

Caudal regression syndrome type 2 associated with tethered cord: review of magnetic resonance images. A case report

Síndrome de regresión caudal tipo 2 asociado a médula anclada: revisión de las imágenes en resonancia magnética. Presentación de caso

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Summary

Caudal regression syndrome, also known as caudal dysplasia sequence, is a rare severe congenital anomaly characterized by variable extension agenesis of the distal vertebral bodies (sacrococcygeal or lumbosacrococcygeal), which is frequently associated with other musculoskeletal malformations of the pelvis and lower extremities; neurological, orthopedic, gastrointestinal, genitourinary and cardiac abnormalities have also been described. In the evaluation of caudal regression syndrome, magnetic resonance imaging MRI) allows an adequate diagnosis not only of congenital anomalies of the spinal cord and spine, but also of most associated anomalies in the pelvic region. We present the case of a 1-year-old male with MRI of caudal regression syndrome type 2, tethered spinal cord, intradural lipoma, presence of butterfly vertebrae, hemivertebrae and duplication. This article describes the imaging findings of caudal regression syndrome as well as the differences in its classification.

Resumen

El síndrome de regresión caudal, también conocido como secuencia de regresión caudal o displasia caudal, es una anomalía congénita severa poco frecuente, caracterizada por la agenesia de extensión variable de los cuerpos vertebrales distales (sacrococcígeos o lumbosacrococcígeos), que se asocia frecuentemente a otras malformaciones musculoesqueléticas de la pelvis y extremidades inferiores; también se han descrito anormalidades neurológicas, ortopédicas, gastrointestinales, genitourinarias y cardiacas. En la evaluación del síndrome de regresión caudal, la resonancia magnética (RM) permite un diagnóstico adecuado no solo de las anomalías congénitas de la médula espinal y la columna, sino también de la mayoría de las anomalías asociadas en la región pélvica. Se presenta el caso de un niño de un año con imagen por RM de síndrome de regresión caudal tipo 2, médula anclada, lipoma intradural, vértebras en mariposa, hemivértebras y duplicación. En este artículo se describen los hallazgos por imagen del síndrome de regresión caudal, así como las diferencias en su clasificación.

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Introduction

The term *caudal regression syndrome* (CRS) was first used by Bernard Duhamel in 1961, who described this syndrome as a spectrum of congenital defects involving varying degrees of musculoskeletal abnormalities of the lumbosacral spine, pelvis, and lower extremities, as well as alterations of the neurological, genitourinary, gastrointestinal, and cardiac systems. Within the spectrum defined by CRS, it is possible to find a variety of malformations ranging from imperforate anus, sacral agenesis, and absence of lumbar and thoracic vertebrae to the most severe cases, which are malformations of major organs and fusion of the lower extremities, a defect known as sirenomyelia (1).

The etiology of this syndrome is still unclear, but it is believed to be caused by a defect in the induction of the caudal primordia of the embryo before the fourth week of gestation (2).

To understand the embryological alterations that lead to CRS, it is essential to analyze the processes of primary and secondary neurulation, as well as neuronal migration.

Primary neurulation is the process by which the neural plate folds and closes to form the neural tube,

the precursor to the central nervous system. This process occurs during the first weeks of gestation and is essential for the proper development of the brain and spinal cord. Abnormalities in primary neurulation can result in neural tube defects, such as spina bifida. However, CRS is not generally associated with neural tube closure defects, suggesting that alterations in primary neurulation are not the primary cause of this syndrome (3).

Secondary neurulation is the process that forms the caudal portion of the spinal cord from a structure called the caudal eminence. This process involves the condensation, cavitation, and fusion of mesenchymal cells to form the caudal neural tube. Alterations in secondary neurulation can lead to malformations in the caudal structures characteristic of CRS. For example, hypoplasia or agenesis of the sacrum and lower lumbar vertebrae can result from defective secondary neurulation (3).

Neuronal migration is the process by which newly formed neurons move from their place of origin to their final location in the brain and spinal cord. Although neuronal migration disorders are often associated with cortical abnormalities and epilepsy, no direct link has been established between abnormal neuronal migration and CRS. The main abnormalities in CRS are related to defects in the formation of caudal structures during secondary neurulation, rather than to problems with neuronal migration (3).

CRS is frequently associated with pregestational maternal diabetes, suggesting that elevated glucose levels and other metabolic problems related to diabetes may have a detrimental effect on fetal development. However, CRS can also occur in the absence of maternal diabetes, indicating that other genetic and environmental factors also play a role in its etiology, such as genetic susceptibility and vascular hypoperfusion (4).

Regarding exposure to medications during pregnancy, the available medical literature does not provide conclusive evidence linking specific drugs, such as sulfonamides or minoxidil, to the development of CRS. Although some studies have suggested possible associations between certain medications and congenital malformations, a direct relationship with CRS has not been established (5). It is important to note that most research focuses on maternal diabetes and genetic factors as the main contributors to CRS.

The incidence of this syndrome is approximately 0.01 to 0.05 per 1,000 births, with a male-to-female ratio of 2.7:1. This anomaly is not believed to be hereditary, and in 16% of these children, the mothers were diabetic during pregnancy, resulting in an incidence 200 times higher than in the general population (2, 6, 7).

Case report

One-year-old boy born to a 32-year-old mother, G3P1C2, with early prenatal checkups, documented with single umbilical artery, clubfoot, and type 1 fetal growth restriction. At 24 weeks, she was diagnosed with gestational diabetes. Amniocentesis in the third trimester documented a 46XY karyotype without alterations. Born at 36.3 weeks; physical examination revealed asymmetrical auricles, single umbilical artery, sacral alterations (fosset), imperforate anus, asymmetrical limbs, and bilateral clubfoot. Magnetic resonance imaging (MRI) of the brain and neuroaxis documented partial absence of the sacrum and total absence of the coccyx in relation to type 2 caudal regression syndrome, tethered cord, and intradural lipoma (Figure 1), butterfly vertebrae at T4, T6, and T8, two hemivertebrae caudal to the T11 vertebral body (partial vertebral duplication, supernumerary or additional vertebrae in the dorsal region) and below these, the T12 vertebral body and lumbar region (Figure 2) with dilation of the central canal of the spinal cord (Figure 3). As an additional finding, right renal agenesis and hepatomegaly were documented.

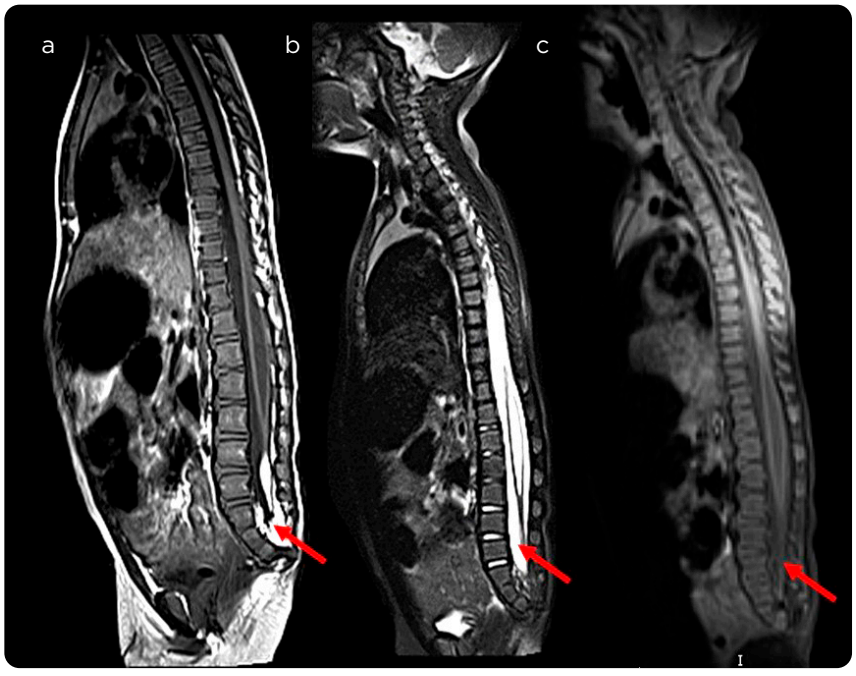


Figure 1. MRI, sagittal images. a) Sequences with T1 information; b) with T2 information; and c) T1 with fat saturation. High signal image (arrow) showing signal loss in fat suppression sequences related to lipoma, located at L4-S1, in the intradural extramedullary space attached to the conus medullaris, which retracts toward the dorsal region.

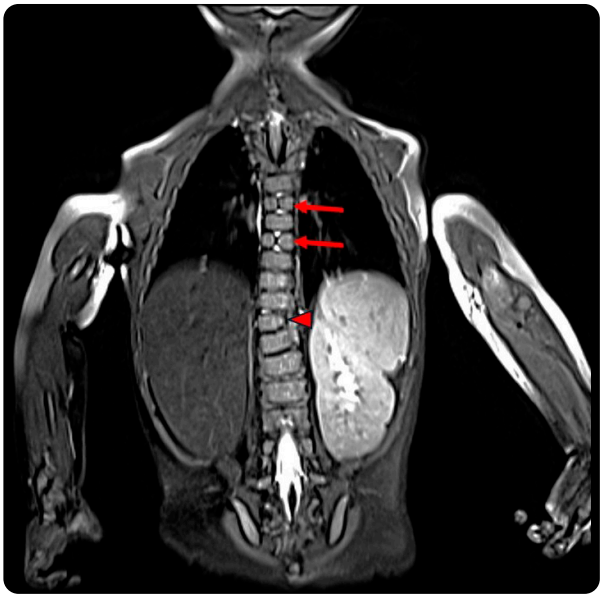


Figure 2. MRI, coronal image, T2-weighted with fat saturation (FS). Failure of fusion (butterfly vertebra) of the lateral halves of the T6 and T8 vertebral bodies (arrows), as well as lack of formation (hemivertebra) of the lateral portion of the vertebral body (supernumerary T11) (arrowhead).

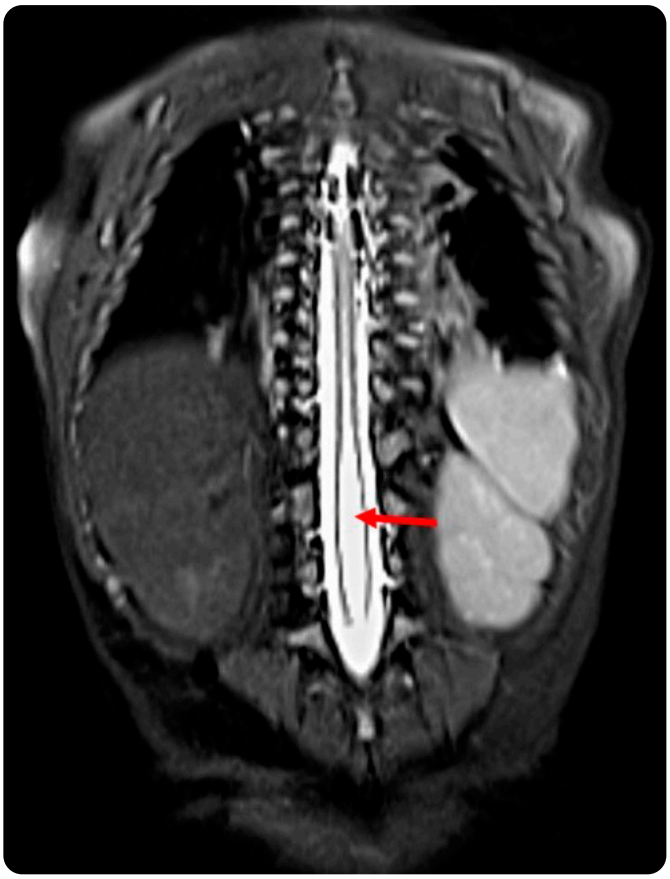


Figure 3. MRI, coronal T2-FS-weighted image. Fluid accumulation and dilation of the ependymal canal (hydroencephalus) within the spinal cord (arrow).

Discussion

The most characteristic MRI finding in CRS is caudal vertebral agenesis and alterations in the conus medullaris and *filum terminale* (2).

The images allow two large groups of CRS patients to be differentiated:

Type 1 is characterized by a blunt conus medullaris that ends above the normal level (lower edge of the first lumbar vertebra or L1) and the nerve roots are arranged in anterior and posterior bundles below this level. Occasionally, there is an associated dilated central canal or a cyst filled with cerebrospinal fluid at the lower end of the cone; these patients have significant sacral deformities (8).

Type 2 presents with an elongated spinal cord cone held in place by a thickened *filum terminale* that ends below the normal level (caudal to the lower edge of L1). The spinal cord is anchored due to associated neural tube defects, such as lipomyelomeningocele, terminal myelocystocele, diastematomyelia, or intraspinal lipoma. Associated spinal cord abnormalities, such as thickening of the *filum terminale*, fatty infiltration of the filum, and spinal cord lipoma, are common and should be accurately noted in radiological reports for appropriate treatment (9).

A thickening of the *filum terminale* refers to a filum measuring more than 2 mm in diameter. An associated syringomyelia may be present, which is more likely in group 2 CRS, but may also be seen in group 1 CRS. This could be due to syringomyelia (abnormal fluid-filled cyst within the spinal cord) or hydromyelia (isolated dilation of the ependymal canal), although these cannot always be definitively differentiated on MRI. Associated dural narrowing and stenosis may occur in any of the groups (8) and are associated with more severe neurological abnormalities (8).

According to Renshaw's classification, sacral agenesis has been divided into four subtypes according to the extent of spinal agenesis without considering the associated spinal cord defect. This is based on the extent of sacral agenesis and the pattern of articulation between the pelvis and the remaining spine.

Type 1 refers to unilateral partial sacral agenesis or isolated coccygeal agenesis. The iliac bones articulate normally with the remaining sacrum (10).

Type 2 refers to bilateral involvement with partial sacral agenesis. The iliac bones articulate with the first sacral vertebra or the remaining sacrum (10).

Type 3 refers to complete sacral agenesis, and the iliac bones articulate with the lowest available lumbar vertebra.

Type 4 refers to complete sacral agenesis where the iliac bones fuse together posteriorly in the midline (10).

The importance of Renshaw's classification is to determine prognosis and plan orthopedic treatment. Renshaw types 1 and 2 are usually treated with non-surgical physical therapy, while Renshaw types 3 and 4 are prone to developing progressive kyphoscoliosis and may require surgical spinal stabilization (10).

The diagnosis of CRS by prenatal ultrasound is possible at the end of the first trimester, despite difficulties due to incomplete ossification of the sacrum at that time. Inadequate cranio-caudal length, which may be the first sign of CRS, and an abnormal appearance of the yolk sac have been proposed as early ultrasound features. At a later stage, ultrasound findings include an abrupt interruption of the spine in its thoracic, lumbar, or sacral segment with the femurs fixed in a charac-

teristic "V" pattern due to external rotation of the hip joints ("Buddha posture") (11).

Plain radiography and computed tomography (CT) of the spine more readily determine bone abnormalities; however, MRI effectively shows the levels of vertebral agenesis and neural tube abnormalities. It is necessary in all cases to assess spinal cord involvement and provide more detailed evidence of the status of intra- and extradural lesions, as well as concomitant anomalies in patients with CRS, in order to guide further treatment.

References

1. Luque H, Fernández R, Tuca M, Luco M, De Barbieri F, Tapia J. Síndrome de regresión caudal. Caso clínico. Rev chil pediatr. 2010;81(2). https://doi.org/10.4067/s0370-41062010000200007
2. Zepeda TJ, García MM, Morales SJ, Pantoja HM, Espinoza GA. Secuencia de regresión caudal: caso clínico-radiológico. Rev chil pediatr. 2015;86(6):430-5. https://doi.org/10.1016/j.rchipe.2015.07.021
3. Trapp B, Freddi TAL, Hans MOM, Calixto LFT, Fujino E, Rojas LCA, et al. A practical approach to diagnosis of spinal dysraphism. Radiographics. 2021;41(2):559-75. https://doi.org/10.1148/rg.2021200103
4. Krishnan V, Jaganathan S, Jayappa S, et al. Clinical and radiological evaluation of caudal regression syndrome. Pediatr Radiol. 2024;54(9):1451-61. https://doi.org/10.1007/s00247-024-05945-1
5. Rojansky N, Fasouliotis SJ, Ariel I, Nadjari M. Extreme caudal agenesis. Possible drug-related etiology? J Reprod Med. 2002;47(3):241-5.
6. Nievelstein RA, Valk J, Smit LM, Vermeij-Keers C. MR of the caudal regression syndrome: embryologic implications. Am J Neuroradiol. 1994;15(6):1021-9.
7. Singh SK, Singh RD, Sharma A. Caudal regression síndrome, case report and review of literature. Ped Surgery Int. 2005;21:578-81. https://doi.org/10.1007/s00383-005-1451-4
8. Unsinn KM, Geley T, Freund MC, Gassner I. US of the spinal cord in newborns: Spectrum of normal findings, variants, congenital anomalies, and acquired diseases. RadioGraphics. 2000;20(4):923-38. https://doi.org/10.1148/radiographics.20.4.g00jl06923
9. Boruah DK, Dhingani D, Achar S, Prakash A, Augustine A, Sanyal S, et al. Magnetic resonance imaging analysis of caudal regression syndrome and concomitant anomalies in pediatric patients. J Clin Imaging Sci. 2016;6:36. https://doi.org/10.4103/2156-7514.190892
10. Diel J, Ortiz O, Losada RA, Price DB, Hayt MW, Katz DS. The sacrum: pathologic spectrum, multimodality imaging, and subspecialty approach. Radiographics. 2001;21(1):83-104. https://doi.org/|10.1148/radiographics.21.1.g01ja0883
11. Baxi L, Warren W, Collins MH, Timor-Tritsch IE. Early detection of caudal regression syndrome with transvaginal scanning. Obstet Gynecol. 1990;75(3 Pt 2):486-9.

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