Currarino syndrome and spinal dysraphism

Case report

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Currarino syndrome is a rare constellation of congenital anomalies characterized by the triad of sacral dysgenesis, presacral mass, and anorectal malformation. It is frequently associated with other congenital anomalies, often including occult spinal dysraphism. Mutations in the MNX1 gene are identified in the majority of cases. The authors report a rare case of Currarino syndrome in an infant with tethered cord syndrome and a dorsal lipomyelomeningocele continuous with a presacral intradural spinal lipoma, in addition to an imperforate anus and a scimitar sacrum. They review the literature to highlight patterns of occult spinal dysraphism in patients with Currarino syndrome and their relationship to tethered cord syndrome. Approximately 60% of the patients with Currarino syndrome reported in the literature have an occult spinal dysraphism. Published studies suggest that the risk of tethered cord syndrome may be higher among patients with a lipoma and lower among those with a teratoma or anterior meningocele.

(Currarino, 2014)

KEY WORDS • Currarino syndrome • lipomyelomeningocele • dysraphism • spina bifida occulta • tethered cord syndrome • congenital

Currarino syndrome, historically known as “Currarino’s triad,” is a rare constellation of congenital anomalies characterized by sacral dysgenesis, presacral mass, and anorectal malformation. Approximately 300 cases have been documented in the literature. Occult neural tube defects are commonly observed in affected patients, although the frequency of this association is unclear. The presacral mass may be a benign or malignant teratoma, a dysraphic lesion such as an anterior meningocele, an intradural spinal lipoma, or a combination. Renal, ureteral, and uterine anomalies have also been described. Because of the broad constellation of anomalies that may be associated with the core clinical triad, the term “Currarino syndrome” is preferred.

There is significant variability in the severity of each anomaly, which is reflected in a wide range of clinical symptoms and ages at diagnosis. Patients with severe anorectal malformations such as imperforate anus typically present at birth, whereas patients with an occult dysraphism and tethered cord syndrome may present as toddlers with neurogenic bladder, frequent urinary tract infections, weakness, sensory loss, and deformity of the lower extremities. Bacterial meningitis in the context of fistula formation between the ventral thecal sac and bladder or colon has also been reported. Older patients with a mild phenotype may present with chronic constipation or scoliosis due to sacral dysgenesis in late childhood or as adults.

Features of this syndrome were noted as early as 1837, but it was not until the 1981 report by Currarino et al. that the clinical triad was defined as a syndrome that could occur from a single embryological process. Early hypotheses suggested that an aberrant association between the endoderm and notochord led to incomplete fusion of vertebral elements, resulting in sacral dysgenesis and dysraphism. Gegg and colleagues noted that many anomalies associated with Currarino syndrome may be explained by an insult during secondary neurulation, during which tail bud formation gives rise to the sacral structures, resulting in sacral dysgenesis and a presacral teratoma adherent to the rectum. Multiple studies report familial cases with autosomal dominant inheritance, and disease-causing mutations in the MNX1 gene have been identified in the majority of cases.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
drome, and there is little detailed information on the associated neurological features and management. We report a rare case of Currarino syndrome associated with a dorsal lipomyelomeningocele continuous with a presacral intradural lipoma, and we review the literature on Currarino syndrome to define patterns of occult dysraphism and their relationship to tethered cord syndrome.25

Case Report

History and Examination. A full-term male neonate with no significant family history had an imperforate anus, talipes equinovarus of the right foot, and a right dorsal lumbar soft tissue mass just above the gluteal crease. Neurological examination revealed decreased sensation and weakness in the right ankle and foot, as well as diminished sacral sensation. Magnetic resonance imaging of the lumbosacral spine demonstrated partial sacral agenesis with a scimitar appearance, a presacral mass consistent with a lipoma and continuous with a dorsal lipomyelomeningocele, as well as syringomyelia and a low-lying conus medullaris terminating at the lumbosacral junction. Alpha-fetoprotein (AFP) levels were within the normal range for a neonate.

A diverting colostomy was performed by pediatric surgeons. A voiding cystourethrogram when the infant was 2 weeks of age demonstrated a neurogenic bladder. His neurological examination was stable at 10 weeks of age, serum AFP remained normal, and MRI of the lumbosacral spine showed a stable appearance of the presacral mass (Fig. 1). Multiple vertebral anomalies were also evident. Chromosomal microarray analysis identified copy number loss within chromosomal band 13q12.11; however, no copy number changes in the region of MNXI (7q36) were found. Detailed sequencing and mutational analysis of MNXI was not performed.

Operation. At 3 months of age, the patient underwent anorectoplasty, followed by laminecctomy, tethered cord release, subtotal resection of the intradural presacral mass, and reconstruction of the ventral thecal sac with neurophysiological monitoring (Fig. 2). The conus medullaris was continuous with the lipomyelomeningocele dorsally and the presacral mass ventrally. Histopathological analysis confirmed the diagnosis of lipoma. Durepair (Medtronic) and Evicel (Johnson & Johnson) were used to reconstruct the ventral thecal sac and isolate it from the residual lipoma. There were no perioperative complications.

Postoperative Course. Six months after surgery, the patient was doing well. The pediatric surgery team performed bowel re-anastomosis, and orthopedic surgeons corrected his right foot talipes deformity. Developmentally, he is not yet ambulating independently, because of right lower extremity weakness, but is otherwise developing appropriately for his age.

Discussion

We report a case of Currarino syndrome with a rare presacral intradural lipoma continuous with a dorsal lipomyelomeningocele. Although the association among Currarino syndrome, occult spinal dysraphism, and tethered cord syndrome has long been recognized, the frequency is unknown, especially as it relates to the type of presacral mass. Despite numerous case reports, very few large series of patients with Currarino syndrome have been reported in the literature,2,5,9,17 and the true incidence of this syndrome is unknown.

Literature Review

We performed a search using PubMed and the search term “Currarino.” We eliminated articles written in languages other than English, as well as articles written by authors named “Currarino” which were not related to the syndrome. We also searched the references of all identified articles for additional sources. We then limited our review to clinical studies reporting at least four cases, revealing 11 studies.2,5,6,14–17,19,21,22,26,27 One group reported an initial series6 that was later updated with additional patients.5

We then completed a data abstraction form for 11 unique studies, recording the total number of patients, the number of patients with a specific type of occult dysraphism (anterior meningocele, presacral tumor, lipoma, or other spinal cord anomaly such as a syrinx, split cord malformation, and so forth), the presence of tethered cord syndrome (no study specifically defined this term), the association of tethered cord syndrome with each type of dysraphism, and the presence of MNXI mutations. We tabulated the results (Table 1) to analyze patterns of occult spinal dysraphism and tethered cord syndrome in patients with Currarino syndrome.

We identified 193 unique cases in these 11 studies, although not all data were reported in some of the studies. Among 171 patients for whom the information was available, 90 (53%) presented with a solid nondysraphic
presacral tumor. Histological analysis of the lesion was reported in 60 patients: 58 of the lesions were teratomas, 1 was a hamartoma, and 1 was a dermoid cyst. The remaining 30 patients each had a presacral solid tumor identified on imaging only. In a series of 17 children with presacral masses from a single center, 11 of whom had Currarino syndrome, 3 patients, including 1 with Currarino syndrome, had a malignant tumor. A retrospective review of 173 children with sacrococcygeal teratoma treated in the Netherlands between 1970 and 2003 demonstrated mature histology in 64.3%, immature histology in 19.3%, and malignant histology in 12.9%; however, the association with Currarino syndrome was not described. Given these findings, early resection of presacral masses in children is recommended, but it is unclear whether the risk of malignancy with Currarino syndrome–associated teratomas differs from that with sporadic sacrococcygeal teratomas.

A presacral anterior meningocele was identified in 58 (43%) of 135 patients, and these occurred together with a presacral nondysraphic tumor in 47% of cases. In studies of spinal cord anomalies, 66 (60%) of 110 patients had at least one spinal cord anomaly consisting of an anterior meningocele, spinal lipoma, diastematomyelia, low-lying conus, or syrinx. A spinal lipoma was identified in 33% of those cases.

The presence or absence of a “tethered spinal cord” was noted in 163 patients, and 70 of them (43%) underwent surgery for untethering. Among those who had tethered spinal cord were 28 (46%) of 61 patients with a nondysraphic presacral solid tumor such as a teratoma, 27 (47%) of 57 patients with an anterior meningocele, and 29 (81%) of 36 patients with a lipoma. Although specific definitions of tethered spinal cord or the criteria for surgical untethering were not included in any of the study reports, these data suggest that the risk of tethered cord syndrome is much higher when a spinal lipoma is identified on MRI.

Tethered cord syndrome, defined as neurological symptoms caused by dysfunction of the lumbosacral spinal cord when it is anatomically fixed or “tethered” to an
inelastic structure such as an occult dysraphism,25 may be more difficult to ascertain in patients with Currarino syndrome because of the presence of anorectal malformations and frequent constipation. Recently, Lee and colleagues18 reported urodynamic findings in 12 patients with Currarino syndrome who had undergone surgery for tethered cord release. While 10 patients had persistent difficulty voiding postoperatively, only 5 patients underwent urodynamic testing before and after surgery, and 3 of these demonstrated improvement.

Genetics

While the molecular pathogenesis of Currarino syndrome is still not completely understood, disease-causing mutations within the MNXI gene (7q36; also known as HLXB9) have been characterized in autosomal dominant familial forms of Currarino syndrome.24 MNXI encodes a homeobox nuclear transcription factor involved in caudal development and is required for pancreatic development and spinal cord motor neuron differentiation.26 More than 50% of sporadic cases of Currarino syndrome have also demonstrated mutations in the MNXI gene; however, more specific genotype-phenotype correlations have been complicated by incomplete penetrance and a wide variation in clinical presentation even among familial cases.5 Overall, 43 different disease-causing mutations in the MNXI gene have been identified in patients with Currarino syndrome. In familial cases, 90% of affected individuals have an identified mutation, and in sporadic cases, mutations have been detected in approximately 50%. Patients with MNXI mutations show incomplete penetrance without a clear genotype-phenotype correlation. Among familial patients with the same mutation, cases with and without spinal dysraphism have both been observed.17 In the studies we reviewed, among the 59 patients with identified mutations in the MNXI gene whose data were available, a spinal cord anomaly was identified in 43 (73%). Chromosomal microarray in the featured case revealed a copy number loss within chromosomal band 13q12.11 spanning 0.290 Mb, encompassing GJB6, and encoding connexin 30. Although mutations in GJB6 are associated with nonsyndromic sensorineural hearing loss,10 there is no known association with caudal tail bud development or dysraphism.

Conclusions

In summary, we report the case of a child with Currarino syndrome and a rare type of occult spinal dysraphism consisting of a dorsal lipomyelomeningocele continuous with an intradural presacral lipoma. Approximately 60% of the patients with Currarino syndrome described in the literature have an occult spinal dysraphism, most commonly an anterior meningocele. Tethered cord syndrome appears to be much more common in patients with a spinal lipoma.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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