Hutchinson-Gilford progeria syndrome

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Abstract

Hutchinson-Gilford progeria syndrome (HGPS) is a rare genetic disease in which symptoms of aging are manifested at an early age. In the present report, we describe a 9 months old female child presented with a history of progressive coarsening of skin, failure to thrive and irregular bumps over thighs, buttocks and lower limbs for the last 7½ months. In the course of time, she developed alopecia, hyperpigmented spots over the abdomen with thickening and a typical facial profile of HGPS including micrognathia, absent ear lobules, prominent eyes, loss of eyelashes, eyebrows and a bluish hue over the nose.

Introduction

Hutchinson-Gilford progeria syndrome (HGPS) is a rare disorder and is found to affect all races and both sexes equally.[1] As of January 2014, not more than 200 cases have been reported.[2] The prevalence of HGPS is approximately one in 4-18 million.[3] A newborn with HGPS may have certain findings present at birth that may lead to the suspicion of the disease, such as hard scleroderma-like skin over the buttocks, legs and lower abdomen that looks shiny and unusually taut, within the mid-portion of the face a bluish tinge (mid-facial cyanosis) and a pinched sculptured nose. Here, we present a case of HGPS.

Case Report

Our patient "N", a 9 months old female child, was admitted with a history of progressive coarsening of skin, failure to thrive and irregular bumps over thighs, buttocks and lower limbs for last 7½ months. In the course of time, she developed alopecia, hyperpigmentation of the abdomen with thickening. The perinatal history was nothing contributory. She was apparently normal till 2½ months of her age and there was no family history of similar illness. General examination revealed the child to be severely underweight (WAZ=-4). Eyes appeared unusually prominent with hypoplastic chin and absent ear lobules. Coarse, thickened skin over the dorsum of the hands, shoulders and brownish spots with scaly areas over abdomen was found. "N" also had prominent scalp veins, alopecia and loss of eyebrows and eyelashes. Un-erupted teeth, lipodystrophic changes over buttocks and thighs, pinched nose, protruding ears with absent ear lobes were noted (Figure 1).

Investigations showed hypertriglyceridemia and the skeletal survey showed dome-shaped calvaria, prominent frontal region, dental crowding, absent lateral part of the clavicle, gross osteopenia of distal phalanges of hands, coxa valga and fish mouth vertebral bodies. Considering clinical, biochemical and radiographic findings we diagnosed this case as HGPS.

Discussion

A newborn with HGPS at birth is suspected when certain findings, such as hard scleraderma-like skin over the buttocks, legs, and lower abdomen that looks shiny and unusually taut, mid-facial cyanosis and a pinched sculptured nose are found.[4] This is followed by growth retardation that becomes quite evident by 24 months of age approximately and is profound and progressive; resulting in extreme short stature and weight for age and weight for height remains extremely low. The face appears small in comparison to the head and skull bones look prominent that leads to frontal and parietal bossing.[5] Hair becomes thin and sparse and alopecia totalis ensues by approxi-mately two years of age and later in childhood patient may also lose his eyelashes and eye brows. Sclerodermatous changes over the buttocks, thighs, and lower abdomen develop soon.

Rastogi and Mohan described a 14 year old girl who presented with growth failure and history of progressive coarsening of skin and she could not properly squat for the past four years.[6] The

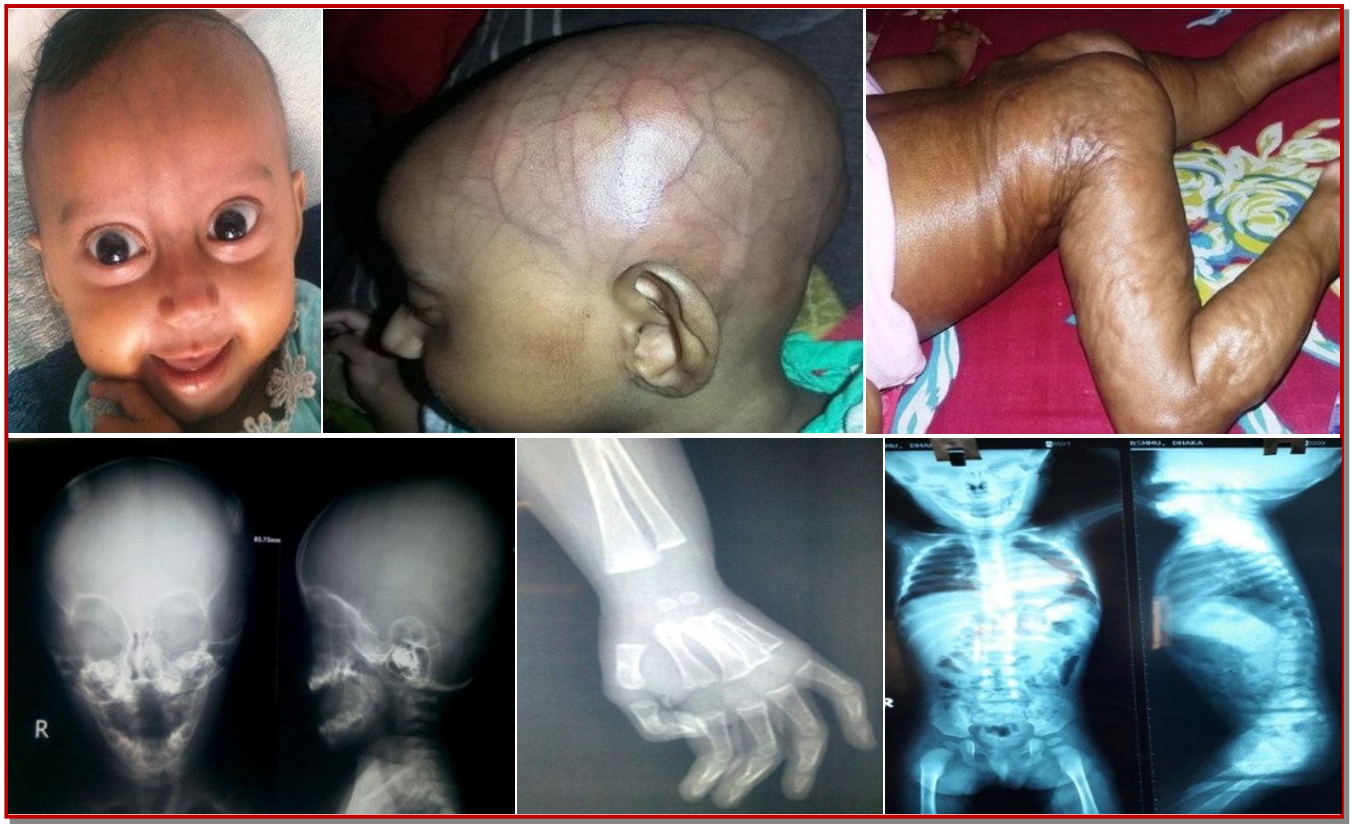

Figure 1: Shows unusually prominent eyes, alopecia, loss of eyebrows and micrognathia (A); prominent scalp veins, absent ear lobules, dome shaped calvaria (B); sclerodermatous skin changes (C). X-Ray findins show dome shaped calvaria, mid facial hypoplasia and micrognathia (D); gross osteopenia of distal phalanges (E); fish mouth vertebrae, absent lateral half of the clavicle and coxa valga

girl also developed alopecia over the past 3 years. The perinatal history was nothing contributory. At one year of her age parents first noticed the above mentioned features. She was intellectually normal. There was no family history of similar illness.

Kashyap et al reported a 3 year old boy having "plucked-bird" appearance, unusually prominent scalp veins and eyes, aged look, alopecia areata, loss of eyelashes and eyebrows, pigmentation with sclerodermatous changes of the body along with stunted growth.[7]

Chu et al. reported a 6 year old male child who was born full term and presented at 1 month of his age with scleroderma-like skin features and later developed a characteristic clinical picture of progeria. Facial features like unusually prominent scalp veins, leg veins, eyes, alopecia, loss of eyelashes and eyebrows with stunted growth were quite characteristic. Later he developed scleroderma -like changes of the skin, and a premature aged appearance.[8]

Delayed eruption of the deciduous and permanent teeth has been noted and teeth formed are irregular, small, discolored or even absent. Teeth in HGPS are prone to dental caries.[9, 10] Likewise, our patient was around 10 months old however no deciduous teeth had erupted yet.

Micrognathia results in dental crowding and in addition other skeletal defects found in HGPS include delayed closure of anterior fontanelle, abnormal calvaria (dome like), absent lateral half of clavicle, gross osteopenia of distal metacarpal bones, coxa valga and fish mouth vertebrae. Skeletal survey of "N" also revealed similar findings.

Research has determined the cause of HGPS to be a single-letter misspelling in a gene present on chromosome 1 that codes for Lamin A (*LMNA*), a protein that is a crucial component of the membrane surrounding the nucleus of the cell.[9] The Lamin A protein produced due to this defect is abnormal and is called as Progerin. Once a case of progeria is found in a family it does not usually pass down further.[10, 11] The gene change is extremely rare. HGPS occurs because of autosomal dominant mutation that is sporadic in nature. It is a new change in the family affected hence it is sporadic and dominant because only one copy of the gene needs to be changed in order to have the syndrome.[9] The chances of having a child with progeria in the family is 1 in 4–8 million but for those parents who already had a child with progeria, the chance to have another child with progeria is much higher about 2-3%. This is due to

mosaicism.

Treatment for HGPS is symptomatic and supportive. A multi-disciplinary approach is required for the management of this disorder including pediatricians, orthopedicians, physiotherapists and other health care professionals.[8] Lonafarnib, a kind of farnesyl transferase inhibitor, is actually developed for the treatment of cancer, is shown to be effective for progeria.[11] Those children treated with lonafarnib showed significant improvement in many ways like better weight gain, hearing, improved bone development and importantly increased the flexibility of blood vessels.

We managed the child with proper counseling of her parents and follow-up advice. Besides that, we prescribed an emollient for her rough skin, along with calcium, folic acid and other multivitamins.

Ethical Issue

Informed consent from parents was taken for publishing this case report.

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