

### Hutchinson – Gilford Progeria Syndrome: A Rare Case Report

Dr. Kajalkumari M. Jain<sup>1</sup>, Dr. Ujjwala Shirsath<sup>2</sup>, Dr. Ramesh Kothari<sup>3</sup>, Dr. Sunil Natha Mhaske<sup>4</sup>

<sup>1</sup>Resident, <sup>2</sup>Assistant Professor, <sup>3</sup>Professor & Head, Department of Paediatrics, <sup>4</sup>Professor & Dean, Dr. Vithalrao Vikhe Patil Foundation's Medial College & Hospital, Ahmednagar-414111, (MS), India

Corresponding Author : Dr. Kajalkumari M. Jain

E-mail : kajaljain1018@gmail.com

Address : Department of Paediatrics, Dr. Vithalrao Vikhe Patil Foundation's Medial College & Hospital, Ahmednagar-414111, (MS), India

#### Abstract :

Hutchinson – Gilford Progeria Syndrome is a rare genetic disorder characterized by premature aging involving the skin, bones, heart, and blood vessels. We report a fourteen year old girl with clinical manifestations characteristic of this syndrome. She had a characteristic “plucked-bird” appearance, prominent eyes and scalp veins, senile look, loss of scalp hair, eyebrows, and eyelashes, stunted growth, and mottled pigmentation with sclerodermatous changes over the trunk and lower limbs. Radiological changes and decreased high-density lipoprotein (HDL) levels were also characteristic of the syndrome. This interesting case is reported for its rarity.

**Keywords:** Hutchinson-Gilford syndrome, Progeria, Premature aging

#### Introduction:

Hutchinson – Gilford Progeria Syndrome was first described in 1886 by Jonathan Hutchinson and by Hastings Gilford in 1897.<sup>(1)</sup> Since then, just over 100 cases of HGPS have been reported and currently, there are approximately 40 known cases worldwide.<sup>(2)</sup> Most cases occur due to de novo mutation and are rarely inherited. Sporadic autosomal dominant mutation in LMNA genes is responsible in most cases.<sup>(3)</sup> These patients exhibit characteristic facies; so, they look alike. The appearance is described as a “plucked-bird” appearance.<sup>(4)</sup> Significant morbidity and mortality result

from accelerated atherosclerosis of the carotid and coronary arteries leading to premature death during the second decade of life.<sup>(5)</sup>

#### Case Report:

A fourteen-year-old girl presented with progressive loss of scalp hair, eyebrows, and eyelashes since six months of age along with stunted growth as a major complaint. The child's antenatal history was normal but was born to third-degree consanguineously married parents. On examination, she had a senile look with prominent eyes, sparse hair with patches of alopecia and visible veins over the scalp, beaked nose, and receded chin. Her voice was high pitched and growth was stunted as parameters were less than the third percentile. Teeth and genitals were normal and intelligence quotient (IQ) was corresponding to the age. Hands were short and clawed with thickening and hardening of the skin over the knuckles with racquet nails. There was mottled pigmentation and sclerodermatous changes over the trunk and lower limbs.

Lower limbs also had prominence of knees and slight valgus deformity. Routine investigations were within normal limits. X-ray of the chest showed a pyriform thorax, overcrowding of proximal ribs, and short clavicle with pointed lateral ends.



Fig 1: Senile look Fig 2: Sclerodermatous changes

#### Discussion:

Most cases of HGPS occur due to de novo autosomal dominant mutation in the LMNA gene, located on band 1q21.1-1q21.3.<sup>(2)</sup> Rarely, transmission can be autosomal recessive or maternal due to gonadal mosaicism. Most commonly, there is transitional mutation replacing cytosine with thymine.

This leads to abnormal transcription of the nuclear lamina structural protein called prelamin A. Normal farnesylation of prelamin A allows it to attach to the nuclear membrane. Failure to remove this farnesyl group, due to the mutation, permanently affixes the protein to the nuclear membrane. This affects nuclear morphology and integrity, deoxyribonucleic acid (DNA) repair, regulation of gene expression, and telomere stability. Ultimately, there is genomic instability, decreased cell proliferation, and premature cell senescence and death.<sup>(6)</sup>

The infant is generally healthy at birth but there may be sclerodermatous skin changes involving the trunk and extremities in some cases. Manifestations appear within one to two years in most of the cases.<sup>(7)</sup> Hair growth decreases over the scalp and other parts of the body with areas of alopecia followed by cardiovascular involvement. IQ remains normal.<sup>(8)</sup> Lipodystrophy involving the face leads to typical facies with senile look, glyphic nose, and "plucked bird" appearance. (Fig 1) Involvement of the lower limbs with valgus deformity and mid flexion leads to a "horse riding" stance.<sup>(9)</sup> (Fig 2) HGPS is considered a segmental progeroid syndrome in the sense that it does not recapitulate all the characteristic phenomena of aging like increased tumor formation and cataract development. Hypertension develops, but unlike arteriosclerosis in the general population, in progeria, the only lipid abnormality is decreased HDL levels.<sup>(10)</sup>

This syndrome should be distinguished from scleroderma, Cockayne syndrome, Rothmund - Thomson syndrome, Werner syndrome, acrogeria, and anhidrotic ectodermal dysplasia. In our case, Cockayne syndrome was ruled out because of lack of photosensitivity, facial erythema, and ocular defects, and normal IQ. Rothmund - Thomson syndrome was ruled out by the absence of erythema, poikiloderma, and cataract. Earlier age of onset ruled out Werner syndrome. Acrogeria also manifests at birth but involves only extremities with no tendency to atheroma or decreased life expectancy.

There was an absence of conical teeth, hypotrichosis, and partial or complete anhidrosis, which ruled out hypohidrotic ectodermal dysplasia. Typical clinical features of the child were sufficient to make the diagnosis. This case is reported for its rarity.

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