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Transient monoparesis following blade plate removal in a Hutchinson-Gilford progeria syndrome patient. A case report

Suzanne M. Yandow, MD^{a,c}, David L. Rimoin, MD, PhD^b, Aimee M. Grace, BA^d, Ramona R. Fillman, MHA, PT^c, and Ellen M. Raney, MD^c

^aCentral Texas Pediatric Orthopaedics & Scoliosis Research

^bMedical Genetics-Birth Defects Institute, Cedars-Sinai Medical Center

^cShriners Hospitals for Children-Honolulu

^dJohn A Burns School of Medicine, University of Hawaii

Abstract

Treating patients with Hutchinson-Gilford progeria syndrome (HGPS) are based on the abnormalities of accelerated aging that affect the healing processes, combined with a fragile cardiovascular status. A classic HGPS case is presented, of Korean ancestry, who was treated for severe coxa valga with bilateral varus osteotomies using blade plate fixation. Complications over the blade plate area required removal of the hardware, after which the patient displayed left-sided hypertonicity--determined to be a cerebrovascular accident. Subsequently, she returned almost completely to her pre-surgical neurologic status. Perioperative planning for HGPS patients should include risks typically considered in the planning for geriatric patient care.

Keywords

progeria; Hutchinson-Gilford syndrome; HGPS; monoparesis; coxa valga

INTRODUCTION

Hutchinson-Gilford progeria syndrome (HGPS) is a rare yet well-recognized genetic disease characterized by accelerated aging.[1] Children with this syndrome tend to exhibit extreme short stature, low body weight, early loss of hair, lipodystrophy, scleroderma, decreased joint mobility, osteolysis, and facial features that resemble aged persons.[2] Cardiovascular compromise causes early demise, whereas cognitive development remains normal.[2] 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 following fracture.[3] Clinically, the diagnosis of HGPS is based on characteristic clinical features as well as detection of a mutation of the *LMNA* gene.[4] Molecular genetic testing

Correspondance to Suzanne M. Yandow, MD, Central Texas Pediatric Orthopaedics & Scoliosis Research, 1301 Barbara Jordan Blvd, Suite 300, Austin, TX 78723. PH: 512-478-8116; Fax: 512-478-9368.smyandow@yahoo.com.

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for this mutation is clinically available.[5] A recent case of HGPS is presented in an infant of Korean ancestry. The patient's mother and father agreed to have her as part of this case report.

CASE

IRB consent was received.

In classic HGPS, the main reasons for presentation include failure to thrive, hair loss, skin problems, lipodystrophy, and rarely other symptoms (i.e., unusual face, small clavicles).[2] Our patient presented at one month of age with skin tightness involving the entire trunk as well as upper and lower extremities, with her abdomen described as being “tight as a drum”—characteristics believed due to a form of scleroderma. She also presented with knee and hip flexion contractures, as well as constipation and “spitting up.” At two months of age (Fig. 1), the differential diagnosis included linear scleroderma, dermatitis, congenital fascial dystrophy (stiff skin syndrome), subcutaneous fat necrosis, and restrictive dermopathy.

At ten months of age, the patient was clinically diagnosed as having a form of Progeria. At age 3 (Fig. 2, A,B), symptoms included tight skin of the entire body causing limited excursion of the knees, significant amount of hair loss, mild thoracic kyphosis, and marked osteopenia (50% of normal age-adjusted bone density). Possible hyperparathyroidism was suggested by resorption of the patient's distal clavicles documented radiographically at age 3 (Fig. 3, A) and resorption of the distal phalanges, documented radiographically at age 4 (Fig. 3, B) and again at age 6 (Fig. 3, C).

By age 7, diagnosis of HGPS became more certain with characteristic features of short stature, weight low for height, disproportionately large head (Fig. 4), diminished subcutaneous fat, prominent scalp veins, generalized alopecia, micrognathia, limited joint range of motion, “shiny” skin with periodic peeling over the abdomen, uneven subcutaneous tissue, minimal edema of the extremities, nail dystrophy, persistent patent anterior fontanel, and characteristic facial features becoming more prominent with age. The patient showed decreased HDL, increased LDL, and an increased cholesterol/HDL ratio, corresponding to the expected risk of early atherosclerotic disease in Progeria. The patient's intelligence remained normal.

Progressive coxa valga bilaterally was first noted at age 4 (Fig. 5). Just prior to surgery, at age 7, the angle of her femoral neck shaft was 180 degrees (normal 135 degrees), with acetabular dysplasia (Fig. 6) and bilateral femoral head subluxation with 40% of the head uncovered. Head coverage improved dramatically on abduction inward rotation film with congruency and 100% femoral head coverage. To improve the acetabular coverage and subluxation of the femoral heads, and to decrease the risk of further acetabular dysplasia and dislocations, the decision was made to precede with bilateral femoral varus osteotomies using blade plate fixation (Fig. 7). Precautions were taken in light of the risks inherent in HGPS, including a cardiology consult with EKG and echocardiogram, and dermatologic consult. During the surgery, the patient was noted to have very friable skin and connective tissue that bled easily.

No immediate intraoperative or postoperative complications were noted. Plates remained very prominent due to the patient's thin skin and sparse subcutaneous fat. The right side osteotomy demonstrated a delayed union. The left side demonstrated union, but with erythema, irritation, and skin breakdown over the prominence of the hardware. The decision was made to remove the hardware on the left side as the bone appeared to be united and the plate was causing skin irritation.

Intraoperatively, during plate removal, there appeared to be granulation and fibrous connective tissue over the plate. Histologically, there was acute and chronic inflammation, but no infection. The patient was noted to have some irregularities on the cardiac tracing intraoperatively, including transient ST elevations indicating ischemia.

Postoperatively, she was noted to have switched her hand dominance from right to left and demonstrated mild-to-moderate right-sided upper extremity hypertonicity. Stroke was considered as an etiology. Subsequent to a previously normal MRI, a newly obtained MRI revealed multiple scattered old cortical infarcts in both cerebral hemispheres, with the largest one in the white matter of the left parietal region, undercutting much of the parietal cortex. This is the infarct that is believed responsible for the new-onset right upper extremity monoparesis. The patient's weakness and spasticity slowly improved, and at the time of this report was completely resolved.

The patient also had a Stage II wound breakdown to the coccyx postoperatively due to the bony prominence of the area, as well as contractures and limited subcutaneous fat. The contractures improved with stretching in addition to range of motion (ROM) and strengthening exercises.

Following bone union, the right sided plate was removed to minimize the risk of further skin breakdown (Fig. 8). The patient has subsequently done well without further complications. Her hips demonstrate abduction in flexion to 70 degrees, external rotation to 60 degrees, internal rotation to 60 on the right and 40 on the left, and no contractures. Thigh-foot angle is 10 degrees external bilaterally. Her knees have 0 to 100 degrees of flexion. She walks well and her spine is straight. Her deep tendon reflexes are 2+ and symmetric with no clonus noted. Hypertonicity has resolved.

Our patient was also noted to have delayed dentition, open fontanels, and delayed skeletal maturity compared to age—all orthopedic manifestations of HGPS. The patient's growth plates were wide open without advanced skeletal age. Joint range of motion demonstrated restrictions in arc of motion in numerous joints due to connective tissue and skin rigidity.

DISCUSSION

Orthopedic manifestations in HGPS are well-established, including coxa valga, joint stiffness, cervicothoracic kypohosis, early osteoarthritis, and osseous necrosis of the femoral head.[2] Other common orthopedic abnormalities in Progeria include osteoporosis, osteolysis, dysplastic skeletal changes, and dislocation of the hip. Scoliosis has also been reported. [6] However, normal growth plate development is generally to be present, as physal closure is under gonadal influence, and children with progeria do not undergo precocious puberty. Such factors continue to support the theory of segmental aging of body systems in HGPS.[7] Bone age assessment should include evaluating for delayed dentition, open anterior fontanel, delayed skeletal maturity with delayed bone age, and open physis.

Our patient had progressive coxa valga requiring surgical attention. Gamble[8] reports that severe coxa valga is the first abnormality of hip disease in HGPS, noting that hips become abnormal early in the disease process, with severe coxa valga apparent by 2 years of age. While acknowledging the problem of valgus hips, this author argued that late operative intervention past 10 years old is inadvisable due to prominent internal fixation devices under thin skin and delayed osteotomy healing. He suggested that the best therapeutic regimen is early osteotomy (age 4-6 years) and a regular exercise program to maintain muscle strength and range of motion.[8] Of note, our patient was under 10 years old at the time of surgery. Gamble also stated that the femoral head in HGPS becomes increasingly uncovered as the acetabulum becomes more dysplastic, with the center edge angle decreasing, the acetabular

index increasing, and the medial wall of the acetabulum widening. He cited two patients, one that had an increase in hip uncoverage from 38% to 62% between age 10 and 13, and another from 17% to 48% between age 10 and 18.[8] Our patient had 30-50% uncoverage of the femoral heads and bilateral hip subluxation. These changes result in hip pain and loss of sphericity, again predisposing to potential complications of hip dislocation and pain and the need for surgical intervention at a later age with even higher perioperative risk.

Detailed pre- and postoperative neurologic examination is needed to assess central nervous system function and risk for development of CVA. Postoperative physical therapy to maintain ROM and physical conditioning despite non-weight bearing status is important to bone union and good functional outcomes. As the integument of HGPS patients tends to be thin and devoid of subcutaneous fat[8], as was the case in our patient, attention to conservation of skin and connective tissue is warranted, as there is scarce subcutaneous fat for support around the surgical site. If hardware is prominent, early postoperative removal may be needed to prevent further skin breakdown. A previous case study by Moen of a Progeria patient similarly reported removal of a fixation apparatus five months after varus derotational osteotomy and hip reduction due to protrusion of the device through the skin, as well as non-union of multiple fractures in this patient.[6]

Our patient's tissue was found to bleed easily, likely due to the tissue hypervascularity as demonstrated on histologic sections. Anticipation of the potentially significant bleeding risks during surgery of HGPS patients is necessary, and the patient's blood should be typed and cross-matched to be available in the case of need for transfusion.

Our patient had marked decreased bone density. This osteoporosis may lead to delayed union and hardware failure. Osteoporotic HGPS patients should be treated with carefully planned osteotomy and monitored regularly postoperatively for any signs of complications. Bisphosphonates, estrogen, or other bone building medications may be warranted.

Due to the premature aging of the cardiovascular system in HGPS, with abnormal lipid profiles and risk of atherosclerosis, surgeons and anesthesiologists should recognize the inherent risks of surgery in a HGPS patient with the cardiovascular status similar to an elderly person. A thorough cardiology consult should be obtained preoperatively, including an EKG and echocardiogram. Cardiac status, including potential myocardial ischemia, should be monitored intraoperatively. Our patient showed transient ST elevations, indicating possible myocardial ischemia.

Our patient was believed to have suffered a CVA intraoperatively, leading to right upper extremity monoparesis, presumed due to the underlying HGPS disease process with its inherent risk factors. Roen's previous case study on the orthopedic aspects of Progeria reported two CVAs causing a left-sided and right-sided hemiparesis, respectively, in a progeroid patient. It was initially presumed that this paralysis caused muscle imbalance leading to hip dislocation, but there may in fact be contributing factors from the underlying progeria disease process.[6] The HGPS patient should be monitored for any new-onset weakness, unsteady gait, upgoing plantar reflexes, change in hand dominance, or other neurological sequelae of any potential CVAs. Fall precautions should also be employed.

Although HGPS patients are children, their disease process has made them analogous to geriatric patients. Any older patient that is kept immobilized is at risk for many complications, including pneumonia, osteopenia, bed sores, stroke, and myocardial infarction (MI). It is imperative to recognize that these HGPS patients should be treated more like fragile geriatric patients than pediatric patients, and providers should be vigilant in addressing perioperative complications. From an orthopedic point of view, the patient should be kept moving postoperatively for the best prognosis.

CONCLUSION

HGPS patients require extensive perioperative evaluation when considering orthopedic surgeries. Their underlying disease process poses inherent surgical risks, including dermatologic, orthopedic, cardiac, and neurologic. Perioperative care and monitoring frequently utilized for high risk geriatric patients may improve outcome in this younger group of high risk surgical patients. Clinical testing for LMNA mutations is available and would help to earlier identify the syndrome. Given the inherent features of HGPS, including dermatologic, orthopedic, cardiac, and neurologic abnormalities, anticipation and special care on the part of both the orthopedic surgeon and anesthesiologist is essential for the successful surgical outcome of an HGPS patient.

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References

1. OMIM. Hutchinson-Gilford Progeria Syndrome; HGPS. 2008 [January 2, 2008]. [Johns Hopkins University web site]Available at: <http://micro189.lib3.hawaii.edu:2198/entrez/dispmim.cgi?id=176670>.
2. Hennekam RC. Hutchinson-Gilford progeria syndrome: review of the phenotype. *Am J Med Genet A*. 2006; 140:2603–24. [PubMed: 16838330]
3. Fernandez-Palazzi F, McLaren AT, Slowie DF. Report on a case of Hutchinson-Gilford progeria, with special reference to orthopedic problems. *Eur J Pediatr Surg*. 1992; 2:378–82. [PubMed: 1477072]
4. McClintock D, Ratner D, Lokuge M, Owens DM, Gordon LB, Collins FS, et al. The Mutant Form of Lamin A that Causes Hutchinson-Gilford Progeria Is a Biomarker of Cellular Aging in Human Skin. *PLoS ONE*. 2007; 2:e1269. [PubMed: 18060063]
5. Brown, W.; Gordon, L.; Collins, F. Hutchinson-Gilford Progeria Syndrome. 2006 [12/05/07]. [GeneTests web site]Available at: www.genetests.org.
6. Moen C. Orthopaedic aspects of progeria. *J Bone Joint Surg Am*. 1982; 64:542–6. [PubMed: 7068697]
7. Halaschek-Wiener J, Brooks-Wilson A. Progeria of stem cells: stem cell exhaustion in Hutchinson-Gilford progeria syndrome. *J Gerontol A Biol Sci Med Sci*. 2007; 62:3–8. [PubMed: 17301031]
8. Gamble JG. Hip disease in Hutchinson-Gilford progeria syndrome. *J Pediatr Orthop*. 1984; 4:585–9. [PubMed: 6490880]

Figure 1. Photographs at 2 months of age showing A: posterior lower extremity/trunk scleroderma and tight skin; B: normal facies with some scleroderma of upper trunk and arms.

Figure 2. Photographs at 3 years/10 months of age showing A: extremely tight skin throughout the entire body with limited excursion of the knees and mild kyphosis; B: pinched facial features, dental crowding and alopecia.

Figure 3. Radiographs showing resorption of A: the distal clavicles at 3 years/7 months of age; B: the distal phalanges at age 4 years/4 months of age; and C: the distal phalanges at 6 years/7 months of age.

Figure 4. Photographs at 7 years/7 months of age showing A: disproportionately large head, beaked nose, prominent scalp veins and forehead, and micrognathia; B: poor axial strength, knee flexion contractures and loss of subcutaneous fat typical with HGPS.

Figure 5.
Radiograph of hips at 4 years showing bilateral coxa valga.

Figure 6.
Radiograph of hips at 7 years showing preoperative coxa valga.

Figure 7.
Radiograph of hips at 7 years/7 months of age showing hips plated bilaterally.

Figure 8.
Radiograph of hips at 8 years/4 months of age showing plating removed bilaterally.