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Case Report

Caudal Regression Syndrome: A Case Report

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ABSTRACT

Background: Lumbosacral agenesis or caudal regression syndrome (CRS) is a rare congenital malformation represented with symmetrical sacrococcygeal or lumbosacrococcygeal agenesis with a varied incidence between 1 per 25000 live births to 2.5 per 100000 live births. Additionally, manifold abnormalities may be associated with CRS, including spinal cord malformations, cardiac malformations, lipomyelomeningocele, orthopedic deformities, renal agenesis, neurogenic bladder, tethered-cord, sacral agenesis, and anorectal atresia.

Case report: We report a case of a male neonate delivered to a 28-year-old diabetic mother at 38 weeks' gestation diagnosed with CRS. In this case, lumbosacral agenesis, hip dislocation, and club foot deformities along with cardiac abnormalities, including small patent ductus arteriosus (PDA), atrial septal defect (ASD), hypertrophic cardiomyopathy (HCM) without left ventricular outlet obstruction were seen.

Conclusion: Having the 200-fold increased relative risk of developing CRS in infants of diabetic mothers in mind, this case report provides evidence that uncontrolled maternal diabetes might increase the risk of CRS in infants.

Keywords: Caudal regression syndrome, Diabetes mellitus, Lumbosacral agenesis, Lumbosacral region, Prenatal diagnosis

Introduction

Lumbosacral agenesis or CRS is a rare congenital malformation that is represented with symmetrical sacrococcygeal or lumbosacro-coccygeal agenesis. Additionally, manifold abnormalities may associate CRS, including spinal cord malformations, cardiac malformations, lipomyelomeningocele, orthopedic deformities, renal agenesis, neurogenic bladder, tethered-cord, sacral agenesis, and anorectal atresia (1, 2). The incidence of CRS varies from 1 per 25,000 live births to 2.5 per 100,000 births (3). However, it should be noted that although maternal diabetes increases the incidence of developing CRS by 200 times, diabetes is not present in all cases (4, 5). Along with hyperglycemia, other contributing factors to CRS include genetic defects, chromosomal abnormalities, trimethoprim-sulfamethoxazole or minoxidil exposure, and vascular hypoperfusion (6). In this context, we report a case of a baby with CRS born to a diabetic mother.

Case report

The patient is a male neonate delivered to a 28-year-old diabetic mother G2P2T2A0L2 (gravida 2, para 2, term 2, aborta 0, live 2) at 38 weeks' gestation by normal vaginal delivery (NVD). Apgar scores in 1 and 5 minutes were 5 and 8, respectively. The mother was diagnosed with overt diabetes from the late trimester of her first pregnancy and was poorly controlled with oral drugs for eight years. Therefore, she was shifted to a twice-daily insulin regimen during this pregnancy. She gave no history of consanguinity with her husband, smoking, alcohol, or illicit drug abuse. Her first child is a healthy eight-year-old boy. The antenatal ultrasounds revealed no special abnormalities, and her glycosylated hemoglobin (HbA1c) was documented as 9.1 within the first trimester of this pregnancy. She was admitted to the hospital in her second trimester of pregnancy additionally for the delivery as a result of the uncontrolled diabetes. The neonate experienced asphyxia as a result of shoulder dystocia leading to prolonged delivery. After cardiopulmonary resuscitation in the delivery room, the baby was shifted to NICU. On physical examination, the baby's birth weight, length, and head circumference were 3850 gm, 49

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cm, and 35 cm, respectively. Bilateral club feet, hyperextension of the knees, fixed flexion, adduction and internal rotation of the left and right hips, was noted in the lower extremities. Three dimples were detected in the midline and lateral aspects of both buttocks in the iliac crest area. The sacral bone was impalpable. The anus was perforated with reduced tone and in a normal position. On further examination of the upper limbs, Erb's paralysis of the left extremity was revealed with a left-sided reduced moro reflex, probably due to birth injury. In the cardiovascular examination, a 2/6 degree midsystolic murmur was heard, and the baby was able to maintain 98% oxygen saturation without supportive oxygenation. The baby's face and abdomen were normal (Figure 1). Meconium and urine passage occurred within the first 24 hours of the baby's life. Voiding problems manifested by dribbling were in favor of a neurogenic bladder.

Further urodynamic studies in the later ages were planned to confirm the diagnosis. The spine X-ray revealed bilateral hip joint dislocation, absence of L4, L5, and sacrococcygeal bones, and apposition of both iliac bones (Figure 2), which was also confirmed with spinal ultrasonography. Cranial ultrasonography was normal. The ultrasonography of the abdomen and shoulder joint revealed no abnormalities. The hip joint ultrasonography was suggestive of a type-4 developmental dysplasia of the hip (DDH), and the sonographic evaluation of the knees was not diagnostic of any deformities.

Echocardiography revealed small patent ductus arteriosus (PDA), atrial septal defect (ASD), hypertrophic cardiomyopathy (HCM) without left ventricular outlet obstruction. After putting on a Pavlik Harness and applying a cast for his club foot deformity, the baby was discharged under good condition. The parents were informed about follow-ups for the baby's orthopedic and urologic problems.

Figure 1. Lower limb with bilateral club feet, hyperextension of the knees, fixed flexion, adduction, and internal rotation of the left and right hips

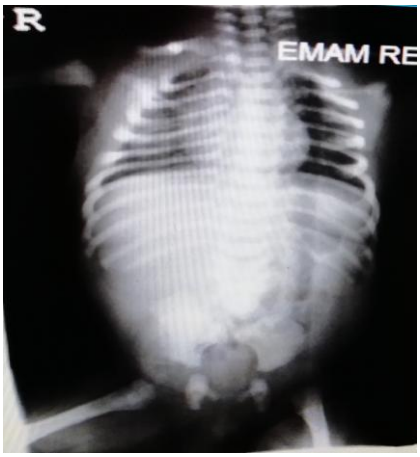

Figure 2. The spine X-ray shows bilateral hip joint dislocation, absence of L4, L5, sacrococcygeal bones, and apposition of both iliac bones

Discussion

Although the exact mechanism of CRS pathogenesis is unknown, interactions between genetic and environmental factors that disturb either primary or secondary neurulation seem to be responsible for CRS pathogenesis (7). Therefore, infectious, ischemic, and teratogenic factors before the fourth week of fetal development are assumed to be associated with the development of CRS (8).

As in the case of identical twins, one of them was diagnosed with CRS; it is shown that CRS etiology is not fully comprehensible with only environmental effects. Also maternal blood glucose level could not be the exclusive factor (9).

Genetic studies on CRS patients have shown that some genes, such as cytochrome CYP26A1 might potentially be contributory to this condition, whereas investigations for homeobox gene HLXB9 were not promising (10, 11). It has recently been reported that biallelic variants in the TBX4 gene are correlated with a syndromic phenotype of sacrococcygeal agenesis along with lower limb defects (12).

Regarding the clinical presentation, Pang has classified CRS into five types varying in severity: type I, total or partial sacral agenesis; type II, includes total sacral agenesis and degrees of lumbar agenesis along with continuity of the lower vertebrae and ilia; type III, absence of lumbosacral bones with the caudal endplate on the iliac amphiarthrosis; type IV, a complete absence of caudal soft tissues separation; and

type V, referred as sirenomelia represents with a single midline femur and tibia (13). In the reported neonate absence of L4, L5, and sacrococcygeal bones manifest a type II CRS in this classification.

Regarding a 200 times increase in the relative risk of developing CRS in infants of diabetic mothers (4), it has been reported that the adequate control of diabetes before gestation and during the first trimester of pregnancy decreased the incidence of the syndrome (14). However, only 16% to 22% of infants with CRS had a positive history of maternal diabetes (15). Indicating a safe level of glycemic control, Miller *et al.* suggested that HbA1c less than 6.9% and 8.5% were associated with no anomalies and remarkably lower incidence of malformations, respectively. (16). On the other hand, in the study conducted by Greene *et al*., HbA1c of less than 9.3% was associated with a 3% risk of major malformations (17). In the presented case, the mother's blood glucose was poorly controlled before and during the pregnancy, and the documented HbA1c was above 9% from the first trimester. A dose-related pattern of hyperglycemia-induced malformations has been reported in an animal study; this study shows a 20% malformation rate in groups with twice normal glucose level versus 100% malformation rate in groups with 950 mg/dl glucose levels (18). Therefore, given the influence of hyperglycemia on free radical excess, it is hypothesized that either by a direct or indirect mechanism, hyperglycemia can lead to the disruption of signal transduction system (19).

Etiologically, common anorectal, renal, neural, and genital anomalies associated with CRS might be due to the juxtaposition of developing hindgut, neural, notochordal, and genitourinary structures within the tailfold during the secondary neurulation (20). In this case, associated genitourinary, cardiovascular, and orthopedic deformities were present.

A critical aspect of prenatal ultrasound is to evaluate the lower extremities and fetal spine. Sacral agenesis, termination of the lumbar spine, and abnormal extremities in prenatal ultra-sonographic evaluations can be suggestive of CRS (21). Transvaginal ultrasound (TVUS) has been introduced as an effective tool for the early diagnosis of CRS. In the CRS case study reported by Baxi *et al*., the diagnosis was made using TVUS at 17th gestational week (22). However, in our case, no abnormalities were reported in the prenatal ultrasound.

Conclusion

In conclusion, this case report provides evidence that uncontrolled maternal diabetes might increase the risk of CRS in infants.

Acknowledgments

None.

Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of the present study.

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