arteries, neurological examination, MRI or MRA of the head and neck, examination for the content of fats in the blood serum (lipid profile), dental examination, X-ray of the thigh, computed tomography to measure bone density, ophthalmological examination, audiometry.

Although it can be treated on the purpose, there is special treatment. Progeria treatment includes the use of a drug called lonafarnib. Originally developed to treat cancer, lonafarnib has been shown to improve many aspects of progeria. The drug has increased the average survival rate of children with the disease by two-and-a-half years.

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