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In utero diagnosis of caudal regression syndrome

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We present a case of caudal regression syndrome (CRS), a relatively uncommon defect of the lower spine accompanied by a wide range of developmental abnormalities. CRS is closely associated with pregestational diabetes and is nearly 200 times more prevalent in infants of diabetic mothers (1, 2). We report a case of prenatally suspected CRS in a fetus of a nondiabetic mother and discuss how the initial neurological abnormalities found on imaging correlate with the postnatal clinical deficits.

Introduction

This case report presents many of the findings associated with CRS on prenatal sonography and magnetic resonance imaging (MRI). The prevalence of CRS is estimated to be one in 25,000 live births (3). Genetic mutations in the coding sequences of HOXD13, CYP26A1, and HLXB9 have been suspected in the pathogenesis of CRS (4). Other factors likely to contribute include chromosomal abnormalities, vascular hypoperfusion, hyperglycemia, and exposure to minoxidil and trimethoprim-sulfamethoxazole (2).

Evaluation for suspected CRS by medical imaging is possible starting at around 20 weeks gestational age (5). Diagnosis in the first trimester is difficult because of incomplete sacral ossification. Here, we review signs of CRS on medical imaging and further discuss its role in differentiation from other skeletal dysplasias.

Case report

A 22-year-old G4P1 was referred for routine obstetric sonography. The medical history was notable only for depression, for which she was treated with sertraline. There was no history of illicit drug use, and prenatal testing, including genetic testing and 100g glucose tolerance test, was normal.

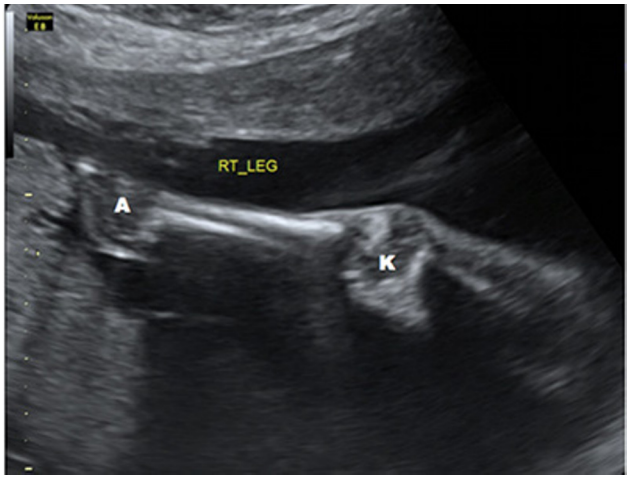

Fig. 1. Fetal sonogram shows muscle atrophy (sarcopenia) of right leg. A, fetal ankle; K, fetal knee.

Initial obstetric ultrasound (US) showed a singleton fetus of gestational age 19 weeks-3 days with normal amniotic fluid volume. However, the feet were poorly visualized. Subsequent US demonstrated relative atrophy of both legs compared to the girth of the upper extremities (Figs. 1 and 2). US also showed atypical position of legs and feet and sacral defects (Figs. 3 and 4). Fetal MRI confirmed these findings (Figs. 5 and 6) and, in addition, showed a dysmorphic conus medullaris that was both short and nontapered (Figs. 7 and 8). The remainder of the cord and the brain (Fig. 9) were normal, as were the fetal lungs, liver, and kidneys. The pregnancy progressed to term uneventfully, although serial sonography showed the fetus to be small for gestational age. Postnatal radiographs confirmed initial in utero findings of dysmorphic conus medullaris (Figs. 10 and 11) and absence of the sacrum (Fig. 12).

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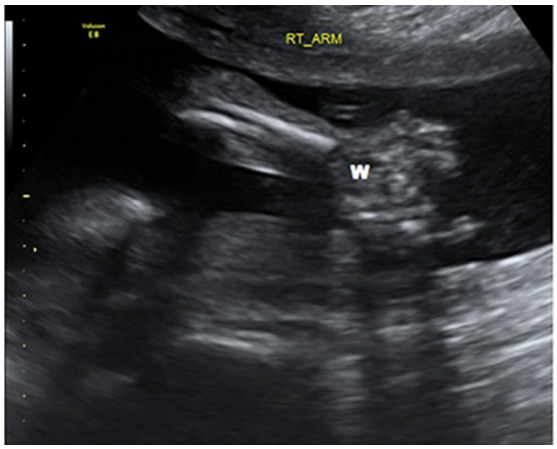

Fig. 2. Fetal sonogram shows normal size of right forearm muscles; radius and ulna are demonstrated. W, fetal wrist.

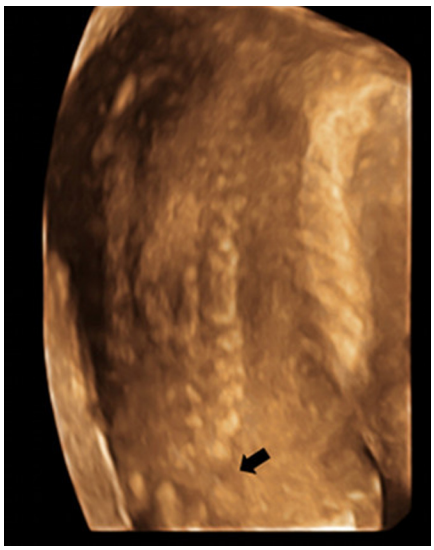

Fig. 3. Fetal sonogram demonstrates absence of sacrum (arrow).

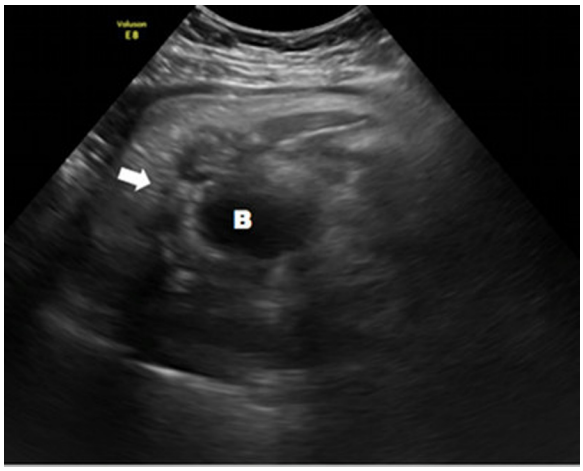

Fig. 4. Transverse axial ultrasound image at level of fetal urinary bladder (B) demonstrates absence of sacrum (arrow).

Discussion

Caudal regression syndrome (CRS), a relatively uncommon congenital anomaly, covers a spectrum of lumbosacral deficiencies and a variable extent of neurologic, genitourinary, musculoskeletal, and cardiac abnormalities. CRS is categorized into two types depending on the location and shape of the conus medullaris (6). Type 1 is typified by distal cord hypoplasia that is club- or wedge-shaped and that terminates abruptly rostral to the first lumbar level. Often there are severe sacral anomalies as well as urinary and bladder dysfunction. In contrast, type 2 CRS is characterized by a tapered and low-lying conus that ends

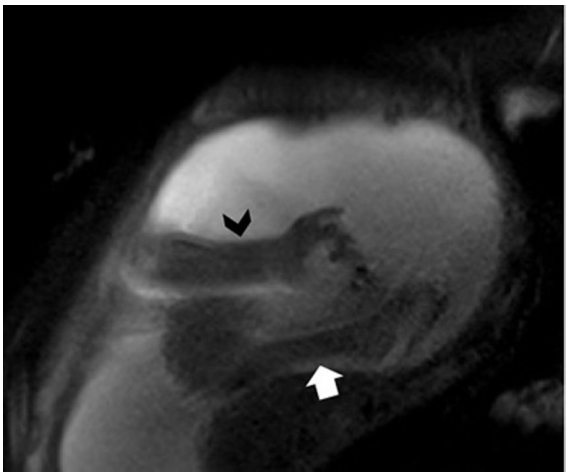

Fig. 5. MRI shows normal size of fetal forearm (black chevron) and sarcopenia of leg (white arrow).

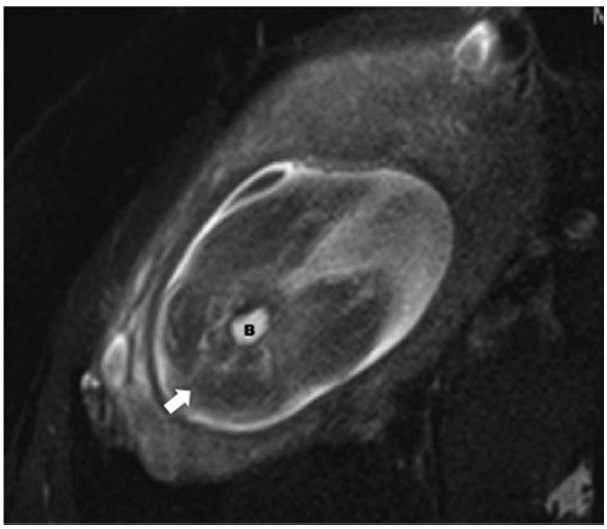

Fig. 6. Transverse image at level of fetal urinary bladder (B) shows normal muscle girth of both thighs and absence of the normal sacrum (arrow).

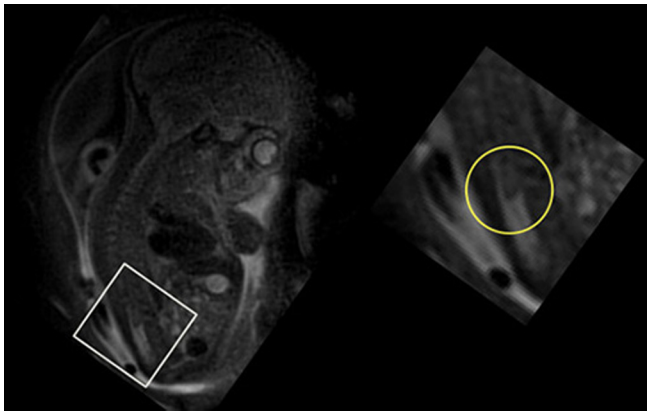

Fig. 7. Box inset of fetal MRI is magnified to demonstrate short and blunted terminus of conus medullaris.

caudal to the first lumbar segment, and the elongated conus is often tethered by a thickened filum terminale, terminal myelocystocele, or transitional lipoma. Less severe sacral anomalies are associated with type 2, but neurologic deficits are more common. The case we present is typical of type 1 CRS (Figs. 7 and 8).

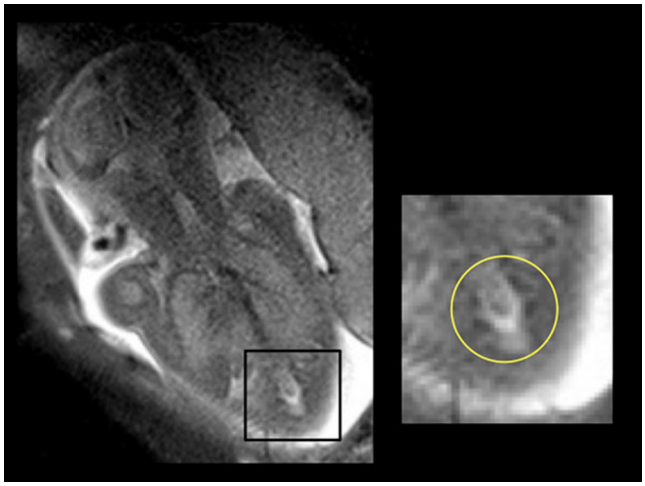

Fig. 8. Box inset of fetal MRI is magnified to demonstrate blunted terminus of conus medullaris.

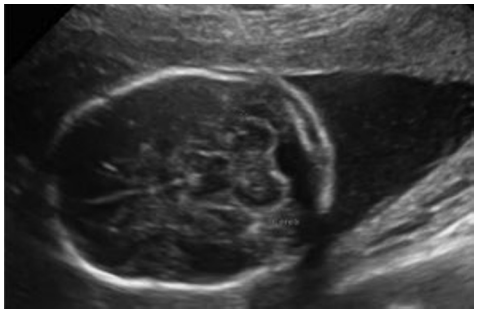

Fig. 9. Transverse US image at 22 weeks gestation age shows normal fetal brain and calvarium. There is no "lemon sign" (flattened or inwardly scalloped frontal bones) or "banana sign" (absent cisterna magna), and other images demonstrated normal ventricular size.

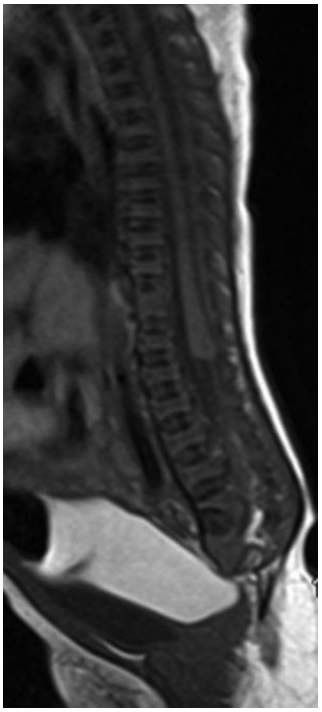

Fig. 10. Sagittal T1-weighted MRI of lower neonatal spine shows dysmorphic conus medullaris and absence of sacrum and coccyx. (TSE T1, TR, 601; TE 12)

Particularly in the setting of oligohydramnios and maternal obesity, MRI is valuable and can be used to assess genitourinary, gastrointestinal, and musculoskeletal anomalies that might be associated with CRS (2). It can be helpful to assess the degree of vertebral body dysgenesis, and to characterize the location and shape of the conus medullaris. US features that may be demonstrated early in gestation include shortening of the crown-rump length, protuberance of the lower spine, and a large nuchal translucency (2). Detailed obstetric sonography later in gestation may reveal a shortened spine with missing sacral and lower

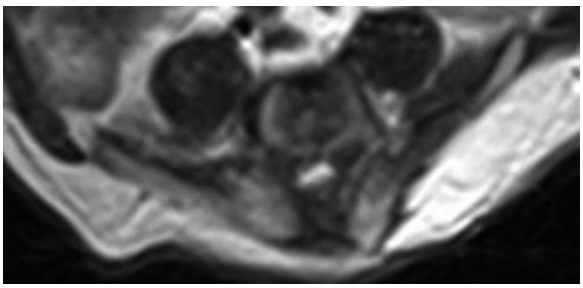

Fig. 11. Transverse axial T2-weighted MRI of the lower neonatal spine shows abnormal approximation of iliac bones and absence of the sacrum. (transverse axial TSE T2; TR, 4,900; TE, 4)

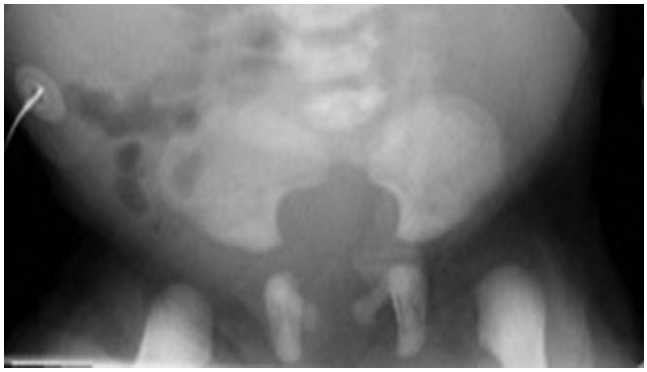

Fig. 12. Frontal radiograph of neonatal pelvis demonstrates absence of sacrum and coccyx.

lumbar vertebrae, short femora, and flexion contractures of the lower extremities.

The motoric deficit and its manifestation may correlate with the level of vertebral dysgenesis and aids the diagnosis (7). The lumbar plexus is formed from the ventral rami of the L1-L4 nerve roots and forms the femoral and obturator nerves. The femoral nerve innervates the iliacus, psoas, and quadriceps femoris muscles and therefore subserves hip flexion and knee extension. The obturator nerve also arises from the lumbar plexus and innervates hip adductor muscles. The sacral plexus is formed from the ventral rami of L4-S4. The sciatic nerve is formed from L4-S3 nerve roots and provides motor innervation of the posterior thigh muscles and all motor function below the knee. Agenesis of the sacral spinal roots in CRS enables unopposed motoric activity of the femoral and obturator nerves. This may be one cause for the abnormal posture--hip flexion and knee extension--of the fetal lower limbs demonstrated in our case. This atypical positioning is not pathognomonic of CRS, since it can also be a normal finding or found in other congenital syndromes. However, hip flexion and knee extension are highly suggestive of CRS when found in the setting of lower limb atrophy and underdevelopment (Figs. 1, 2, and 5). Girth of the extremities should be compared, particularly the relative muscle mass surrounding the fibula/tibia and that surrounding the radius/ulna.

The majority of children afflicted by CRS have deficits in their lower extremities only; 40% are weak and 86% have abnormal deep tendon reflexes (8). In the child we present, hypotonia and leg weakness were evident after delivery. As predicted by the prenatal imaging, the lower extremities were disproportionately underdeveloped and hypotonic compared to the normal girth and tone of the upper extremities. Other pertinent neurologic manifestations on the postnatal examination included absence of the toe grasp and plantar reflexes and normal upper extremity reflexes, including moro, grasp, and suck.

US findings of an abrupt cord termination and diminished tone of lower limbs might suggest other diagnoses including neural tube defects, sirenomelia, sacrococcygeal teratoma, or arthrogryposis-akinesia (2, 9). Neural tube defects such as myelomeningocele are almost invariably associated with Chiari type 2 malformation (10). On US, antenatal diagnostic clues include an open neural arch and flared laminae, a protruding myelomeningocele sac, and intracranial signs of Chiari 2. The lethal condition of sirenomelia can also be diagnosed on prenatal sonography by presence of a single lower extremity, oligohydramnios, and renal agenesis (2). The presence of a sacrococcygeal mass without sacral agenesis would suggest the diagnosis of teratoma (3). Sonography in this case showed none of these findings.

Arthrogryposis-akinesia represents a complex of multiple different etiologies leading to absent fetal movement. In utero, it could be difficult to differentiate arthrogryposis-akinesia from a mild case of CRS, since either could present with signs of decreased extremity motion, intrauterine growth retardation, and flexion-extension contracture (9, 11). However, in arthrogryposis-akinesia the spinal column is normal (2).

The prognosis for children with CRS largely depends on the severity of vertebral anomalies and associated malformations (1, 8). The best prognosis is associated with unilateral or partial bilateral sacral agenesis. A stable midline spinal column provides sacroiliac stability and a greater likelihood of ambulation, especially with orthopedic intervention. The prognosis is poor for patients with total sacral agenesis, since associated musculoskeletal, respiratory, cardiac, gastrointestinal, and genitourinary malformations predispose to early neonatal death. Intrauterine intervention does not exist, and postnatal treatment is mainly supportive.

In conclusion, imaging professionals must be cognizant of CRS and carefully investigate the lower spine, conus medullaris, and lower-extremity muscle girth when they encounter fetal malposition. Early recognition is important because the imaging specialist may be the first to suggest the in utero diagnosis of CRS to the obstetrical care provider. Familiarity with the range of imaging findings, which may vary depending on the severity of sacral agenesis, is critical for timely prenatal counseling, appropriate management of delivery, and effective postnatal treatment.

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