CASE STUDY

Hyperkyphosis and Diffuse Platyspondyly in a 20-Year-Old Woman with Laron Syndrome: A Case Report

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Submission: 16 Jan. 2023
Accepted: 01 Dec. 2023

Citation
Alrehaili AA, Alyami JH, Alahmadi AAS, Aldusary NO, and Mohamed AM. Hyperkyphosis and diffuse platyspondyly in a 20-year-old woman with Laron Syndrome: A case report. JKAU Med Sci 2023; 30(2): 59-64. DOI: 10.4197/Med.30-2.6

Abstract

Background: Laron syndrome (LS) is a rare genetic disorder caused by mutations in the growth hormone receptor gene. It is characterized by severe dwarfism resistant to growth hormones, metabolic abnormalities, and an increased risk of developing type 2 diabetes. Patients with LS often present with spinal abnormalities, including hyperkyphosis. However, hyperkyphosis and diffuse platyspondyly are unusual features in patients with LS; to our knowledge, no case has been reported to date.

Case Report: This report presents the case of a 20-year-old woman with LS who visited the orthopedic outpatient clinic with hyperkyphosis. She received an LS diagnosis during childhood, and her family members also had hyperkyphosis. The patient reported a gradual worsening of her condition, accompanied by back pain and difficulty in daily activities. Physical examination showed increased thoracic curvature and reduced height. Radiographic investigations included long spine radiographs, a computed tomography scan, and magnetic resonance imaging. The radiographs revealed kyphosis with flattened vertebral bodies, and the magnetic resonance imaging demonstrated degenerative changes and spinal cord assessment. Diffuse platyspondyly, kyphosis centered around the T11 level, and degenerative changes were observed.

Conclusion: The case report highlights hyperkyphosis in a patient with LS and emphasizes the importance of further investigation for hereditary skeletal dysplasia. This case report contributes to the understanding of the musculoskeletal manifestations of LS, specifically hyperkyphosis and spinal abnormalities. Further research is warranted to explore the underlying mechanisms and develop targeted treatment strategies for individuals with LS and its associated spinal deformities.

Keywords

Laron syndrome, Hyperkyphosis, Hereditary skeletal dysplasia, MRI, CT

INTRODUCTION

Genetic Causes of Laron Syndrome (LS) and Prevalence

Laron syndrome (LS), also known as Laron-type dwarfism, is a rare genetic disorder caused by mutations in the growth hormone receptor gene (GHR)[1]. Mutations or deletions in the GHR lead to congenital insulin-like growth factor-1 (IGF1) deficiency. Patients with LS have low IGF1 levels despite normal or increased growth hormone (GH) levels. Exogenous GH does not induce a subsequent IGF1 response or restore normal growth due to the dysfunction of GHR[2]. The inheritance pattern of LS is autosomal recessive[1]. A new splice-site mutation in the growth hormone receptor gene probably causes LS, and the mutation leads to the synthesis of a receptor protein with an eight amino acid deletion from the extracellular domain[3].

LS was first described in 1966[4]. The prevalence of LS is about one in one million[1]. It has been estimated that the total number of patients worldwide is about 350[1].

Characteristics of Dwarfism in LS and Infertility

Patients with LS typically manifest severe dwarfism[4]. Patients tend to have a characteristic doll-like face[5] but typical craniofacial features[2]. Patients may also have metabolic abnormalities, including severe obesity, metabolic syndrome, abnormal glucose levels, insulin resistance, and an increased risk of developing type 2 diabetes[5]. Individuals with LS have torsal obesity and are prone to hypoglycemic episodes[2].

LS is characterized by delayed bone age, absent or delayed puberty, and infertility[6]. Women with LS are usually subfertile, mainly due to obesity and metabolic dysregulation[5]. The low IGF1 levels in patients with LS lead to disturbances in hypophysis-gonads interactions, affecting reproductive function and, hence fertility[7]. In one case study, an infertile patient with LS had hyperprolactinemia, which can cause anovulation and eventually infertility[8].

LS Diagnosis

LS is usually diagnosed in infants or young children[9]. LS diagnosis is based on clinical and biochemical findings, including height and weight measurements, growth charts, IGF1 levels, and GH levels[10]. In untreated patients with LS, marked dwarfism, high plasma human growth hormone (hGH), low serum IGF-1, and development of progressive and marked obesity are observed[11]. Genetic testing can confirm the diagnosis of LS[6].

LS Management

There is no definitive treatment for LS, and growth hormone treatment is ineffective. The management of LS focuses on treating the symptoms. Nutritional counseling, a low-calorie diet, and exercise are recommended to manage obesity and metabolic syndrome. Specialized care with monitoring and management of glucose intolerance, diabetes, and other metabolic complications is important in the long-term management of LS[5]. Treatment with IGF-1 results in a significant decrease in subcutaneous fat in all patients[11].

Hyperkyphosis and LS

One of the notable findings in patients with LS is the abnormal development of the spine. Individuals with this condition often exhibit distinct features such as short stature, delayed bone age, and skeletal abnormalities, including spinal curvature. The spine findings in LS patients can manifest as scoliosis, kyphosis, or lordosis, depending on the specific changes in the curvature of the spine. These abnormalities can vary in severity, with some individuals experiencing mild curvature while others may have more significant spinal deformities. However, hyperkyphosis and diffuse platyspondyly are unusual features in patients with LS; to our knowledge, no case has been reported to date. Hyperkyphosis is an exaggerated anterior curvature of the thoracic spine, typically defined as a Cobb angle exceeding the normal range of 20–40°. It can lead to various musculoskeletal and clinical consequences, such as impaired mobility and chronic pain.

In conclusion, LS is a rare genetic disorder caused by mutations in the GHR gene. It is characterized by severe dwarfism resistant to growth hormone, metabolic abnormalities, abnormal glucose levels, insulin resistance, and an increased risk of developing type 2 diabetes. Women with LS are usually subfertile due to metabolic dysregulation causing infertility. The diagnosis of LS is based on clinical and biochemical findings. There is no definitive treatment for LS, and growth hormone treatment is ineffective.

CASE REPORT

This report describes the case of a 20-year-old woman with LS who presented with hyperkyphosis at the orthopedic outpatient clinic in King Salman bin Abdulaziz Medical City (KSAMC). Laron syndrome had been diagnosed during childhood.

The patient reported a gradual worsening of her kyphosis over the past few years, accompanied by occasional back pain and difficulty in performing daily activities. Her medical history revealed that some of her family members, including her father and sister, also had hyperkyphosis. She was advised to undergo further workup for hereditary skeletal dysplasia. Upon physical examination, the patient had a noticeably increased thoracic curvature and a reduced height compared to individuals of her age. Neurological examination revealed no signs of sensory or motor deficits.

Given the patient's symptoms, the orthopedic specialist recommended further radiographic investigations to assess the spinal pathology. The patient received a long spine radiograph to assess the state of her spinal condition. The examination involved anteroposterior (AP) and lateral views of the spine (see Figures 1A and 1B). The radiographs showed relatively normal proximal limb length with short femoral necks bilaterally. The computed tomography (CT) scan of the thoracic spine (see Figure 2) revealed kyphosis with flattened vertebral bodies.

The magnetic resonance imaging (MRI) screening (see Figure 3A, 3B, and 3C) demonstrated further degenerative changes, including disc dehydration and loss of disc height. Additionally, the MRI allowed for the assessment of the spinal cord and neural structures. The MRI scan demonstrated diffuse platyspondyly that was more severe at the thoracic and lower cervical levels, resulting in kyphosis centered around the T11 level. Degenerative changes were noted at the mid and lower thoracic level, including disc dehydration, endplate irregularities, and early marginal bony lipping. Small posterior disc bulges at T4/5 through T11/12 levels were causing bilateral foraminal impingement, slightly more on the right side due to the loss of vertebral body

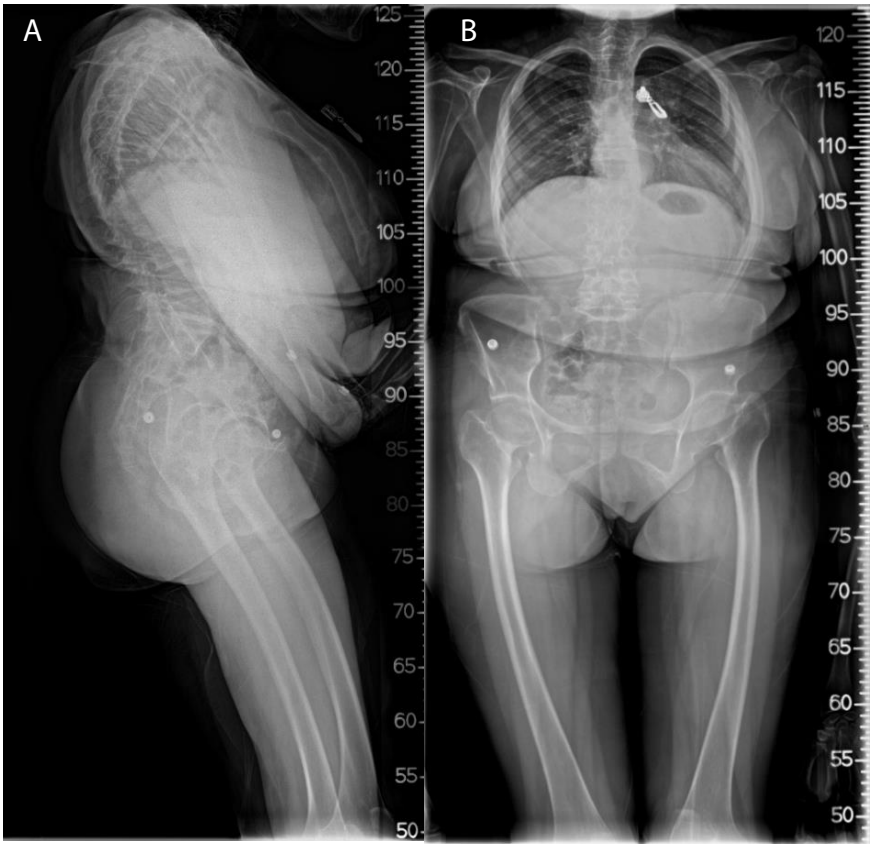

Figure 1. X-RAY long film images showed relatively normal proximal limb length with short femoral necks bilaterally (A) shows a lateral view of the spine. (B) shows an anteroposterior (AP) view of the spine.

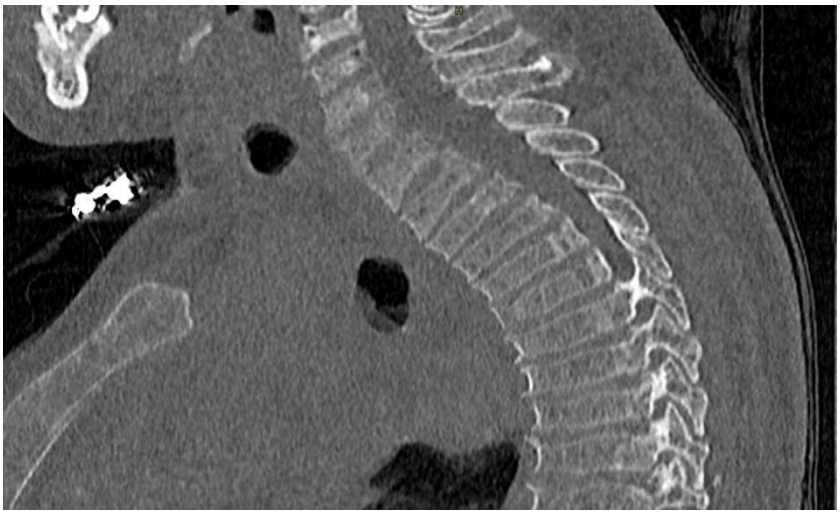

Figure 2. **CT image of the thoracic spine revealed severe thoracic kyphosis, accompanied by platyspondyly and a generalized decrease in bone density.**

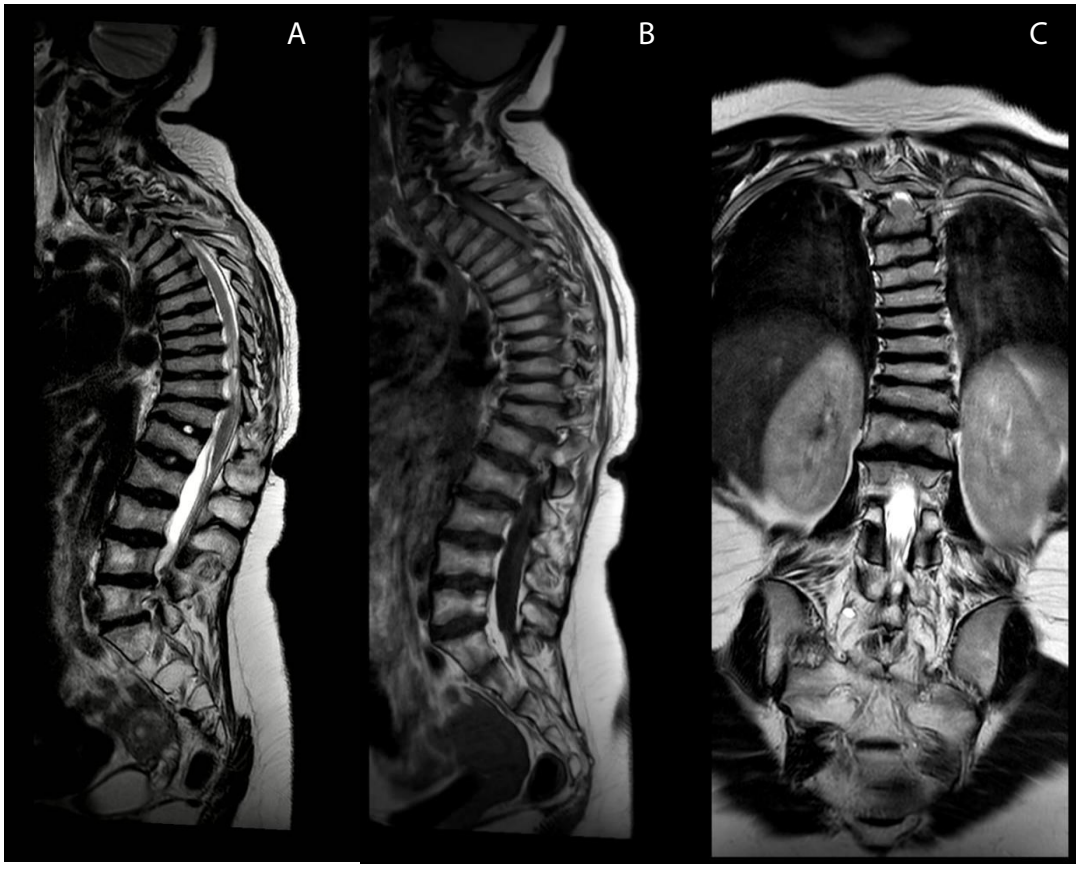

Figure 3. **MRI images of the whole spine indicate kyphosis around T11. Degenerative changes in the mid and lower thoracic spine included disc dehydration and irregularities in endplates. Small posterior disc bulges from T4/5 to T11/12 caused bilateral foraminal impingement. Dehydrated lumbar discs with small bulges at L3/4 and L4/5. (A) shows a sagittal view with a T2-weighted image of the whole spine. (B) shows a sagittal view with a T1-weighted image of the whole spine. (C) shows a coronal view with a T2-weighted image of the whole spine.**

heights. Milder cervical disc bulges were also present, causing mild foraminal impingement. The lumbar discs showed dehydration with small bulges at L3/4 and L4/5 levels, resulting in mild bilateral foraminal impingement.

In conclusion, the findings indicate thoracic hyperkyphosis with diffuse platyspondyly and early degenerative spine, requiring further investigation for hereditary skeletal dysplasia. Treatment options were discussed with the patient. Non-surgical interventions, including physiotherapy, postural exercises, and bracing, were recommended to improve spinal alignment and mitigate symptoms. Regular follow-up appointments were scheduled to monitor the patient's progress and evaluate the need for additional interventions, such as surgical correction.

DISCUSSION

Hyperkyphosis and diffuse platyspondyly are unusual features in patients with LS; to our knowledge, no similar case has been reported to date. Here we described a rare case of hyperkyphosis and diffuse platyspondyly in a 20-year-old woman with LS.

The hyperkyphosis and diffuse platyspondyly in our patient suggest skeletal system involvement. Conditions resembling our patient's condition, such as Morquio syndrome or Morquio-Brailsford syndrome, usually present with marked deformities of the extremities[12]; no similar deformities were present in our patient. Platyspondyly in Morquio syndrome affects the entire spine, and the upper and lower surfaces of the vertebral bodies are generally smooth, unlike the hyperkyphosis and diffuse platyspondyly observed in our patient. In addition, the present case's clinical findings did not fully correspond to the Kozlowski's spondylometaphyseal dysplasia described elsewhere[13] because asymptomatic hypocalciuric hypercalcemia in Kozlowski's spondylometaphyseal dysplasia was not observed in our patient.

In conclusion, we report a rare case of hyperkyphosis and diffuse platyspondyly in a 20-year-old woman with LS. Non-surgical interventions, including physiotherapy, postural exercises, and bracing, were recommended. The hyperkyphosis and diffuse platyspondyly are unlikely to be related to Morquio syndrome, Kozlowski's spondylometaphyseal dysplasia, or any metabolic complications of LS reported in the literature. This case report contributes to the understanding of the musculoskeletal manifestations of LS, specifically hyperkyphosis and spinal abnormalities. Further research is warranted to explore the underlying mechanisms and develop targeted treatment strategies for individuals with LS and its associated spinal deformities.

Author Contributions

All authors contributed scientifically and declared no conflict for this research.

Conflicts of Interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript, and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

Disclosure

The authors did not receive any form of commercial support, either in the form of compensation or financial assistance, for this case report. The authors have no financial interest in any of the products, devices, or drugs mentioned in this article.

Ethical Approval

The study had been approved by the Institutional Review Board of King Salman bin Abdulaziz Medical City (IRB log No: 22-063)

Informed Consent Statement

Not applicable

Data Availability Statement

The data were collected at Al-Madinah Al-Munawarah Hospital, King Salman Bin Abdulaziz Medical City, Madinah, Saudi Arabia

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