Case Report

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A case report of Jarcho–Levin syndrome

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Abstract:

Jarcho–Levin syndrome (JLS) is a rare, congenital disorder, inherited in an autosomal recessive pattern, that represents a spectrum of clinical and radiographic abnormalities of the spine and chest. The present case report discusses two siblings, an 11 year old girl and a 6 year old boy, diagnosed as cases of JLS based on family history and clinical-radiological findings. The main features of the syndrome are shortness of stature with a spinal abnormality, multiple abnormal vertebral defects, and a small malformed "fan-like" or "crab-like" rib cage due to posterior fusion and anterior flaring of the ribs, leading to short-trunk dwarfism. The spinal and rib malformations result in a small thoracic cavity, not capable of accommodating the growing lungs, causing thoracic insufficiency resulting in severe cardiac and respiratory complications and frequent chest infections. The diagnosis is based on clinical and radiological findings, characteristic physical appearance, symptoms of thoracic insufficiency, family history, consanguineous parents, skeletal survey, or specialized genetic tests for mutations. Milder forms are compatible with life.

Keywords:

Clinical-radiological findings, congenital disorder, Jarcho–Levin syndrome, physical appearance

Introduction

We present a case of two siblings, two children, an 11 year old girl and a 6 year old boy, diagnosed as cases of Jarcho-Levin syndrome (JLS) based on family history and clinical-radiological findings. The siblings were referred from the pediatric department to the radiology department with complaints of short stature, deformity of the spine and bony cage, and breathlessness on exertion. The referral was for radiological skeletal survey and ultrasound of the abdomen.

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The children were born of a second-degree consanguineous marriage and were normally delivered. The mother did not undergo any antenatal investigations in the course of both pregnancies. No antenatal ultrasonography was performed. No other family member had had a similar problem. The children exhibited an average level of intelligence for their age, and except for physical athletic activities, their performance at school was sound.

The siblings had the characteristic physical appearance of a short stature with a short trunk, the spine appeared kyphoscoliotic, and the chest seemed to be asymmetric and "crab like" due to mal-aligned ribs. They had a short webbed neck with restricted mobility, and the limbs though of healthy appearance appeared relatively longer. The trunk seemed short with a mildly protuberant abdomen. There was no evidence of any mental or neurologic deficit [Figure 1].

Ultrasound of the abdomen was normal except for small for age uterus in the female child. The skeletal survey was

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performed by imaging the cervical and dorsolumbar spine in anteroposterior and lateral positions using an X-ray [Figure 2].

The cervical spine in both siblings showed partially and completely fused vertebrae, and complete and incompletely blocked vertebrae. The radiograph of the dorsolumbar spine in both siblings showed kyphoscoliotic curvature. There were deformed vertebrae such as hemivertebrae, butterfly vertebrae, fused vertebrae, and hypoplastic vertebrae seen at multiple levels. The limb survey revealed standard shape, length, and density of the bones of the limbs.

The chest cavity appeared small and asymmetric. The ribs were malformed, and a few were fused, bifid, or missing. There was a posterior crowding of the ribs owing to their fusion at the next costovertebral junction and anterior flaring, giving a crab-like or fan-like appearance to the rib cage.

The diagnosis of JLS or spondylothoracic dysostosis was reached based on a detailed history and clinicoradiological findings. The findings of the patients who are siblings, born of second-degree consanguineous marriage, were the absence of any mental retardation or neurological deficit and clinical results of kyphoscoliotic spine and small malformed chest with "crab-like" or "fan-like" ribcage. There was short stature with a short trunk, a short neck with disproportionately long limbs and radiographic findings of multiple vertebral segmentation defects including hemivertebrae, butterfly-absent, or block vertebrae, and a small malformed chest with malformed and mal-aligned ribs, and normal ultrasound examination of the abdomen corroborated the diagnosis.

Discussion

JLS is a congenital skeletal disorder inherited in an autosomal recessive pattern.[1] It is characterized by abnormalities in the spine with malformed vertebrae and chest with a crab-like appearance of rib cage.[1] It was first described in 1938 by Jarcho and Levin in cases of thoracic insufficiency due to vertebral and rib anomalies.[2] As it is a rare genetic disorder, its exact prevalence is unknown.[3] Many cases may have gone undiagnosed or misdiagnosed.[3] Only 400 cases have been described in the world and about 15 cases in the Indian literature.[4] JLS includes two distinct genetic disorders, spondylocostal dysostosis (SCD)

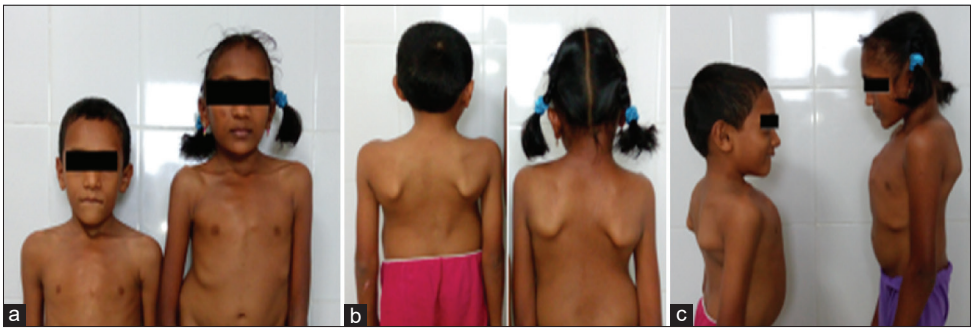

Figure 1: Physical examination of case (a and b) shows short-trunk dwarfism, short neck, malformed chest, and abnormal curvature of spine abnormality in stature with asymmetric thoracic cage and scoliotic spine. (c) Short torso, crab-like appearance of rib cage with protuberant abdomen. The limbs appear normal for the age

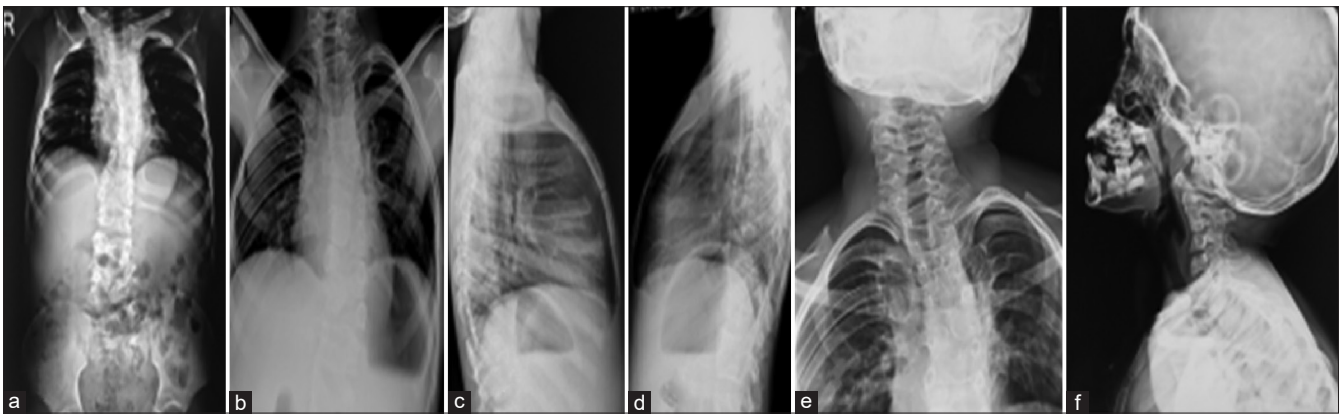

Figure 2: Radiological investigation of case (a-d) anteroposterior and lateral radiographs of the thoracolumbar spine of the siblings with kyphoscoliosis with multilevel vertebral anomalies such as hemi-, wedged, and butterfly vertebrae. The chest cavity appears "crab like" due to mal-aligned, crowed, fused, irregular, or bifid ribs with posterior symmetric fusion of all the ribs at the costovertebral joints. (e and f) Anteroposterior and lateral radiographs of the cervical spine showing short neck with block vertebrae with fusion of C2, 3, 4, and asymmetry of the visualized portion of the chest

and spondylothoracic dysplasia, which present with multiple vertebral and costal anomalies. SCD, classified into two major types, is best applied to those phenotypes with generalized multiple segmentation defects of the vertebrae and a broadly symmetric thoracic cage.[5,6]

SCD type 1 (severe form), which can be diagnosed *in utero*, follows an autosomal recessive pattern of inheritance, with critical spine involvement, in people of Puerto Rican descent. It generally causes death in affected children as a result of respiratory failure. SCD type 2, the milder form, which cannot be diagnosed *in utero*, follows an autosomal dominant pattern, with milder manifestations compatible with life.

The precise genetic basis of JLS is not clear, but it has been attributed to a mutation in one of at least five different genes, specifically DLL3, MESP2, LFNG, HES7, and TBX6. Still, the most common is the DLL3 gene mapped to the 19q13.1-q13.3 region. Milder forms of mutations have been reported in the MESP2 gene. Many people do not have a mutation in any of these genes, suggesting that there is an as-yet-unidentified gene as an etiological factor.[7]

The clinical findings are an abnormality in the spine and chest. The patient has a short-trunk dwarfism and a short neck with restricted mobility and limbs that appear disproportionately long. The small malformed chest cannot expand for the developing lungs resulting in reduced lung capacity, difficulty in breathing, and repeated infections (pneumonia) of the lungs, which can be mild, moderate, or life-threatening. These can be associated with complications like hypertension with an increased risk of heart failure.[8] Only milder forms reach adulthood.[9] Imaging findings show mostly kyphoscoliotic curvature of the spine and segmentation defects at least at ten contiguous levels in the way of vertebral anomalies such as hemi-, butterfly, wedged, fused, or absent vertebrae. The chest shows malformed ribs which are mal-aligned, crowded, fused, and bifid with posterior symmetric fusion of all the ribs at the costovertebral joints and flared anteriorly giving "crab-like" or "fan-like" appearance to the chest. In the absence of clear genetic markers for JLS, reliance is placed on physical appearance characteristic symptoms, a detailed patient and family history, and a thorough clinical and imaging. It can be suspected on antenatal fetal ultrasound at 16 weeks because of some defects associated with the spine and chest, such as irregular short "pebble-like" spine with poorly formed vertebrae, normal amniotic fluid, standard limb length, and biparietal diameter.[7] At birth, diagnosis is most commonly based on physical appearance and skeletal survey of the chest and spine. Although molecular genetic testing can detect mutations, it is only available in specialized laboratories. Diagnosis cannot be confirmed in patients who have no mutations in any of the genes known to cause the following disorders:[10] Alagille syndrome, campomelic dysplasia, oculo-auriculo-vertebral syndrome, Klippel–Feil syndrome, Robinow syndrome, multiple pterygium syndrome, sirenomelia, and Vacterl syndrome. In Casamassima–Morton–Nance syndrome, there are urogenital abnormalities as well as spinal and rib malformations.[11,12] Treatment of JLS cases depends on the degree of skeletal deformity (especially of the chest) and thoracic insufficiency. Initial management aims at aggressive neonatal care, by providing respiratory support to prevent pulmonary infections and avoid respiratory compromise, which is the primary cause of mortality and morbidity in infancy. At later stages, orthopedic procedures can be planned depending on the evolutionary course. In 2004, the Food and Drug Administration approved the vertical expandable prosthetic titanium rib (VEPTR), which can improve thoracic function by increasing the thoracic volume as it reasonably straightens the spine and separates the ribs to allow room for the lungs to grow with age. This device, which requires specialist teams, is designed to maintain these improvements throughout the patient's growth and grow with the child.[13,14]

Conclusion

Modern imaging and orthopedic techniques and respiratory technology have improved the survival of infants with JLS, but those who survive beyond early childhood have progressive scoliosis, neurological dysfunction and paraplegia secondary to spinal cord compression, etc., However, the advent of newer techniques like VEPTR has not only improved the survival but also improved the quality of life, allowing them to lead near-normal and professional lives as adults.

Declaration of patient consent

The author certifies that all appropriate consent forms were obtained from the patients' parents for the publication of the case report. The consent covers images and other clinical information being reported. They were assured that patients' names and initials will not be published and every effort will be made to conceal the patients' identity, but that anonymity could not be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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