Simultaneous Shoulder and Hip Dislocation in a 12-Year-Old Girl with Hutchinson-Gilford Progeria Syndrome

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Abstract- Hutchinson-Gilford progeria syndrome (HGPS) is a rare premature ageing disorder that is characterized by accelerated degenerative changes of the cutaneous, musculoskeletal and cardiovascular systems. Mean age at diagnosis is 2.9 years and generally leading to death at approximately 13 years of age due to myocardial infarction or stroke. Orthopedic manifestations of HGPS are multiple and shoulder dislocation is a rare skeletal trauma in progeria syndrome. Our patient had simultaneous shoulder and hip dislocation associated with a low energy trauma. This subject has not been reported. Treatment accomplished as close reduction under general anesthesia and immobilization.

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Keywords: Accelerated aging; Hutchinson-Gilford progeria syndrome

Introduction

Hutchinson-Gilford progeria syndrome (HGPS) is an extremely rare hereditary disease that affects the skin, musculoskeletal system, and vasculature. HGPS is characterized by dramatic signs of premature aging and generally leading to death at approximately 13 years of age due to myocardial infarction or stroke. Many orthopedic abnormalities have been reported in HGPS, including delayed closure of the skull, bone dysplasias, osteoporosis, osteolysis, especially in terminal phalanges and clavicles, osteonecrosis of the femoral head, dislocated hips, and delay in the union of bone after fracture (1,3,5). The genetic basis of most cases of this syndrome is a change from glycine GGC to glycine GGT in codon 608 of the lamin A (*LMNA*) gene, which activates a cryptic splice donor site to produce abnormal lamin A; this disrupts the nuclear membrane and alters transcription (8).

Case Report

A 12-year-old girl, known case of HGPS was admitted to the hospital because of pain and limitation of range of motion in the left shoulder and left hip after simple falling. She could not weight bearing. On examination, the arm was supported by the contralateral hand and hold in an abducted and externally rotated position. Lower extremity was shortened but position of limb appeared normal. Range of motion of shoulder and hip was limited. Careful examination of the neurologic and vascular status was normal. Radiographic studies displayed anterior shoulder and posterior hip dislocation (Figures 1, 2 and 3).

In the operation room, successful closed reduction for left shoulder was achieved but multiple reduction maneuvers were tried for left hip.

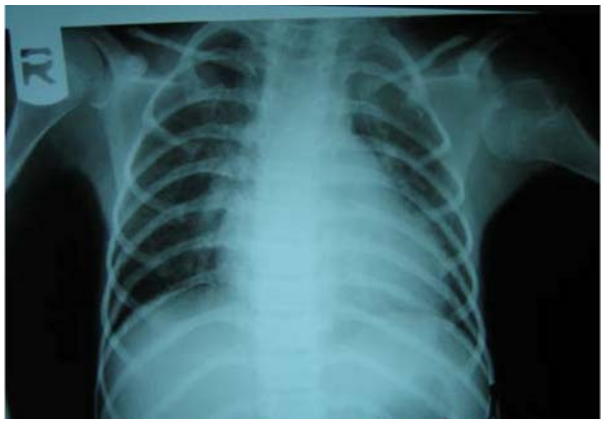

Figure 1. Chest X ray of a 12-year-old girl with Hutchinson-Gilford progeria syndrome displayed left anterior shoulder dislocation

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Table 1. Hematology laboratory data.

Hematocrit (%)	41.6
Hemoglobin(g/dl)	14.1
White cells (per mm^3)	11800
Neutrophils (%)	75
Lymphocyte (%)	20
Monocyte (%)	5
Eosinophils (%)	0
Basophils (%)	0
Platelets (per mm^3)	672000
Mean corpuscular volume (μm^3)	87.9
Red cell morphology	Normal
Prothrombin time (sec)	13
Partial thromboplastin time (sec)	26
INR	1

Table 2. Chemistry laboratory data.

Fasting blood sugar (mg/dl)	92
Creatinine (mg/dl)	0.5
Sodium (mM)	142
Potassium	4.1
Triglyceride (mg/dl)	199
Cholestrol (mg/dl)	161
HDL. Cholestrol (mg/dl)	32
LDL. Cholestrol (mg/dl)	90
Calcium (mg/dl)	10
Phosphorus (mg/dl)	5.2

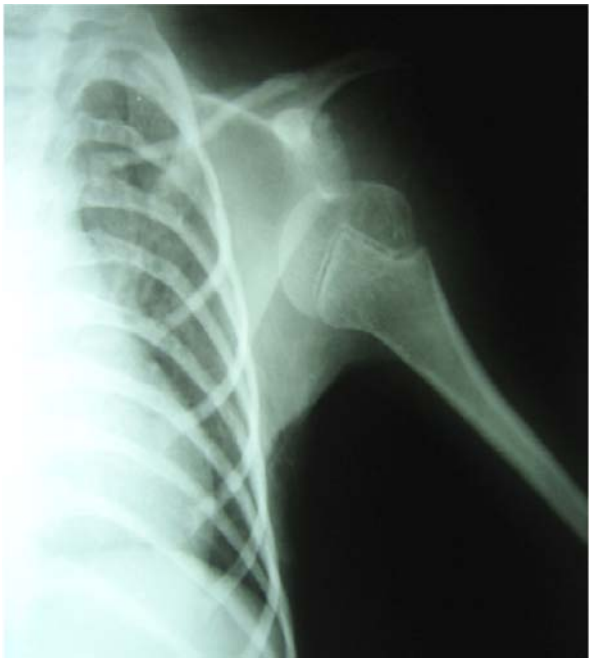

Figure 2. Shoulder X ray of the patient with Hutchinson-Gilford progeria syndrome displayed left anterior shoulder dislocation

Left hip joint was unstable but finally successful closed reduction was achieved with IV sedation and a Spica cast used for 6 weeks. Laboratory values are shown in table 1 and table 2. Blood pressure was normal. An echocardiogram showed minimal mitral regurgitation and aortic insufficiency, aberrant chordae attached to IVC without significant stenosis and moderate concentric left ventricular hypertrophy. There was no history of parental consanguinity.

Discussion

HGPS is a rare premature ageing disorder that affects the skin, musculoskeletal system, and vasculature. The characteristic phenotype of progeria was first recognized more than a century ago. Hutchinson-Gilford syndrome was initially reported by Johnathan Hutchinson in 1886 and further described by Hastings Gilford in 1904. He suggested naming the entity ‘progeria,’ ‘pro’ meaning early and ‘geras’ meaning old age in ancient Greek (1,3,5,6,8).

Progeria has an incidence of 1 in 4 million live births and is one of a number of “aging syndromes”. Approximately 100 cases of HGPS have been reported in the literature (3,9,10). Males are affected one and a half times more often than females (M:F=1.5:1) .White persons represent 97% of reported patients. HGPS become generally apparent after the first year of life, the children appearing healthy at birth although somewhat small for gestational age. The mean age at diagnosis is 2.9 years (3,11-13). Typical facial features include: protruding ears with absent lobes, beaked nose, thin lips with centrofacial cyanosis, prominent eyes, frontal and parietal bossing with pseudohydrocephaly, midface hypoplasia with micrognathia, large anterior fontanel (Figure 4).

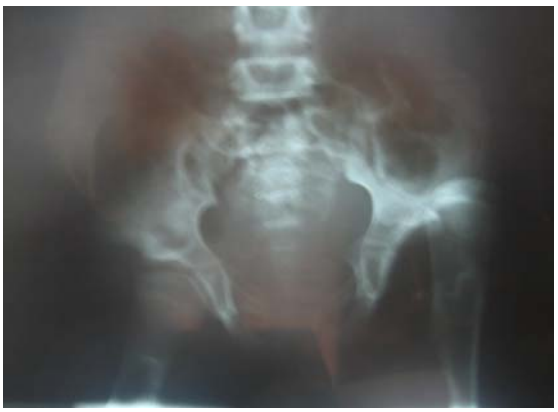

Figure 3. Pelvic X ray of the patient with Hutchinson-Gilford progeria syndrome revealed left posterior hip dislocation.

Figure 4. Characteristic facies of HGPS include: Prominent scalp veins, protruding ears with absent lobes, beaked nose , thin lips with centrofacial cyanosis, prominent eyes, frontal and parietal bossing with pseudohydrocephaly, midface hypoplasia with micrognathia, large anterior fontanel.

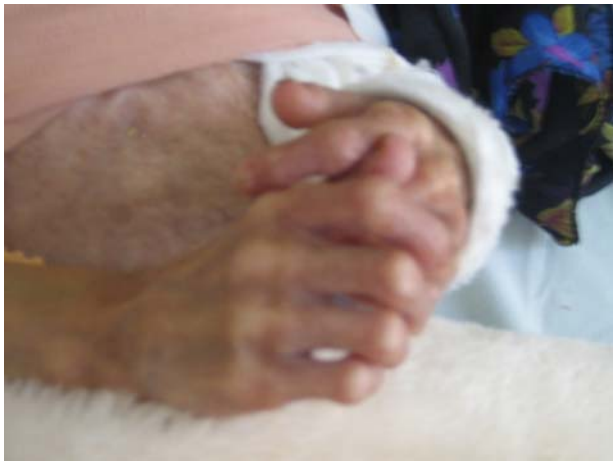

Figure 5. Patient with Hutchinson–Gilford progeria syndrome presented with Sclerodermatous skin changes and Thin limbs with prominent joints

Skin is thin, atrophic and sclerodermatous changes involving the trunk and extremities but sparing the face (Figure 5). Other abnormalities include Prominent scalp veins, circumoral cyanosis, generalized lipodystrophy with loose, aged-appearing skin, progressive freckle-like hyperpigmentation in sun-exposed areas Hair loss. Sweat glands and sebaceous glands are reduced in number and

Subcutaneous adipose tissue is atrophic. Tooth eruption is delayed and anodontia, hypodontia, dental crowding is often observed. The cardiovascular system is severely affected with small diameter of the intima and media and extensive loss of vascular smooth muscle cells with fibrous replacement (3,5,11-15).

Morbidity and mortality in persons with HGPS occur primarily as a result of atherosclerosis of the coronary and cerebrovascular arteries that result in premature death between the ages of 7 and 27 years with average life expectancy is 13 years. Myocardial infarction is the most frequent cause of death (1,3,13-16).

Typically, there is no significant obstetrical history given by the mother. The children generally have normal intelligence, cognitive functions, mood, affect and personality. There have been reported cases of siblings with progeria, cases of monozygous twins with progeria, and rare reports of siblings from consanguineous marriages. Progeria children do not reproduce. *De novo* mutations associated with advanced paternal age are responsible for most cases (1-3,13-18). Aortic atherosclerosis displayed ulceration and ostial stenosis of segmental branches, but extreme severity and aortic aneurysms has not been reported. Cardiovascular studies revealed diminishing vascular function with age, including elevated blood pressure, reduced vascular compliance, decreased ankle-brachial indexes, and adventitial thickening (17-20). In a review of serum cholesterol levels of 13 progeric patients, each had at least one estimation above 184 mg/dl, but the figures suggested high normal adult values rather than a traditional hypercholesterolemic state (2,3,20).

Clinical features have been divided into characteristics that are always present, as follows: plucked bird appearance; scalp alopecia; prominent scalp veins; prominent eyes; micrognathia; delayed, abnormal dentition; pear-shaped thorax; short clavicles; horse-riding stance; thin limbs with prominent joints (Figure 5); short stature; weight decreased for height; functional oral deficits, incomplete sexual maturation, normal intelligence and personality, resorption of distal phalanges, hyaluronuria and decreased subcutaneous fat.

Clinical features also have been divided into characteristics that are usually present, as follows: sclerodermatous skin; generalized alopecia; eyebrow/eyelash alopecia; protruding ears, with absent lobes; glyphic-beaked nose; thin lips with circumoral cyanosis; patent anterior fontanel; high-pitched voice, low-frequency conductive hearing loss, hypertension, diffuse osteoporosisand dystrophic nails (2,3,18-23). In HGPS, the most important biochemical changes occur within the connective tissue, mainly of mesodermal origin. The most useful finding in this syndrome appears to be the urinary excretion of hyaluronic acid. There are at least two studies that demonstrated 10-20 times greater urinary excretion of hyaluronic acid in patients with HGPS than with controls (2,8,22).

Orthopedic manifestations of HGPS are including coxa valga, joint stiffness, cervicothoracic kypohosis, early osteoarthritis, osseous necrosis of the femoral head, osteoporosis, osteolysis, dysplastic skeletal changes, scoliosis, pyriform (pear-shaped) thorax with short, decrease in joint range of motion, stooped shoulders, calcaneovalgus, subluxed finger joints, genu valgum, kyphosis, calcaneo varus and dislocation of the hip (11,19). Bilateral shoulder dislocation also been reported but simultaneous shoulder and hip dislocation associated with a low energy trauma have not reported (Figure 1, 2 and 3). Some form of osteolysis is invariably present in any patient with HGPS. It can be found at the distal phalanges, clavicles, mandible, neurocranium and viscerocranium. There are also reports of osteolysis involving the first ribs. All these bones are formed by membranous ossification including the middle part of the distal phalanges. In classical HGPS, osteolysis seems to be restricted to these bones. Osteolysis of the distal phalanges usually starts between 1 and 2 years of age, but can be as early as the first months of life or later than 5 years. The process starts in the index and little fingers, and gradually extends. The ring finger is usually the least affected. The osteolysis starts at the acromial ends of the clavicles, and is only slowly progressive (3,6,11). Despite radiologic evidence of bone resorption, laboratory evidence suggests a normal rate of bone turnover. Growth impairment was not related to inadequate nutrition, insulin unresponsiveness, or growth hormone deficiency. Growth hormone treatment in a few patients increased height growth by 10% and weight growth by 50%. Muscle volume remained proportional to body mass, as indicated by normal production of creatinine per kg of body weight. (8,20-22).

Normal results of blood tests included the absolute neutrophil and lymphocyte counts and hemoglobin, glycated hemoglobin, C-reactive protein, homocysteine, sodium, potassium, calcium, alkaline phosphatase, aspartate aminotransferase, total bilirubin, lactic dehydrogenase, creatine kinase, uric acid, blood urea nitrogen, total protein, albumin, prealbumin, thyroid-stimulating hormone, free thyroxine, vitamin D, IgM, IgG, and IgA levels. HGPS usually has prolonged prothrombin times, elevated platelet counts and serum phosphorus levels. Some children with HGPS had elevated levels of serum triglycerides, total cholesterol low-density lipoprotein cholesterol and reduced levels of high-density lipoprotein cholesterol (3,8,11). Elevated levels of hyaluronic acid excretion are seen in the urine of patients with HGPS but are not diagnostic.

The diagnosis of HGS relies on the combination of the clinical features as there is no diagnostic test. HGPS should be easily differentiated from other progeroid syndromes such as Werner's syndrome, acrogeria, Rothmund-Thomson syndrome and Cockayne's syndrome.

Most of the physical characteristics of patients with progeria described in the literature (1-3,5,8) could be seen in our patient.

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