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Hutchinson - Gilford progeria syndrome: A rare case report of two siblings

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Abstract
Hutchinson-Gilford progeria syndrome (progeria) is a rare, fatal, autosomal dominant also autosomal recessive, segmental syndrome which has striking feature resembling premature aging. Children develop the appearance of accelerated aging involving the skin, bones, heart, and blood vessels. We report two male siblings of age 8 years and 13 years with clinical manifestations characteristic of this syndrome. Both had characteristic features like frontal bossing, prominent eyes, pointed nose and dilated visible scalp veins, sparse immature scalp hair, no eyebrows, and scant eyelashes, micrognathia, stunted growth, senile look, and mottled pigmentation over the trunk and lower limbs, coxa valga, "Horse riding stance", club foot acroosteolysis of distal phalanges, high pitched voice, intelligence quotient (IQ) corresponding to their age. We present these two cases of progeria with all the classical physical & radiological findings

Keywords: no eyebrows, prominent eyes, scant eyelashes

Introduction
Hutchinson – Gilford Progeria Syndrome (HGPS; MIM 176670) is a rare premature ageing syndrome which was first described by Jonathan Hutchinson, in 1886 and Hastings Gilford in 1897 gave the name progeria to this syndrome [1]. Progeria is caused by a single base mutation in LMNA gene. The disease has incidence of 1 in 4,000,000 live births and prevalence of 1 in 18 million, there were a total of 350 children living with progeria in 2013 worldwide [2] Males are affected more than females 1.5:1 [3]. These children develop progressive atherosclerosis and die due to heart attacks or strokes at a median age of 14.5 yr, most often between ages 5 and 20 yr [2].

Case Report
Two male siblings of age 8 years and 13 years, both presented with complains of failure to thrive, abnormal gait, progressive loss of scalp hairs. Both these children had an uneventful antenatal & perinatal history and born to third-degree consanguineous marriage. Both children were apparently normal till 1 year of age and from their parents started noticing abnormal body features. There was no history of similar complaints in family. On examination both were short statured and malnourished, had senile look with large cranium, wide open anterior and posterior fontanelle, frontal and parietal bossing, soft; downy; sparse immature hair, dilated visible veins over the scalp, face appears disproportionately small in comparison to the head, eyes appeared prominent, beaked nose, delayed eruption of the primary (deciduous) and secondary (permanent) teeth; irregularly formed, small, discoloured, and absent teeth; and also presence of dental caries, micrognanthia, narrow shoulders; prominent ribs, Small thorax (pyriform thorax) with a prominent abdomen. Long bones of both upper and lower limbs were thin, and visible veins over lower limbs were present. Hands and Fingers were short and clawed with thickening and hardening of the skin over the knuckles. Both had laxed and atrophic skin over dorsum of hands and feet with scleradermatous changes. Both had prominence of knees and wide based, "horse-riding stance". Elder sibling had bilateral CTEV deformity and weight of 11.2 kg. And height of 95.5cm. On examination the child found to have horizontal nystagmus. Younger sibling had right sided CTEV deformity and weight of 10.1 kg. and height of 93.0cm.

Growth parameters were less than third percentile. In both genitalia were normal. Both had high pitched voice and Intelligence quotient was corresponding to the age.

Based on the history and clinical findings a provisional diagnosis of progeria was made, routine haematological, biochemical, endocrine investigations were normal. X-ray of the chest showed a pyriform thorax, with thinning and overcrowding of proximal ribs and short clavicle with pointed lateral ends. X-ray of the skull showed widely opened anterior and posterior fontanelle and micrognathia. X-ray lower limbs shows coxa valga deformity i.e. straightening of the femoral head-neck axis to >125 degrees also thinning of long bones and flaring of the humeral and femoral metaphyses. X-rays of hands and feet showed acro-osteolysis of phalanges and tarsals also showed CTEV.

Retinitis pigmentosa seen to elder child on ophthalmological examination while younger sibling has normal study. Echocardiography revealed mild Aortic regurgitation due to degenerative changes in Aortic Valve in younger sibling while other sibling has normal heart study. Hearing assessment of both children were normal. Ultra-sonography abdomen, Electrocardiogram, MRI brain not show any abnormalities. Genetic studies were however not performed.

Discussion

Mutations in the *LMNA* gene (located on band 1q21.1-1q21.3) that causes progeria [4]. Most cases of HGPS occur due to *de novo* autosomal dominant mutation in the LMNA gene [5]. Rarely, transmission can be autosomal recessive or maternal due to gonadal mosaicism. The normal *LMNA/C* gene encodes the proteins lamins A and C, of which only lamin A is associated with human diseases. The lamin proteins are the principal proteins of the nuclear lamina, a complex molecular interface located between the inner membrane of the nuclear envelope and chromatin. The integrity of the lamina is central to many cellular functions such as DNA replication, RNA transcription, organization of the nucleus, nuclear pore assembly, chromatin function, cell cycling, and apoptosis. It is important in creating and maintaining structural integrity of the nuclear scaffold. Translation followed by posttranslational processing of the altered messenger RNA produces progerin, a shortened abnormal lamin a protein with a 50-amino-acid deletion near its C-terminal end [2].

Normal farnesylation of prelamin A and progerin during posttranslational processing allows them to attach to the nuclear membrane. Because of mutation there is failure to remove this farnesyl group, permanently affixes these protein to the nuclear membrane, which affects nuclear integrity and morphology, DNA repair, regulation of gene expression, and telomere stability. All these factors causes genomic instability, decreased cell proliferation, blebbing of the nucleus, disrupting mitosis, and altering gene expression. and premature cell senescence and death [6].

Overall, the group of pattern of small body habitus, hair, bone, subcutaneous fat, and skin changes results in the marked physical resemblance among patients with progeria [2]. The infant is generally healthy and asymptomatic at birth but there may be sclerodermatous skin changes which involves the trunk and extremities in some cases [7]. Manifestations appear within one to two years in most of the cases. Hair growth decreases over the scalp, absent eyebrows, thin eyelashes. Loss of subcutaneous fat over face leads to typical facies with senile look, pointed nose, and "plucked bird" appearance [8]. Involvement of the lower limbs with coxa valga deformity and mid flexion leads to a "horse riding" stance. Joint contractures, a result of ligamentous and skin changes, limit range of motion. Contractures in multiple joints including fingers, elbows, hips, knees and ankles may be present at birth and/or in later years [2, 9]. children with progeria reach a final height of approximately 1 m and weight of approximately 14 kg. Liver, kidney, thyroid, immune, gastrointestinal, and neurologic systems remain intact [2]. IQ remains normal [8].

Death occurs primarily from myocardial infarction, and less often from strokes. Progeria is a primary vasculopathy, characterized by pervasive accelerated vascular stiffening, followed by large and small vessel occlusive disease as a result of atherosclerotic plaque formation, with valvular and cardiac insufficiency in later years. Hypertension, angina, cardiomegaly, metabolic syndrome, and heart failure are common end-stage events [2, 10].

In our case elder sibling found to have horizontal nystagmus, on detailed examination there was changes of retinitis pigmentosa rest was normal study. Younger sibling had mild Aortic regurgitation due to degenerative changes in Aortic Valve.

The disorders that resemble progeria are those grouped as the senile-like syndromes and include Wiedemann-Rautenstrauch syndrome, Werner syndrome, Cockayne syndrome, Rothmund-Thomson syndrome, restrictive dermopathy, and Nestor-Guillermo progeria syndrome.

Wiedemann-Rautenstrauch syndrome has oncet at newborn period and associated with diabetes. Presence of coxa valga deformity and voice abnormality and absence of diabetes in our cases rule out Wiedemann-Rautenstrauch syndrome.

Werner syndrome is also known as progeria adultorum (progeria of the adult).The onset might occur in individuals in their mid-teens or individual is as old as 30 years. Both sexes are affected equally. Death occurs when patients are having atherosclerosis or malignant tumors. Earlier age of onset, absence of cataracts, skin calcification, Diabetes and presence of coxa valga ruled out Werner syndrome.

Cockayne syndrome characterised by premature aging pigmentation and growth deficiency. The syndrome was ruled out because of lack of photosensitivity, ocular defects, facial erythema, and normal IQ Acroosteolysis of the distal phalanges, delayed cranial sutural bones, short stature, baldness, linear lucent defects of the metaphyses are the predominant features of Rothmond Thomson syndrome which is a hereditary and familial disease which is ruled out because by the absence of erythema, poikiloderma and cataract.

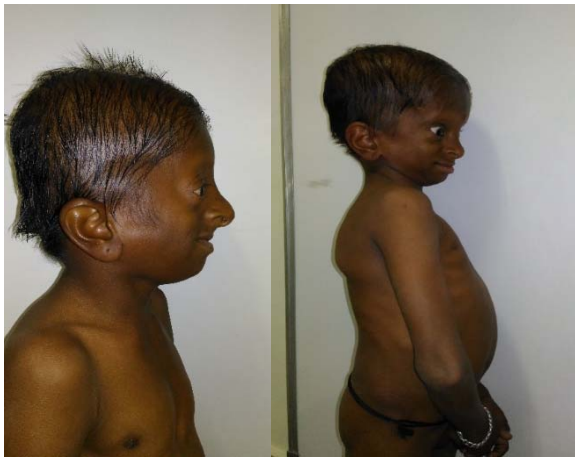
Presence of coxa valga, voice abnormality, loss of subcutaneous fat and infantile onset rule out Restrictive dermatopathy Absence of eyebrows and eyelashes, crowding of teeth and oncet before 1 year of age rule out Nestor-Guillermo progeria syndrome.

Acrogeria is a progeriod syndrome of premature ageing of the skin and internal organs manifests at birth but involves only extremities with no tendency to atheroma or decreased life expectancy. It is seen mainly in females and in familial cases are also seen (Gottron type). Congenital cataracts, bilateral microphthalmia rule out Hallermann-Streiff syndrome.

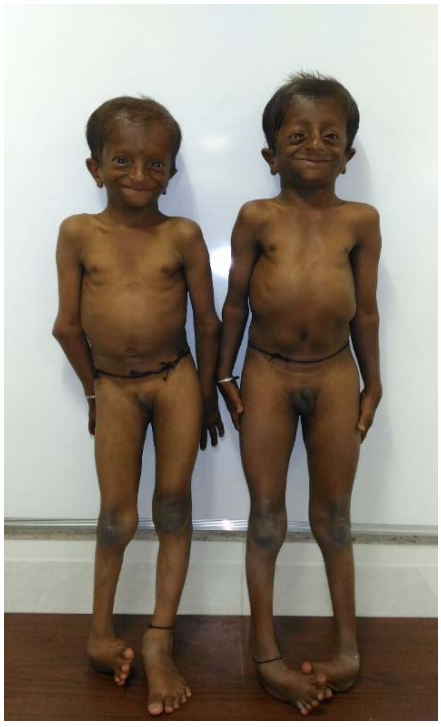
Management of the case is mainly by counselling and symptomatic treatment, which includes early identification and prompt management of the complications.

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. Proper counselling 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.

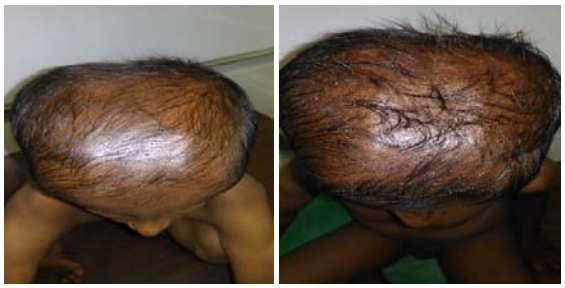
This case is reported for its rarity.



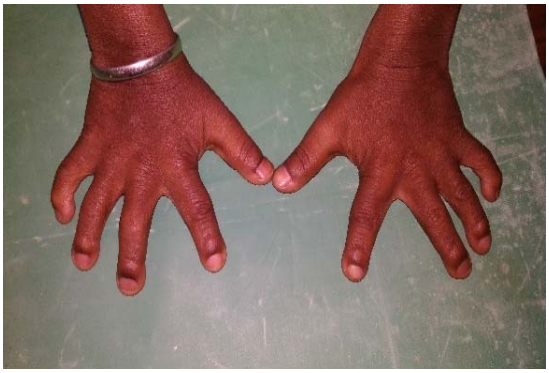
Side Photograph of the children showing the typical phenotypic features of the Hutchinson-Gilford progeria syndrome. On left older sibling and on right younger sibling

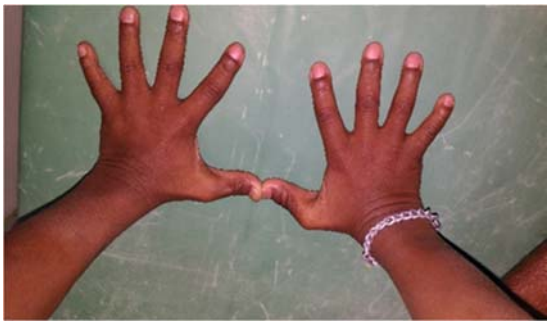


Front Photograph of the children showing the typical phenotypic features of the Hutchinson-Gilford progeria syndrome. On left younger sibling and on right older sibling



Features of the Hutchinson-Gilford progeria syndrome: sparse immature hair, dilated visible veins over the scalp





Hands and Fingers are short and clawed with thickening and hardening of the skin.

References

1. Hutchinson J. Case of congenital absence of hair with atrophic condition of the skin and its appendages in a boy whose mother had been almost wholly bald from alopecia areata from the age of six. Lancet, 1886; 1:923.
2. Nelson Textbook of Pediatrics, 20th Edition, 2(90):753-756.
3. DeBusk FL. The Hutchinson-Gilford progeriasyndrome. Report of 4 cases and review of the literature. J Pediatr. 1972; 80(4):697-724.
4. Pollex RL, Hegele RA. Hutchinson – Gilford progeriasyndrome. Clin Genet, 2004; 66:375-81.
5. Shumaker DK, Kuczmarski ER, Goldman RD. The nucleoskeleton: lamins and actin are major players in essential nuclear functions, Current Opinion in Cell Biology, 2003; 15(3):358-366.
6. Ding SL, Shen CY. Model of human aging: Recent findings on Werner's and Hutchinson-Gilford progeria syndromes. Clin Interv Aging. 2008; 3:431-44.

7. DeBusk FL. The Hutchinson-Gilford progeria syndrome. Report of 4 cases and review of the literature. J Pediatr. 1972; 80:697-724
8. DeBusk FL. The Hutchinson-Gilford progeria syndrome. Report of 4 cases and review of the literature. J Pediatr. 1972; 80:697-724
9. Silverman FN. Miscellaneous forms of short stature. In: Silverman FN, Kuhn JP, editors. Caffey's pediatric X-ray diagnosis: An integrated imaging approach. Mosby, 1993, 1725-7.
10. Badame Progeria AJ. Arch Dermatol. 1989; 125:540-4.