

## **Jarcho Levin Syndrome and Renal Abnormalities**

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### **ABSTRACT**

**Jarcho Levin syndrome is a rare genetic disorder characterized by malformations of the vertebrae at different levels of the spine and ribs. We present a case of Jarcho Levin Syndrome diagnosed prenatally and was associated with renal abnormalities.**

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### **INTRODUCTION**

Jarcho Levin Syndrome is a congenital disorder of the skeleton inherited in an autosomal recessive pattern, but variants of an autosomal dominant pattern have been also reported<sup>1</sup>.

The autosomal recessive types described in the literature were two types; one was indistinguishable from the dominant type and the condition was compatible with life; the other was incompatible with life and usually present with respiratory difficulty and other anomalies of the ribs and vertebrae<sup>2</sup>.

The skeletal disorders of the spine include multiple vertebral anomalies, such as “butterfly vertebrae”, hemivertebrae and fused hypoplastic vertebrae.

This syndrome is more common in females. It was found more in Spanish ancestry with frequency of 0.2 per 100,000 live births by the Spanish Collaborative Study of Congenital Malformations<sup>3</sup>.

The aim of this presentation is to highlight the abnormal ultrasonic findings of this rare syndrome.

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### **THE CASE**

A twenty-eight-year-old Bahraini lady (gravid 4, Para 3, living 1) presented at 12 weeks of gestation for first trimester routine ultrasound. Her first pregnancy ended in lower segment cesarean section due to fetal compromise. The baby died on the fifth day of the neonatal period. He had a solitary non-functioning kidney and was diagnosed as Potter syndrome.

The second delivery was a full-term normal vaginal delivery and the baby was alive and well. The third delivery was a lower segment cesarean section due to breech presentation and the

baby expired at the age of 7 months. The baby was in NICU on ventilator with the diagnosis of bilateral polycystic kidneys and small dysmorphic rib cage. The spinal cord showed no herniation or deformities.

The family history did not reveal any congenital anomalies or hereditary diseases. The marriage was non-consanguineous.

The fourth pregnancy had no history of exposure to radiation or teratogenic agents during early pregnancy. The diagnosis was achieved using ultrasonography in a 12 weeks fetus; the mother had bad obstetrical history.

Ultrasound at 12 weeks of gestation showed that the nuchal translucency measurement was 0.96 cm, which was above the 95<sup>th</sup> percentile, and skin edema detected all around the body.

The serum markers [PAPP-A and free BHCG] with nuchal translucency, in addition to maternal age, revealed the fetus to be in the high risk group. Both the parents refused the offer of amniocentesis.

At a 14-week scan, the fetus showed evidence of skin edema all over the body. The spine was seen up to thoracic region; bladder and kidneys could not be visualized, see figure 1.



**Figure 1: A Fetus with Skin Edema All over the Body**

At 20 weeks, transverse view of the fetal head was normal, see figure 2. There was severe disruption of the normal spine with kyphoscoliosis and segmentation abnormalities with hemivertebrae. The chest looked narrow in comparison with the abdominal circumference seen in figures 3, 4, 5 and 6.



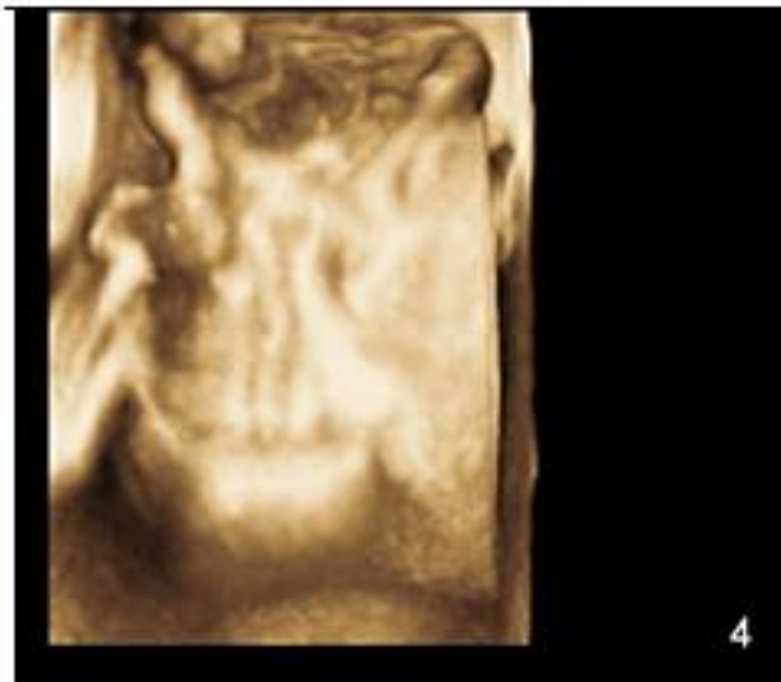
**Figure 2: A Transverse Normal View of Fetal Head at 20 Weeks Gestation**



**Figure 3: A Sagittal Section at 20 Weeks of Gestation: Thoracic and Lumbar Hemivertebrae with Abnormal Alignment of the Vertebral Bodies**



**Figure 4: A Sagittal View Showing Kyphoscoliosis of the Thoracolumbar Spine**



**Figure 5: Widening of Spinal Canal and Disarrangement of Vertebrae**



**Figure 6: Fetal Spine with Malalignment of Vertebral Bodies**

The kidneys were normal in size, hyperechoic and cystic in appearance, with dilatation of both renal pelvises, see figures 7 and 8.



**Figure 7: Bilateral Dilatation of Renal Pelvises, More on the Left Side**



**Figure 8: Hyperechoic and Cystic Kidneys**

Prenatal echocardiography did not detect cardiac abnormalities. The limbs' lengths were corresponding to gestational age. The amniotic fluid index was normal.

The baby girl was born by cesarean section at 38 weeks of gestation. Apgar score was 6 at five minutes and 8 at ten minutes. The birth weight was 2,130 grams. Her cephalic, thoracic, and abdominal circumferences were 32, 30 and 31 cm respectively, and the fetal length was 48 cm.

At birth, she had pulmonary complication and expired after 48 hours due to respiratory failure from severe pulmonary hypoplasia.

A radiographic study performed for the parents did not reveal any spinal abnormalities. The couples were seen by the obstetrician and pediatric genetics during the postnatal period. Genetic counseling regarding the mode of inheritance for an autosomal recessive was discussed and a plan was made to assess any subsequent pregnancy with ultrasound.

## **DISCUSSION**

Cases of Jarcho Levin Syndrome (JLS) with multiple anomalies have been reported by several authors. Short trunk skeletal dysplasia, vertebral and ribs are the main anomalies in JLS<sup>4</sup>.

The spectrum of other associated anomalies which were described are urogenital anomalies, lower limb anomalies, neural tube defects (spina bifida), anal anomalies, inguinal hernias, and Meckel's diverticulum<sup>5-7</sup>.

Other studies have described two subtypes of Jarcho Levin syndrome: spondylocostal dysplasia and spondylothoracic dysplasia. Survival rate is higher in the former, but the latter is almost always fatal.

Both subtypes have an abnormal vertebral column with segmentation defects including absent vertebrae, hemivertebrae and fused vertebrae.

The two subtypes are distinguished by the ribs' abnormalities; 'crab-chest' deformity of spondylothoracic dysplasia is due to fusion of the posterior elements of the ribs with flaring of the anterior ends; spondylocostal dysplasia, have intrinsic abnormalities of fusion and bifurcation of the ribs but no flaring. In both subtypes, the karyotypes are typically normal<sup>8</sup>.

A mutation in the delta-like 3 gene (DLL3) on chromosome 19 and MESP2 gene are responsible for the development of spondylocostal dysplasia in Jarcho Levin syndrome<sup>9-11</sup>. But chromosome 2q32.1 is associated with spondylothoracic dysplasia.

The etiology of JLS and related disorders is due to significant reduction in levels of Pax1 and Pax9 protein expression in chondrocytes of the vertebral column by immunochemical analysis<sup>12</sup>.

Dias and Pang et al found that embryological failure of mid axial integration have resulted in split cord malformation during the period of gastrulation<sup>13,14</sup>.

The babies with Jarcho Levin Syndrome were described as having multiple vertebral anomalies at different levels of the spine associated with short and rigid neck, short thorax, inguinal and umbilical hernias and protuberant abdomen. Major features are seen in vertebral and rib malformations<sup>15</sup>. The prognosis is directly related to respiratory complications.

Our case illustrates the importance of an accurate early ultrasound examination (first and second trimester) and early diagnosis of uncommon syndromes such as Jarcho Levin Syndrome<sup>3</sup>.

Ultrasound could reveal the prenatal diagnosis at 16 weeks of gestation; the diagnostic criteria could be unpaired or poorly formed vertebrae, indistinct or fused posterior ribs, irregular short 'pebble-like' appearance of the spine, short trunk, protuberant abdomen, hernias, normal amniotic fluid, normal limb length and normal bi-parietal diameter<sup>16</sup>.

## CONCLUSION

**A case of a lethal type of Jarcho Levin Syndrome was presented. The case was suspected prenatally by using Nuchal translucency screening, anatomy scanning at second trimester and three-dimensional ultrasound.**

**Although it has a low incidence, it is important to be considered in the differential diagnosis in fetuses with spinal and rib abnormalities.**

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