Magnetic Resonance Imaging Analysis of Caudal Regression Syndrome and Concomitant Anomalies in Pediatric Patients

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ABSTRACT

Objective: The aim of this study was to evaluate the magnetic resonance imaging (MRI) findings of caudal regression syndrome (CRS) and concomitant anomalies in pediatric patients. Materials and Methods: A hospital-based cross-sectional retrospective study was conducted. The study group comprised 21 pediatric patients presenting to the Departments of Radiodiagnosis and Pediatric Surgery in a tertiary care hospital from May 2011 to April 2016. All patients were initially evaluated clinically followed by MRI. Results: In our study, 21 pediatric patients were diagnosed with sacral agenesis/dysgenesis related to CRS. According to the Pang’s classification, 2 (9.5%) patients were Type I, 5 (23.8%) patients were Type III, 7 (33.3%) patients were Type IV, and 7 (33.3%) patients were of Type V CRS. Clinically, 17 (81%) patients presented with urinary incontinence, 6 (28.6%) with fecal incontinence, 9 patients (42.9%) had poor gluteal musculatures and shallow intergluteal cleft, 7 (33.3%) patients had associated subcutaneous mass over spine, and 6 (28.6%) patients presented with distal leg muscle atrophy. MRI showed wedge-shaped conus termination in 5 (23.8%) patients and bulbous conus termination in 3 (14.3%) patients above the L1 vertebral level falling into Group 1 CRS while 7 (33.3%) patients had tethered cord and 6 (28.6%) patients had stretched conus falling into Group 2 CRS. Conclusion: MRI is the ideal modality for detailed evaluation of the status of the vertebra, spinal cord, intra- and extra-dural lesions and helps in early diagnosis, detailed preoperative MRI evaluation and assessing concomitant anomalies and guiding further management with early institution of treatment to maximize recovery. Key words: Lipomeningomyelocele, magnetic resonance imaging, sacral agenesis, tethered cord

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INTRODUCTION

Caudal regression syndrome (CRS) is a rare congenital abnormality, in which a segment of the lumbar, lumbosacral, or coccygeal spinal agenesis or dysgenesis occurs in association with an abnormality in spinal cord and nerve roots.\(^1\) In CRS, spectrum lumbosacral agenesis lies at the one end, and partial coccygeal agenesis lies at the other extreme of the spectrum. Various genitourinary, anorectal, Mullerian-duct, cardiovascular, orthopedic, and other spinal anomalies have been associated with CRS.

The progressive neurological deficits associated with CRS patients can be corrected with early diagnosis, detailed preoperative magnetic resonance imaging (MRI) evaluation of spine, spinal cord status and associated anomalies with early institution of treatment help in early recovery, especially in Pang Group 2 CRS patients.

It has been recognized that the degree of vertebral agenesis does not always correspond to the severity of coexisting genito-urinary, anorectal, and other neurogenic anomalies; hence, active search for other associated anomalies even in cases with mild degree of sacral agenesis is important by detailed MR evaluation as early correction of such anomalies might have profound effect on the clinical outcome of these patients.

The aim of this study was to evaluate the MRI findings in CRS and concomitant anomalies in pediatric patients.

MATERIALS AND METHODS

After approval from the Institutional Ethics Review Committee, a hospital-based cross-sectional retrospective study was conducted. The study group comprised 21 pediatric patients presenting to the Departments of Radiodiagnosis and Pediatric Surgery in a tertiary care hospital from May 2011 to April 2016.

Patient selection

We included both outpatients and inpatients up to the age of 16 years of both genders presenting with urinary, bowel, and spinal problems related to congenital or neuromuscular conditions. We have included only those children in whom imaging studies were performed. Children in whom imaging studies were not done were excluded from the study. Informed consent was obtained from parents/guardian before undergoing MRI scan.

Magnetic resonance imaging protocols

All patients were subjected to MRI scan using Siemens Avanto 1.5 Tesla B15 machine (Siemens Medical Systems, Erlangen, Germany). MRI of the spine was performed in sagittal, coronal, and axial planes using a combination of pulse sequences. MRI was performed with the patient in supine position with or without sedation under the guidance of anesthetist. Sagittal T2- and T1-weighted spin-echo images, sagittal short-tau inversion recovery (STIR), coronal STIR, and axial T2-, T1-weighted fast spin-echo images of the lumbosacral spine and pelvic regions were obtained routinely. Additional gradient-recalled echo (GRE) images were obtained in the sagittal plane in all patients for more detailed evaluation of vertebral defects or anomalies.

Sagittal spin-echo T1-weighted images (T1WIs) were acquired with 450–500/9–15 (repetition time/echo time). Sagittal T2-weighted images (T2WIs) were acquired with 4000–4600/110–120 (repetition time/echo time). All sagittal and coronal images were obtained with 3 mm slice thickness. Sagittal and coronal fat suppression sequences were employed on the long TR sequences. Sagittal GRE images were obtained with 650–750/24–32 (repetition time/echo time) with a flip angle of 24°–28°. Screening of brain was done in all patients.

Evaluation

Twenty-one CRS pediatric patients were examined to study the presence of congenital anomalies concomitant with CRS. The following conditions were given close attention: A family history of maternal diabetes mellitus, any medication used during pregnancy, a history of genetic illness, pediatric anorectal malformation, cleft mouth, diaphragm hernia, anomalies in the urinary, cardiovascular and respiratory systems, sirenomelia, spinal deformities such as lumbar, sacral, coccygeal partial or total agenesis/hypoplasia, or hip dysplasia.

On MRI, we evaluated type of CRS according to the Pang’s classification, level of conus termination, shape of conus, causes of cord tethering or cord stretching, level of termination of thecal sac, height of syrinx formation in spinal cord according to vertebral height, vertebral segmentation defects, last present vertebra, anorectal malformation, or other associated anomalies. The presence of neurogenic bladder and hydroureteronephrosis was also evaluated.

Statistical analysis

Data were presented in terms of percentage and mean value. Calculations were done using Microsoft Excel.

RESULTS

In our study, 21 pediatric patients were diagnosed with sacral agenesis/dysgenesis related to CRS. Age of presentation varied from 3 days to 16 years with the
mean age of 5.36 year. Male: female sex ratio was 1:3.2. Mother of Pang Type I patients was diabetic. Clinically, 17 (81%) patients presented with urinary incontinence, 6 (28.6%) with fecal incontinence, 9 patients (42.9%) had poor gluteal musculatures and shallow intergluteal cleft, 7 (33.3%) patients had associated subcutaneous mass over spine, 5 (23.8%) patients had skin dimple over back, and 6 (28.6%) patients presented with distal leg muscle atrophy. According to the Pang’s classification, 2 (9.5%) patients were defined as Type I, 5 (23.8%) patients were Type III, 7 (33.3%) patients were Type IV (5 were Type IVb and 2 were Type IVc), and 7 (33.3%) patients were defined as Type V CRS. According to conus termination, CRS patients were categorized into Groups I and II. MRI showed wedge-shaped conus termination in 5 (23.8%) patients [Figure 1] and bulbous conus termination in 3 (14.3%) patients [Figure 2] above the L1 vertebral level falling into Group 1 CRS while 7 (33.3%) patients had tethered cord and 6 (28.6%) patients had stretched conus falling into Group 2 CRS. The cause of tethered spinal cord in Group 2 CRS patients in our study was due to lipomeningomyelocele (Lipo-MM) [Figure 3] in 4 (19%) patients, intraspinal lipoma in 2 (9.5%) patients, and 1 (4.8%) patient had terminal cistocoele. Syrinx formation noted in 7 (33.3%) patients of Group 2 CRS, whereas 3 (14.3%) patients had syrinx <3 vertebral height and another 3 (14.3%) patients had >6 vertebral height.

Table 1 shows the MRI findings in CRS patients with concomitant spinal anomalies.

Concomitant spinal or other system anomalies/conditions were demonstrated in our study as follows:

**Genitourinary**
Seventeen (81%) patients had a neurogenic bladder, 5 (23.8%) patients had bilateral hydroureteronephrosis, and 1 (4.8%) had a hypoplastic uterus (Type I Mullerian agenesis) [Figure 4].

**Gastrointestinal**
Nine patients (42.9%) had an imperforated anus, 8 (38.1%) had anorectal stenosis, 1 (4.8%) had anal stenosis, and 2 (9.5%) had a local anomaly [Figure 5], whereas one patient had omphalocele, cloacal extrophy, imperforate anus, and spinal (OEIS) complex [Figure 6].

**Associated other spinal dysraphism**
Four (19%) patients with CRS had LipoMMC (1 had anterior LipoMMC), 4 (19%) had a high termination of thecal sac terminal above L5 vertebra, and 1 (4.8%) patient had a high termination of thecal sac above S1 vertebra. Six (28.6%) patients had tight filum terminale with fatty tissue which stretches the cord. One each of CRS patients had both intra- and extra-dural lipomas, intrasacral lipoma, diastematomyelia, terminal myelocystocele, both cervical intramedullary and intradural extramedullary neuroenteric cysts [Figure 7], and intrasacral meningocele.

**Vertebral anomaly**
Fifteen (71.4%) CRS patients had vertebral segmentation defects, of which 13 (86.7%) patients had spina bifida, 4 (26.7%) had hemivertebra, 5 (33.3%) had butterfly vertebra, 2 (13.3%) had block vertebra, and 1 (6.7%) had reversed sacral curvature.

The present last vertebra in our study was S5 in 8 (38.1%) patients, S4 in 6 (28.6%) patients, S3 in 1 (4.8%) patient, S2 in 4 (19%) patients, and L5 in 2 (9.5%) patients.
Musculoskeletal
Two CRS patients had pubic diastases, and one patient had bilateral congenital talipes equinovarus.

Miscellaneous
One CRS Type III patient had associated T1WI hypo- and T2WI hyper-intense intergluteal cleft cyst [Figure 8]. Brain
screening showed Type II Chiari malformation in a patient of Type III CRS.

DISCUSSION

CRS is an uncommon malformation of the caudal spine and spinal cord malformation. CRS comprises developmental anomalies of the caudal vertebrae, neural tube, urogenital and digestive organs, and hind limbs, the precursors of all of which are derived from the caudal eminence. Its incidence is estimated approximately 0.1–0.25:10,000 of normal pregnancies. The incidence is higher about 1:350 infants of diabetic mothers and which representing an increase of risk about 200 times. The CRS had a male: female ratio of 2.7:1.
The term CRS was first used in 1961 by Duhamel[27] to describe a syndrome incorporating vertebral agenesis of the variable level with urinary and digestive malformations. Pregestational diabetes is undoubtedly a teratogen, and there is good evidence that gestational diabetes can be involved in the development of the most severe form of CRS.[16] The other possible risk factors include genetic susceptibility and vascular hypoperfusion.[9]

The degree of spinal cord aplasia correlates with the severity of the spinal malformation, with a greater degree of vertebral aplasia in Group 1 than in Group 2.[10]

Clinically, most patients with sacral agenesis exhibit poorly developed “rumps” with short, shallow intergluteal clefts and poor gluteal musculature. They show narrow hips, distal leg atrophy, and talipes deformities. Approximately 20% have subcutaneous lesions such as skin-covered lipomeningoceles (6%), terminal myelocystoceles (9%), or limited dorsal myeloschisis (3%).[11] In our study, we encountered 33.3% of patients with CRS had subcutaneous mass.

Various genitourinary, gastrointestinal, musculoskeletal, and cardiothoracic anomalies are associated with caudal spinal agenesis or dysgenesis.

Motor deficits are present and correspond to the level of vertebral agenesis.[12] The sensation is better preserved in CRS patients than somatic motor function.[13,14] The discrepancy between neurological symptoms and the extent of the spinal defect may be due to the persistence of nerve fibers beneath the vertebrae or enhanced capabilities of sensitive ganglions.[15] Urinary and bladder dysfunctions are constant with CRS.[11]

Agenesis of the sacrococcygeal spine may be a part of syndromic complexes such as OEIS,[16] VACTERL (vertebral abnormality, anal imperforation, cardiac anomalies, tracheoesophageal fistula, renal abnormalities, and limb deformities),[16,17] and the Currarino triad (partial sacral agenesis, anorectal malformation, and presacral mass: teratoma and/or meningocele).[9,18,19]

Antenatal ultrasound (USG) diagnosis of CRS is possible at the end of the first trimester;[20] inappropriate crown-rump length may be the first sign of CRS in the first trimester. At a later stage, USG findings include abrupt interruption of the spine at dorsal, lumbar, or sacral level with the femurs fixed in a characteristic “V” pattern due to external rotation of the hip joints (“Buddha’s attitude”).[20,21]

The Pang’s classification of lumbosacral agenesis with five types: where Types I and II represent total sacral agenesis with and without associated lumbar vertebral agenesis; Type III represents subtotal sacral agenesis with at least S1 present; Type IV has a hemisacrum; and Type V includes coccygeal agenesis.[11]

In Group 1 (41%), the conus ends cephalic to the lower border of L1. In Group 1 with high conus, the sacral deficit is typically large, and the sacrum usually ends at or above S1. These patients have a stable neurological defect due to their “fixed” spinal cord dysplasia. In Group 2 (59%), the conus ends lower, below L1, and is elongated, stretched caudally, and tethered. Progressive neurological deterioration is frequent in these patients due to the low-tethered cord.[22] In our study, 8 patients (38.1%) had conus termination above the L1 vertebral level falling into Group 1 while 13 patients (61.9%) had tethered or stretched low-lying conus falling into Group 2.

The dural sac in CRS patient shows nonstenotic tapering and shortening in around 47% cases. The tapering is greater, and the sac ends higher with higher levels of spinal agenesis.[11] In our study, 5 (23.8%) patients had a high termination of the thecal sac.

Even plain radiography and computed tomography of spine more readily determine osseous anomalies, MR effectively depicts the levels of vertebral agenesis, and it also allows exact identification of dysgraphic-dysplastic anomalies in all patients.[10]

Management is primarily directed toward correction of genitourinary and anorectal anomalies with the goals being to preserve renal function, achieve continence, and prevent infection. Surgical untethering, release, or neuroplasty are procedures that may be necessary to improve neurological function in CRS patients.

Limitations
We could not perform MRI in many cases of clinically suspected spinal dysraphism or caudal spinal anomalies due to cost constraints and those patients who were not suitable for sedation by an anesthesiologist.

CONCLUSION
MRI is the ideal modality for detailed evaluation of the status of the vertebra, spinal cord, intra- and extra-dural lesions, and associated concomitant anomalies of pediatric CRS patients and helps in guiding further management of CRS.

In MRI, a thorough search for caudal spinal, anorectal, and genitourinary anomalies should be pursued even with milder vertebral agenesis if patient presents with progressive neurologic deficits.
In our study of 21 pediatric patients diagnosed as CRS, MRI allowed us to see the various concomitant conditions which often occur with CRS.

A better understanding of such coexisting pathologies with the help of MRI will allow us to not only prevent a progressive neurological deficit in relevant cases at an early stage but also focus attention toward the correction of other associated anomalies. Apart from complex intradural and neurogenic anomalies, detection of other genitourinary and anorectal anomalies helps the clinicians to have an overall assessment of the case and its prognosis earlier, decide management, and counsel the family members accordingly.

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Conflicts of interest
There are no conflicts of interest.

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