Original Research Article

Clinical Evaluation of the Condition of Symptomatic Lower Urinary Tract Dysfunction in Sacral Agenesis

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Abstract

From a urologic perspective, SA has an association with neurogenic bladder dysfunction (80%). However, the level of skeletal and spinal bony defect does not necessarily predict the severity or type of lower urinary tract dysfunction. Thus, patients merit formal evaluation, including a neurologic and urodynamic assessment at diagnosis, as such studies guide initial and long-term management. Although more recent reports have provided insight with long-term follow-up in SA patients, little has been reported regarding the stability, or lack thereof, of the neurogenic component of the lower urinary tract and long-term renal function. Hence present study was planned for clinical evaluation of the condition of symptomatic lower urinary tract dysfunction in sacral agenesis.The present study was planned in the Department of UrologyHanumantHospital,Bhavnagar Gujarat and Kurji Holy Family Hospital, Patna, Bihar, India. The study was performed from the Jan 2016 to Dec 2018. Patients with symptomatic isolated Sacral agenesis (SA), those having SA along with other obvious anomalies of caudal regression syndrome, and those with ARM or cloaca without SA were analyzed and compared.The data generated from the present study concludes that Isolated SA is an uncommon cause for neurogenic bladder that often presents late and may result in renal damage. Careful examination and plain radiograph of the spine in children with unexplained lower urinary tract symptoms may enable early identification. Severity of the bony abnormality does not correlate with severity of lower tract abnormalities and once identified, all patients should undergo formal urological and neurological assessment.

Keywords: Symptomatic Lower Urinary Tract Dysfunction, Sacral Agenesis, neurogenic bladder dysfunction, etc.

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Introduction

Caudal regression syndrome, or sacral agenesis (or hypoplasia of the sacrum), is a rare birth defect. It is a congenital disorder in which the fetal development of the lower spine—the caudal partition of the spine—is abnormal.[1] It occurs at a rate of approximately one per 25,000 live births. Some babies are born with very small differences compared to typical development, and others have significant changes. Most grow up to be otherwise normal adults who have difficulty with walking and incontinence.

This condition exists in a variety of forms, ranging from partial absence of the tail bone regions of the spine to absence of the lower vertebrae, pelvis and parts of the thoracic and/or lumbar areas of the spine. In some cases where only a small part of the spine is absent, there may be no outward sign of the condition. In cases where more substantial areas of the spine are absent, there may be fused, webbed or smaller lower extremities and paralysis. Bowel and bladder control is usually affected.

The condition arises from some factor or set of factors present during approximately the 3rd week to 7th week of fetal development. Formation of the sacrum/lower back and corresponding nervous system is usually nearing completion by the 4th week of development. Due to abnormal gastrulation, the mesoderm migration is disturbed. This disturbance results in symptoms varying from minor lesions of the lower vertebrae to more severe symptoms such as complete fusion of the lower limbs. While the exact cause is unknown, it has been speculated that the condition has a combination of environmental and genetic causes, and that various types of the condition may have differing causes.

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Sacral agenesis syndrome (agenesis of the lumbar spine, sacrum, and coccyx, and hypoplasia of the lower extremities) is a well-established congenital anomaly associated with maternal diabetes mellitus (not gestational diabetes). However, other causes are presumably involved, as demonstrated by the rare incidence of caudal regression syndrome (1:60,000) compared to diabetes. The dominant inherited sacral agenesis (also referred to as Currarino syndrome) is very often correlated with a mutation in the Hb9 (also called HlxB9) gene (shown by Sally Ann Lynch, 1995, Nature Genetics). There are four levels (or "types") of malformation. The least severe indicates partial deformation (unilateral) of the sacrum. The second level indicates a bilateral (uniform) deformation. The most severe types involve a total absence of the sacrum.

Depending on the type of sacral agenesis, bowel or urinary bladder deficiencies may be present. A permanent colostomy may be necessary in the case of imperforate anus. Incontinence may also require some type of continence control system (e.g., self-catheterization) be utilized. The condition often impacts the formation of the knees, legs or feet that is sometimes addressed through surgery. For some with tightly webbed, bent knees or knees that are fused straight, disarticulation surgery at the knee may be a viable option to maximize mobility options.

Before more comprehensive medical treatment was available, full amputation of the legs at the hip was often performed. More recently, the 'amputation' (actually a disarticulation because no cutting of the bone is involved) is done at the knee for those who have bent knee positions and webbing between thigh and calf to enable more ease of mobility and better seating. Some children with knee disarticulation use prosthetic legs to walk. Prosthetics for children without substantial hip and trunk control is usually abandoned in favor of faster and easier wheelchair mobility as the child's weight and age increases. Children may 'walk' on their hands and generally are able to climb and move about to accomplish whatever they need and want to accomplish. Children more mildly affected may have normal gait and no need for assistive devices for walking. Others may walk with bracing or crutches. There is typically no cognitive impairment associated with this disability. Adults with this disability live independently, attend college, and have careers in various fields. In 2012, Spencer West, a man with sacral agenesis and both legs amputated, climbed Mt. Kilimanjaro using only his hands.[2]

The term myelodysplasia includes a group of developmental anomalies that result from defects that occur during neural tube closure. Lesions may include spina bifida occulta, meningocele, lipo myelomeningocele, or myelomeningocele. Myelomeningocele is by far the most common defect seen and is the most devastating. This article focuses on identifying neurogenic bladder dysfunction, defining treatment options, and outlining follow-up care in children with myelodysplasia.Spinal cord and vertebra formation begin at approximately 18 days' gestation. Closure of the spinal canal begins at the cephalad end, proceeds caudally, and is complete by 35 days' gestation. The exact cause of neurospinaldysraphism is unknown, but it appears to be multifactorial. Genetic, environmental, and nutritional factors have been implicated; however, no specific etiology has been pinpointed.

An increased frequency of neural tube defects appears to occur in the offspring of mothers who had folic acid deficiency during pregnancy. Based on these data, the current recommended daily allowance (RDA) of 400 µg/day of folic acid was established for women during pregnancy.Spina bifida is a broad term that may be used to describe a number of open defects of the spinal column. A meningocele occurs when the meningeal sac (the sac that envelops the spinal cord) extends beyond the confines of the vertebral canal but does not contain any neural elements. A myelomeningocele occurs when neural tissue (nerve roots, spinal cord tissue, or both) is included in the sac. A lipomyelomeningocele is defined by the presence of fatty tissue and neural elements within the sac.

Myelomeningoceles account for 90% of open spinal dysraphic states. The overwhelming majority of myelomeningoceles are directed posteriorly, with most defects involving the lumbar vertebrae. In decreasing order of frequency, sacral, thoracic, and cervical vertebrae are affected. In the rare case of an anteriorly directed defect, the sacral vertebrae are most commonly involved.An Arnold-Chiari malformation is associated in 65-85% of children with a myelomeningocele. [3] This occurs when the cerebellar tonsils herniate through the foramen magnum and obstruct the fourth ventricle, which prevents cerebrospinal fluid (CSF) from entering the subarachnoid space. These children require shunting of the ventricles, most commonly to the peritoneum. A small number (~5%) of patients with myelomeningoceles do not have a neurogenic bladder, but this is the exception.

Congenital defects of spinal column formation that are not open defects are often termed spina bifida occulta. The lesions can be subtle, often with no obvious signs of motor or sensory denervation; however, in many patients, a cutaneous abnormality can be seen overlying the lower spine. This can vary from a dimple or a skin tag to a tuft of hair, a dermal vascular malformation, or an obvious subdermal lipoma.Alterations may be found in the arrangement or configuration of the toes, along with discrepancies in lower extremity muscle size and strength, weakness, or abnormal gait. Back pain and an absence of perineal sensation are common symptoms in older children. The frequency of abnormal lower urinary tract function in patients with spina bifida occulta has been reported to be as high as 40%.

Sacral agenesis, defined as the absence of two or more lower vertebral bodies, is another defect that can produce voiding dysfunction. Because perineal sensation is usually intact and lower-extremity function is normal, the only clue is often a flattened buttock and a short gluteal cleft. However, in many patients, no external signs are evident. If suspected, diagnosis is made using a lateral film of the lower spine. Even at best, only 50% of affected infants are identified in the newborn period.The neurologic lesion produced by the dysraphism can vary widely, depending on the neural elements that have everted with the meningocele sac. The bony vertebral level correlates poorly with the neurologic lesion produced.Additionally, different growth rates between the vertebral bodies and the elongating spinal cord can introduce a dynamic factor to the lesion. Fibrosis may surround the cord at the site of meningocele closure, and the cord can become tethered during growth. This can lead to changes in bowel, bladder, and lower-extremity function. If these are noted, investigation is warranted to exclude cord tethering.

From a urologic perspective, SA has an association with neurogenic bladder dysfunction (80%) [4]. However, the level of skeletal and spinal bony defect does not necessarily predict the severity or type of lower urinary tract dysfunction [5]. Thus, patients merit formal evaluation, including a neurologic and urodynamic assessment at diagnosis, as such studies guide initial and long-term management [6]. Although more recent reports have provided insight with long-term follow-up in SA patients [6-10], little has been reported regarding the stability, or lack thereof, of the neurogenic component of the lower urinary tract and long-term renal function.Hence present study was planned for clinical evaluation of the condition of symptomatic lower urinary tract dysfunction in sacral agenesis.

Methodology

The present study was planned in the Department of UrologyHanumant Hospital ,Bhavnagar, Gujarat and Kurji Holy Family Hospital, Patna, Bihar, India. The study was performed from the Jan 2016 to Dec 2018. Patients with symptomatic isolated Sacral agenesis (SA), those having SA along with other obvious anomalies of caudal regression syndrome, and those with ARM or cloaca without SA were analyzed and compared.

Group A: Patients with symptomatic isolated Sacral agenesis (SA),

Group B: Patients having SA along with other obvious anomalies of caudal regression syndrome

Group C:Patients with ARM or cloaca without SA

All the patients were informed and consents taken. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

Despite earlier diagnosis of many patients with SA, a significant proportion is detected later in childhood – near or after the time of expected toilet training. This may be related to subtle physical signs noted only on a careful history and/or physical examination, including, in some, delays in toilet training.

Urodynamic testing is a key component to the evaluation and identification of the neurogenic bladder lesion associated with SA. These studies can comprehensively assess lower urinary tract function or dysfunction, and in these instances provide insight and help guide management toward maintaining low-pressure safe storage bladders with adequate compliance to preserve the upper urinary tract. For example, this data may help determine if a patient's current bladder management is appropriate. This information can guide treatment – whether to adjust medical management or prompt consideration for surgical intervention. The present institutional experience has been limited by the amount of available serial UDS, due to deferred or missing documentation, and varied practice patterns among healthcare teams. For patients diagnosed with SA at the present institution, UDS is performed to establish a baseline and then at intervals based on changes in clinical picture.

Table 1: Description of patients

Group	Group A	Group B	Group C
Description	Patients with symptomatic isolated Sacral agenesis (SA)	Patients having SA along with other obvious anomalies of caudal regression syndrome	Patients with ARM or cloaca without SA
No. of Cases	6	6	4
Age in years	8 -19	5 – 20	0 - 4
Compliance (ml/ Cm H2O)	4 – 15	2 -12	3 – 24
Compliance reduced <12.5ml/cm H2O(Cases)	7	3	6
Detrusor overactivity (Cases)	5	4	2
End-fill pressure cm H2O	11 – 28	21 – 25	7 – 38

Most patients with SA had abnormality of bladder storage and combined with the late presentation resulted in a high prevalence of hydronephrosis. There was a high prevalence of secondary reflux in these. Secondary reflux might have caused underestimation of the pressures and the actual compliance might have been worse than observed. Voiding phase abnormality was noted in a majority of children with detrusor muscle weakness the commonest cause. Given these facts, antimuscarinics with clean intermittent catheterization is likely to be the mainstay of care. Similar to children with spinal dysraphism and ARM, follow-up UDS is likely to be crucial for the evaluation of response and identification of nonresponders for escalation of treatment. For those with refractory storage pressures, the high prevalence of poor compliance could be a potential marker for a less than optimal response to salvage intravesicalbotulinum toxin A injections.[11]

Sacral agenesis (SA) is a rare and severe sacral developmental abnormality. [12] It has been defined as the absence of part or all of two or more lower vertebral bodies. Insulin-dependent diabetes in the mother has been shown to be associated with sacral agenesis but in most of the cases cause is uncertain. [13] The presentation is usually bimodal, with more than three fourths presents in early infancy and the remainder discovered between 4 and 5years of age. [13] Sacral agenesis may also be associated with abnormal development in other organs such as the anus/rectum, the bones and joints of the leg and spine.[14] When these all occur together, this is referred to as Caudal Regression syndrome. [15] Familial cases of sacral agenesis are seen to be associated with the Currarino syndrome (presacral mass, sacral agenesis, and anorectal malformation). [16]

Nerves from the spinal cord pass through a bony canal within the sacrum and exit to supply the bowel, anus, bladder, and to the muscles and sensory organs in the lower limbs. Due to absence of two or more bony segment of sacrum, this agenesis leads to injury to these nerve fibres. [17]

Conclusion

The data generated from the present study concludes that Isolated SA is an uncommon cause for neurogenic bladder that often presents late and may result in renal damage. Careful examination and plain radiograph of the spine in children with unexplained lower urinary tract symptoms may enable early identification. Severity of the bony abnormality does not correlate with severity of lower tract abnormalities and once identified, all patients should undergo formal urological and neurological assessment.

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