Pulmonary Hypoplasia in Jarcho-Levin Syndrome

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Jarcho-Levin syndrome, also known as spondylothoracic dysplasia and characterized by short trunk dwarfism, "crab-like" rib cage, with ribs and vertebral defects; it is not uncommon in Puerto Ricans. Many patients die in early infancy due to respiratory compromise associated to lung restriction and the reported cases emphasize mostly the skeletal malformations associated to the syndrome. We report the autopsy findings in a newborn with isolated Jarcho-Levin syndrome emphasizing pulmonary pathology. He was a pre-term male who died of respiratory failure at three hours old and, autopsy findings confirmed the clinical diagnosis. Internal examination showed hypoplastic lungs with normal lobation. The histological structure appeared normal and relatively mature; the diaphragm showed eventration and unilateral absence of musculature. This case shows the worst spectrum of the Jarcho-Levin syndrome: pulmonary hypoplasia not compatible with extrauterine life. Since thoracic restriction is present during the fetal period, the degree of pulmonary hypoplasia probably defines survival beyond the neonatal period.

Keywords: Dwarphism, Puerto Rico, Spondylothoracic dysplasia, Vertebral defects, Jarcho-Levin syndrome.

The Jarcho-Levin syndrome, also known as spondylothoracic dysplasia was described in 1938. It is an autosomal recessive disorder characterized by short trunk dwarfism, prominent occiput, a short thorax with "crab-like" rib cage, absence of ribs, and multiple vertebral defects (1,2). The syndrome is commonly seen in Puerto Rican individuals. Many of these patients die in early infancy due to severe respiratory compromise. Reported cases in the literature mostly emphasize the skeletal malformations associated to the syndrome. We report autopsy findings in a newborn with isolated Jarcho-Levin syndrome emphasizing pulmonary pathology.

Case Report

A pre-term male baby was born to a 17-year-old primigravida after 34-weeks of gestation by a spontaneous vaginal delivery. The fetus had been diagnosed in utero as a Jarcho-Levin syndrome. There was no family history of skeletal dysplasias, there was no parental consanguinity and both parents were Puerto Rican. Upon delivery, the baby presented generalized cyanosis, bradycardia and poor respiratory effort, requiring immediate orotracheal intubation. The baby had an APGAR score of five and six at one and five minutes, respectively. He was admitted to the Neonatal Intensive Care Unit and placed on mechanical ventilation. His clinical status progressively deteriorated, developed pneumothorax and died three hours after birth, despite resuscitation efforts. Roentgenographic examination showed a small chest with "crab-like" appearance, low lung volume, and multiple vertebral segmentation defects with associated ribs anomalies as shown in Figure 1. Autopsy findings confirmed the clinical diagnosis of Jarcho Levin syndrome. It disclosed a dysmorphic white Hispanic male baby that weighed 2010 gm (expected 1720 ± 580 gm) and measured 19 cm crown to rump (expected 29.3 ± 3.3 cm), 35 cm crown to heel (expected 40 ± 3.5 cm) and 7.0 cm toe to heel (expected 6.3 ± 0.7cm). The upper segment measured 19.3cm, and the lower segment 15.7cm. Externally, he presented a short trunk with a small chest and an increased anteroposterior chest diameter, a globose abdomen, a short neck, and a low posterior hairline (Figure 2). The limbs were normally formed with the impression of being long, at the expense of the short trunk. This was supported by the upper/ lower segment ratio of 1.2, slighter lower than normal due

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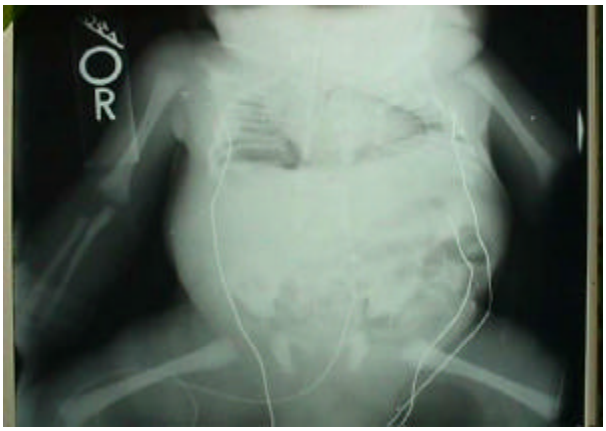

Figure 1. Roentgenographic examination showing a small chest with "crab-like" appearance, low lung volume, a pneumomediastinum, and multiple vertebral segmentation defects with associated ribs anomalies.

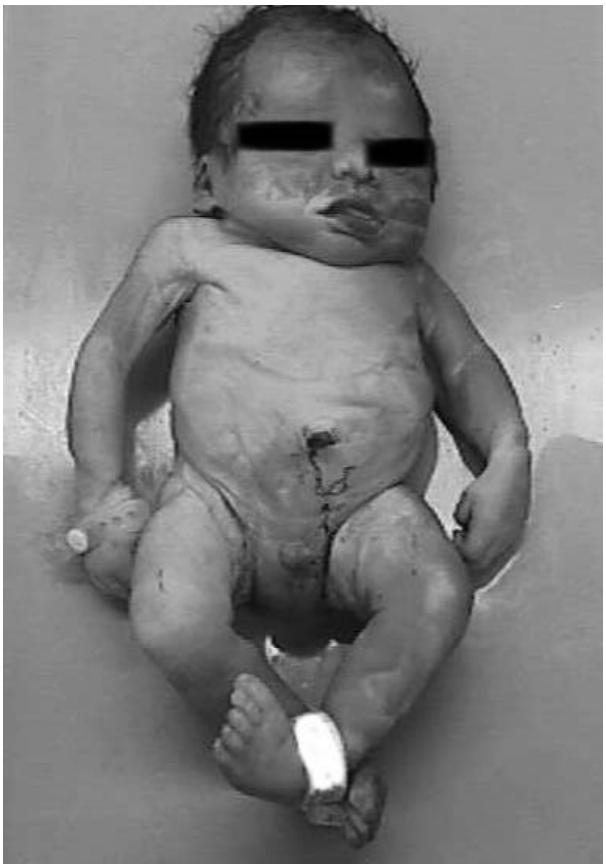

Figure 2. Typical patient with Jarcho- Levin syndrome showing short trunk and small chest.

to the short trunk (normal upper/lower segment is 1.7 at birth). There were also bilateral simian creases in his hands, a left foot equinovarus and acrocyanosis. Upon opening the crab-like rib cage, only eight poorly developed ribs were present on the left side and six on the right, with flaring in a fan-like fashion and multiple vertebral segmentation defects were also observed. The lungs had normal lobation but were hypoplastic, with a combined weight of 11 gm (expected 31.8 ± 13.5 gm) and a lung to body weight ratio of 0.005, when the expected is 0.012 for babies of 28 weeks gestation or more (3). Microscopically, they presented pulmonary hypoplasia with relatively increased number of airways in relation to the lung parenchyma, and the presence of bronchioles very close to the visceral pleura. A radial alveolar count disclosed 3-4 alveolar septa, in the areas where the distal bronchioles were closer to the pleura. Hypertensive vascular changes and focal pulmonary hemorrhages were also present. Other than hypoplasia, the histological structure appeared normal, and relatively mature. The diaphragm was intact but there was eventration, with absent diaphragmatic musculature on the left side. The other internal organs showed normal anatomical relations and no structural defects were observed; The skull bones were essentially unremarkable. Other autopsy findings included focal interstitial hemorrhages of the kidneys and a small hepatic infarct in the gallbladder bed. Sections of the brain revealed acute ischemic neuronal injury with moderate microglial proliferation, and marked congestion.

Discussion

After Jarcho and Levin described two siblings with vertebral and costal malformations, more cases of this syndrome have been reported. In 1991, Karnes et al (4) reviewed 61 cases, reporting two subtypes of the Jarcho-Levin syndrome, spondylocostal dysostosis and spondylothoracic dysostosis. Each of these entities presents different prognoses, in spondylocostal dysostosis there are vertebral malformations and short stature but individuals do not present the fan-like rib abnormalities. Spondylothoracic dysostosis presents a worst prognosis with a high mortality rate due to progressive thoracic restriction.

Although the exact incidence of the Jarcho-Levin syndrome in Puerto Rico has not been clearly established, at least one newborn with this syndrome is admitted each year to the University Pediatric Hospital. The autopsy rate for infants with this syndrome at our institution is low, since parents feel they already know the cause of death and there is no need for an autopsy. Most of the surviving infants have required oxygen supplementation at home suggesting respiratory compromise in survivors. The high mortality in these patients has been associated to lung restriction. Since this is a developmental

abnormality, thoracic restriction is present during the fetal period and probably the degree of pulmonary hypoplasia defines survival beyond the neonatal period.

The case presented in this report shows the worst spectrum of the Jarcho-Levin syndrome with pulmonary hypoplasia not compatible with extrauterine life. Pulmonary hypoplasia is defined as defective or incomplete development of lungs that are immature for gestational age (5). Lung weight to birth weight ratio, radial alveolar count, and tissue maturity have been used to define pulmonary hypoplasia (5-7). This patient presented a low lung-to body weight ratio and decreased radial alveolar count but the lungs were histologically mature. The reported case, in addition to the restrictive thorax, showed clear evidence of pulmonary hypoplasia. There was also absence of diaphragmatic musculature, which further compromised the respiratory effort. Based on our findings we can conclude that determination of the degree of pulmonary hypoplasia may help clinicians ascertain neonatal survival prognosis in newborns with Jarcho-Levin syndrome.

Resumen

El síndrome de Jarcho-Levin, también conocido como displasia espondilotorácica, se caracteriza por enanismo de tronco corto, caja torácica en forma de cangrejo y defectos en las costillas y vértebras y no es raro en personas de origen puertorriqueño. Muchos pacientes mueren en la infancia temprana debido a compromiso respiratorio severo asociado a la restricción pulmonar. Los casos reportados previamente hacen énfasis a las malformaciones esqueletales asociadas a este síndrome. Reportamos hallazgos de autopsia en un recién nacido con el síndrome de Jarcho-Levin aislado, enfatizando la patología pulmonar. El paciente era un varón pre-término que falleció por insuficiencia respiratoria severa a las 3 horas de vida. Los hallazgos de autopsia confirmaron las manifestaciones clínicas demostrando pulmones con lóbulos normales, pero hipoplásicos. La estructura histológica tenía apariencia normal y estaba relativamente madura y el diafragma demostró eventración y ausencia unilateral de la musculatura. Este caso muestra el peor espectro del síndrome de Jarcho-Levin con hipoplasia pulmonar incompatible con la vida extrauterina. Debido a que la restricción torácica está presente durante el período fetal, el grado de hipoplasia pulmonar probablemente define la sobrevivencia más allá del período neonatal.

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