

Hutchinson – Gilford Progeria Syndrome with associated hypothyroidism: A rare case report

Siddhi Tiwari¹, Vikas Meena², Chaitra Prakash³, Deepak Kumar Mathur⁴, Puneet Bhargava⁵

¹Department of Dermatology, Seth G.S. Medical College and K.E.M. Hospital, Mumbai (Maharashtra), India

^{2,3,4,5}Department of Dermatology, S.M.S. Medical College and Hospital, Jaipur (Rajasthan), 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 five year old female child with clinical manifestations characteristic of this syndrome. This child had a senile look with large cranium, frontal bossing, sparse light brown hair and dilated visible veins over the scalp. Other features were prominent eyes, beaked nose, micrognathia, sclerodermatous changes in both feet and legs, lax and atrophic skin over dorsum of both hands and mottled pigmentation over trunk. Decreased high-density lipoprotein (HDL) levels was characteristic of the syndrome. This case is reported for its rarity and uncommon relationship with hypothyroidism.

Keywords: Hutchinson, Gilford Progeria Syndrome, Hypothyroidism.

I. INTRODUCTION

Hutchinson – Gilford Progeria Syndrome (HGPS; MIM 176670) is a rare premature ageing syndrome which was first described in 1886 by Jonathan Hutchinson and by Hastings Gilford in 1897.¹ Since then, just over 100 cases of HGPS have been reported.² Most cases occur due to *denovo* mutation and are rarely inherited. Males are commonly affected than females in the ratio of 1.5.³ These patients exhibit characteristic facies, similar to that of “plucked-bird”.⁴ The classical clinical presentation, conventional radiological & biochemical investigations confirm the diagnosis. Significant morbidity and mortality results from accelerated atherosclerosis of the carotid and coronary arteries.⁵

II. METHODOLOGY

A five year old female child presented with complaints of progressive loss of scalp hair, eyebrows and eyelashes since nine months of age along with stunted growth. She was presented in skin OPD in Charak Hospital attached to SMS Medical College, Jaipur (Rajasthan) India. This case was seen as a very piculear case. So case was thoroughly observed and explores to find out the diagnosis for proper management. This case was found to be Hutchinson – Gilford Progeria Syndrome. As it is a rare premature ageing syndrome, so case report was presented.

III. CASE REPORT

This 5 year aged female child was of presented with complaints of progressive loss of scalp hair, eyebrows, and eyelashes since nine months of age along with stunted growth. Her mother gave an uneventful antenatal and perinatal history. There was no history of similar complaints in family. This child was apparently normal till 9 months of age and thereafter started developing abnormal features. On examination; she had a senile look with large cranium, frontal bossing, sparse light brown hair and dilated visible veins over the scalp, prominent eyes, beaked nose, micrognathia (Figure 1) and sclerodermatous changes in both feet and leg. She also had lax and atrophic skin over dorsum of

hands and feet [Figure 2(a) & 2(b)] and mottled pigmentation over trunk. Growth was stunted with parameters less than third percentile. Teeth and genitalia were normal. Intelligence quotient was corresponding to the age.

Figure 1
Typical Facies of Progeria

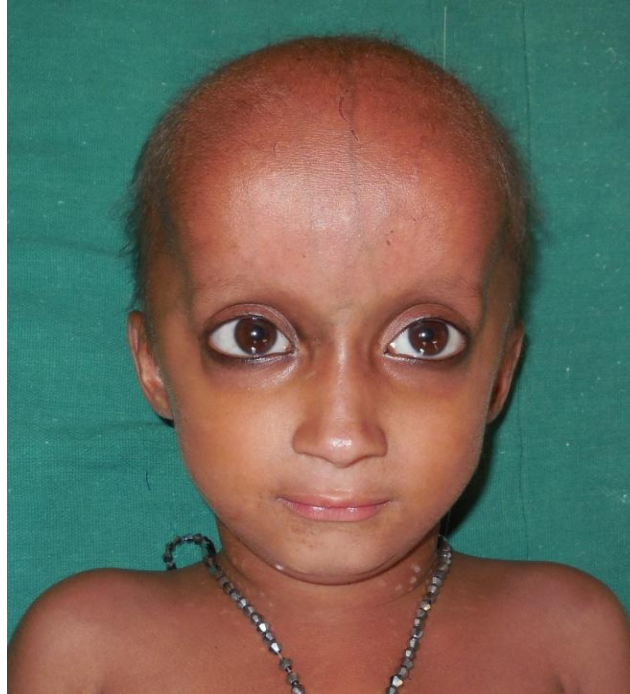


Figure 2(a)

Lax and atrophic skin over dorsum of hands



Figure 2(b)

Lax and atrophic skin over dorsum of feet



Routine investigations including hemogram, liver function test and renal function test were within normal limits. Serum lipid profile showed a decrease in high-density lipoproteins (HDL) and an increase in low-density lipoproteins (LDL). Thyroid profile showed hypothyroidism with borderline anti- TPO antibody. Non contrast computerized tomography brain, X-ray of hands and feet, ultra sonography abdomen, Electrocardiogram, Echocardiography, carotid Doppler did not show any abnormalities. Genetic studies were however not performed.

IV. DISCUSSION

Most cases of HGPS occur due to *de novo* autosomal dominant mutation in the lamininA (LMNA) gene, located on band 1q21.1-1q21.3.² 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.⁶ Generally the rate of ageing in progeria is accelerated to 7 times that of normal. The average life span is 13 years with a range of 7-27 years. There are reports of survival till the age of 45 years.⁷ The infant is generally healthy at birth. Manifestations appear within one to two years of age in most of the cases.⁸ Hair growth decreases over the scalp and other parts of the body with areas of alopecia followed by cardiovascular involvement. Lipodystrophy involving the face leads to typical facies with senile look, beaked nose, and “plucked bird” appearance. Mental age remains normal.⁹ In progeria, HDL cholesterol level is decreased.¹⁰

In our case typical facial appearance and sclerodermatous changes were present with abnormal lipid profile. Hypothyroidism in our case was an additional finding. The differential diagnosis considered were Cockayne syndrome, Rothmund – Thomson syndrome, Werner syndrome and acrogeria. 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. Management of the case is mainly by counseling and symptomatic treatment, which includes early identification and prompt management of the complications. Farnesyltransferase inhibitors (FTIs) such as lonafarnib have shown some promise in reversing the structural abnormalities of the nucleus (prelamin A). The statin drug pravastatin normally used for lowering cholesterol and preventing cardiovascular disease, and the bisphosphonate drug zoledronic acid used for improving osteoporosis are the other drugs advocated for management of HGPS patients.^{11,12} Proper counseling of the parents about this condition is important. Long-term follow-up is needed to observe the cardiovascular and skeletal complications in these patients. There is no definitive cure to the disease. Regular follow up should include blood cholesterol levels and radiological investigations to monitor bone changes.

V. CONCLUSION

This case of Hutchinson – Gilford Progeria Syndrome is reported due to its rarity and associated hypothyroidism which is new to the literature.

Although there is no cure, early recognition of these hereditary premature ageing diseases is essential to be prepared for anticipated complications and their timely management

CONFLICT

None declared till date.

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