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Case Report

Early-onset renal dysfunction in Jeune syndrome: A case report with atypical presentation ☆,☆☆

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ABSTRACT

Jeune syndrome, a rare autosomal recessive disorder, is characterized by skeletal abnormalities, particularly a narrow, bell-shaped chest, leading to severe respiratory distress in newborns. This case report details a full-term female neonate presenting with significant respiratory challenges, typical skeletal features, and early-onset renal dysfunction. Despite normal initial imaging, persistent renal abnormalities were observed, underscoring the need for early diagnosis, vigilant monitoring, and a multidisciplinary management approach to optimize outcomes for patients with Jeune syndrome.

Introduction

Jeune syndrome, also referred to as asphyxiating thoracic dystrophy, represents a severe and extremely rare genetic bone development disorder in relation to the bones of the chest and ribs. The syndrome was described by a French pediatrician named M. Jeune in the 1950s and is therefore named after him. It results in a narrow and bell-shaped chest due to the abnormal development of the rib cage; as such, there is less room for the expansion of the lungs. This thoracic constriction, the most critical aspect of this disorder, may lead to acute respiratory distress and be life-threatening. The constriction of the thorax is probably the most critical as-

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pect of the disorder since it leads to life-threatening respiratory distress, especially in newborns and young children [1–3].

The disorder follows an autosomal recessive pattern of inheritance, meaning that the child needs to inherit 2 copies of the mutated gene, 1 from each parent, to be affected [4]. Interindividual variability in the expression of Jeune syndrome has been associated with several genes like IFT80, DYNC2H1, and WDR19, all implicated in the etiology of this disease [5]. These genes encode proteins necessary for the function of cilia, small hair-like projections on the surface of cells that might be very important in signaling and development and that have been most prominently characterized in skeletal and organ development [6].

In addition to usual thoracic abnormalities, patients suffering from Jeune syndrome usually have short-limbed dwarfism, a disease characterized by proportional shortening of the arms and legs. This skeletal dysplasia may further include hands and feet and thus lead to brachydactyly. In rare cases, it also leads to complications outside the bones—for example, abnormalities of the kidneys in the form of nephronophthisis, liver fibrosis, or retinal degeneration.

The severity differs from 1 person to another, where some affected people with Jeune syndrome have mild respiratory problems while others relapse badly at birth. For those surviving neonatal death, many interventions may be required, like continuous respiratory support, surgical expansion of the chest cavity, and close vigilance for other possible complications like kidney disease [4].

We describe a Jeune syndrome patient whose case exemplifies the early rise of renal markers—a little-emphasized feature of this condition. This case underlines the importance of timely recognition and follow-up of renal dysfunction, in addition to the typical respiratory and skeletal challenges, to guide timely interventions and improve patients' outcomes.

Case presentation

A full-term, small-for-gestational-age female neonate was born at 39 weeks of gestation to a 28-year-old primigravida mother after an uneventful pregnancy course. Her neonate at birth had Apgar scores of 5 at 1 minute and 6 at 5 minutes, thereby showing moderate distress. She lay in significant respiratory distress characterized by tachypnea, nasal flaring, and subcostal retractions that required continuous supplemental oxygen. Her initial vital signs were the following: heart rate, 170 beats per minute; respiratory rate, 80 breaths per minute; blood pressure, 60/40 mmHg; and oxygen saturation, 85% on room air, which improved to 92% with supplemental oxygen. The neonate weighed 2,200 grams; his length was 46 cm on the supine side, and his head circumference was 34 cm, with a chest circumference of 28 cm, hence a ponderal index of 2.35, placing him at a normal birth weight.

On physical examination, she had micrognathia, shortened limbs, a narrow and bell-shaped chest, and bilateral pedal edema (Fig. 1). Her cardiovascular and gastrointestinal evaluation was essentially within normal limits, as was her neurological evaluation.

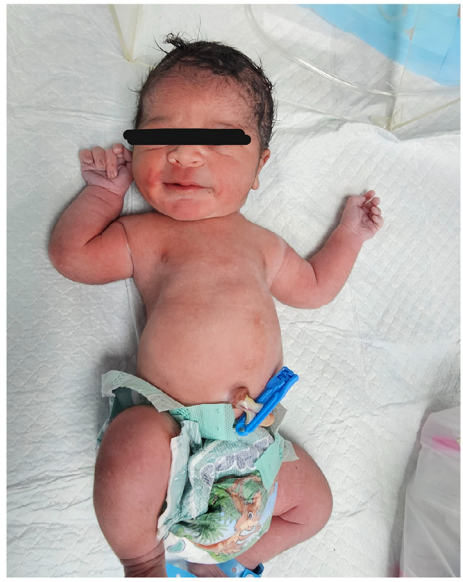

Fig. 1 – physical characteristics of the patient showing shortened limbs, a narrow and bell-shaped chest, and bilateral pedal edema.

Laboratorians demonstrated high serum creatinine at 2.1 mg/dL and BUN at 36 mg/dL. Despite such high renal markers, a renal ultrasound did not demonstrate any structural abnormality and both kidneys were of normal size. Urine specific gravity was normal at 1.018. By the fourth week of age, the patient's renal markers continued to increase, reaching of the serum creatinine to 2.5 mg/dL and BUN 47 mg/dL. An echocardiogram was likewise performed, and cardiac function proved to be normal.

Laboratory results were followed by postnatal radiological evaluation, which included a chest X-ray showing a small and bell-shaped rib cage with decreased volumes bilaterally, thus suggesting lung hypoplasia (Fig. 2). Further imaging confirmed a very narrow thorax with short and horizontally running ribs and low lung volumes. The skeletal survey on the overall skeleton also showed shortened long bones, irregularly formed costal cartilages, and hypoplastic iliac bones.

She was treated with supplemental oxygen due to respiratory distress, which gradually improved. She required close follow-up with Nephrology for his elevated renal markers. Orthopedic follow-up was arranged to track skeletal development. She had nutritional support for growth. The family received genetic counseling on the nature of Jeune syndrome—it is autosomal recessive in inheritance; thus, it risks recurrence in future pregnancies and has long-term implications for this child.

A multidisciplinary care plan was initialized that included pulmonology, orthopedics, nephrology, and genetics for comprehensive treatment and monitoring. Key elements of long-term management include frequent follow-up visits and anticipatory guidance toward addressing the changing needs associated with the condition.

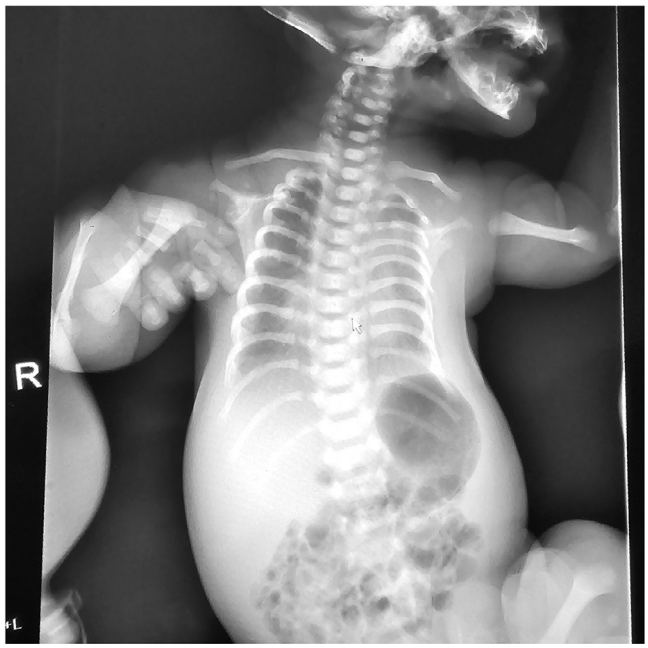

Fig. 2 – Anteroposterior (AP) view chest X-ray showing a small and bell-shaped rib cage with decreased volumes bilaterally, thus suggesting lung hypoplasia.

Discussion

Jeune syndrome, also known as asphyxiating thoracic dystrophy, is a very uncommon autosomal recessive genetic disorder. It was first described in 1955. The syndrome is mainly characterized by a narrow chest, usually resulting in severe respiratory distress at birth due to reduced lung volume secondary to the small size of the thoracic cage [7].

This neonate showed typical features of Jeune syndrome with a narrow, bell-shaped thorax and shortened ribs, which were also in the investigated imaging. The severe respiratory distress right after birth supported the literature findings that, among babies, respiratory complications in the neonatal period are the leading cause of morbidity and mortality in Jeune syndrome [8]. Our findings are in agreement with previous reports of such infants often requiring respiratory support and that the amplitude of breathing difficulty was directly proportional to the severity of chest constriction. In our patient, supplemental oxygen improved the condition and correlated well with the effectiveness of noninvasive respiratory support, as reported in other cases [9]. However, more aggressive interventions, such as mechanical ventilation or surgical implementations of chest expansions, are required to be implemented in severe cases [10].

This case, however, depicts very early-onset renal involvement. The patient's serum creatinine was elevated at 2.1 mg/dL and BUN of 36 mg/dL from birth, with these levels increasing to 2.5 mg/dL and 47 mg/dL, respectively, by the fourth week. Notably, no specific cause for this renal impairment was identified, as the renal ultrasound was unremarkable, excluding any anatomical abnormalities and genetic testing was not performed because it was unavailable. So, the diagnosis of renal involvement due to Jeune syndrome was established by exclusion. This finding contrasts the existing literature, where renal involvement in Jeune syndrome typically manifests much later in the disease course. For example, a case series reported renal issues in only 1 out of 9 cases, noted at 2 years of age; a review of 110 reports found renal involvement in just 34% of cases [11]. There also have been several studies demonstrating that chronic renal failure may appear as late as 6, 4, and 3 years [12]. Typically, renal complications in Jeune Syndrome are expected to manifest after the second year of life [13]. With early and persistent renal impairment in this case, against the background of initially negative imaging and a later reported onset, these renal issues may very well arise sooner and more unexpectedly, making early monitoring essential.

Other conditions involving renal impairment in the neonatal period, such as autosomal recessive polycystic kidney disease (ARPKD), cystinosis, and nephronophthisis, were excluded based on specific diagnostic criteria and clinical findings.

Firstly, the diagnostic criteria for ARPKD require the absence of any other congenital anomalies. In our case, congenital skeletal deformities ruled out this condition [16]. Secondly, cystinosis is characterized by wide systemic involvement, affecting multiple organs, including the cornea, thyroid, liver, spleen, muscles, and peripheral nerves. Our patient's absence of these manifestations further excludes cystinosis as a diagnosis [17,18]. It was ruled out for nephronophthisis, which is an autosomal recessive disease. The juvenile form typically leads to renal failure in the second decade of life, beginning with a urine concentration defect in the first decade. The juvenile form is mostly associated with ultrasound findings of hyperechogenic kidneys without cysts at presentation, while the infantile form is more aggressive with symptoms before age 5. Symptoms include renal failure at an early age, often combined with cystic dilatations of the collecting ducts and a moderate degree of kidney enlargement. Moreover, the infantile form is often associated with severe hypertension and extrarenal symptoms such as retinitis pigmentosa and cerebellar ataxia. As we did not find these in our case, nephronophthisis was ruled out [19].

Lastly, there is a rare genetic disorder called brachymesomelia-renal syndrome. Although it shares similarities with Jeune Syndrome in terms of renal and skeletal involvement, brachymesomelia-renal syndrome was excluded from our case because it primarily includes limb deformities rather than thoracic cage abnormalities. In contrast, Jeune Syndrome is characterized by a narrow thoracic cage, leading to respiratory distress [20].

Ongoing orthopedic follow-up in this case was necessary to monitor the child's skeletal development in view of the skeletal abnormalities associated with Jeune syndrome. These include shortened long bones, irregular cartilage of the ribs, and underdeveloped pelvic bones. These findings correlated well with other reports of Jeune syndrome. Genetic counseling was also conducted to advise the family regarding the recessive trait inheritance pattern and the possibility of recurrence in future pregnancies. This aspect of care is most important because an early diagnosis with complete genetic counseling

empowers the family to be aware and make informed decisions about further planning and management [14,15].

Conclusion

This case underscores the importance of early detection and management of renal involvement of Jeune syndrome, as evidenced by the atypical early elevation of renal markers. With emphasis laid heavily on respiratory care, this case points out very clearly that it is the manifestation of nephrological complications, which do manifest much earlier than is appropriately recognized and hence should be screened for from birth itself. The findings call for a comprehensive and coordinated approach to care, meaning that every dimension of the syndrome needs to be managed optimally.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Patient consent

Informed written consent was obtained from the parents of the neonate for the publication of their child's anonymized information in this article.

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