Urological outcome in patients with Currarino syndrome

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A B S T R A C T

Introduction: Currarino syndrome is a type of caudal regression syndrome characterized by the association of hemisacrum, anorectal malformation and presacral mass. Only few studies on small series report the incidence of urinary dysfunction in Currarino syndrome. Our aim was to evaluate the urological outcome in patients with Currarino syndrome.

Patients and methods: We retrospectively reviewed all Currarino syndrome patients treated in our institution. Of 20 patients, we could evaluate the urological outcome in 16. This group of patients underwent clinical, radiological and urodynamic evaluation.

Results: All 16 patients had a sacral defect, fourteen of them presenting a presacral mass (87.5%), eight a tethered cord (50%), and 7 anorectal malformations (43.7%). Eight patients underwent neurosurgical treatment for neural tube defects. In 14 patients, the presacral mass was resected. One case presented detrusor overactivity, 2 recurrent urinary tract infections and 2 vesicoureteral reflexes. Both patients with lipomyeloschisis had a neuropathic bladder. All the other patients could void the bladder spontaneously. Renal function was normal in all.

Conclusion: Currarino syndrome is a rare congenital disorder presenting a variable phenotype. Urological outcome is good in the majority of patients.

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Currarino syndrome (CS) was first described by Currarino et al. [1] as a congenital disorder characterized by the triad of anorectal malformation (ARM), sacrococcygeal defect, and presacral mass. The only mandatory clinical feature for diagnosis of CS is the sacral anomaly. Mutations of MNX1 gene have been reported in nearly all familial CS patients, with a 30% of CS sporadic patients. Current studies reported a mutation of MNX1 that is detected in about 50% of affected patients [2]. The presacral mass can be a teratoma, a dermoid cyst, a rectal duplication, or a combination of them. Different spinal abnormalities can be associated, such as anterior meningocele, tethered cord, or lipoma.

The most frequent type of ARM in CS is rectoperineal fistula [3]. However, different types of ARM were described in CS (rectourethral fistula, rectovestibular fistula, cloacal malformation).

Among the many different types of sacral agenesis described [4] and classified into 5 categories, the sacral anomaly in CS belongs to the 4th group (hemisacrum). Many associated congenital spinal abnormalities were described [5]. Neural tube malformations, particularly tethered cord, can be associated with CS, and spinal magnetic resonance imaging (MRI) is the gold standard for detection of these anomalies. CS has variable phenotypes: some patients presented with only asymptomatic hemisacrum without other anomalies, others presented the complete triad and other associated gynecologic or urologic malformations. Due to this great variability of penetrance, the name of Currarino syndrome is more appropriate than Currarino triad [6].

Associated gynecologic malformations include bicornuate uterus, septate vagina, and bifid clitoris [7]. Urologic involvement may be characterized by duplex ureter, horseshoe or duplex kidney, vesicoureteral reflux (VUR), dysplastic kidney, or hypospadias.

There are only few reports about the therapeutic management and long-term follow-up [8,9] and even less analyzing the urological outcome in patients with CS. In the largest reported series including 205 CS patients, 35% had urinary tract dysfunction [4], in other series the incidence of urological complications was about 20% [9]. A study performed by Crétolle reported an incidence of 3.4% of neuropathic bladder and 14% of urinary incontinence in a series of 29 patients [8]. Another study performed by Lee reported an incidence of 36% of urinary incontinence in a series of 14 patients [9]. However, in none of these studies it was possible to identify individual risk factors for urological dysfunction. In particular, owing to the small number of patients, no significant relation among the type of sacrococcygeal defect, treatment of presacral mass or anorectal anomaly, and urological sequelae was reported. Another confounding factor is the treatment received, that can

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obviously influence the final urological outcome. In patients treated for sacrococcygeal teratomas long-term sequelae, including neuropathic bladder or bowel abnormalities, have been observed in 11%–41% of survivors [10–13].

Our aim was to evaluate the urological outcome in a series of CS and try to elucidate if bladder function disorders could be owing to a congenital malformation or be the sequelae of surgical treatment.

1. Materials and methods

We studied retrospectively 20 CS patients (13 girls and 7 boys) evaluated in a single center from 1991 to 2010 (Table 1).

Inclusion criterion for diagnosis of CS was the presence of hemisacrum. Every case underwent history and physical evaluation, renal function assessment, urinalysis, ultrasound examination, sacrum radiograph, genetic molecular analysis of the MNX1 gene, cystogram, magnetic resonance and urodynamic studies.

Sacrum radiograph was performed in 2 projections (anteroposterior and lateral). MRI was always performed in patients with diagnosis of hemisacrum.

Urodynamics was performed in children more than 2 years old with suspect of neuropathic bladder owing to their voiding habits (dropping, using diapers, not toilet trained) or some radiological signs (bladder profile at cystogram or ultrasound) after the last surgical treatment. In toilet trained children without any voiding trouble urodynamics and in infants, urodynamics was not performed in order to avoid any undue invasiveness. Urodynamics study included cystometry, electromyography (EMG) and uroflowmetry, electromyography (EMG) was not performed.

The decision to perform detethering surgery was ultimately made by the neurosurgeon and based on MRI findings, somatosensory evoked potential and symptoms. Cases of tethered cord were identified by magnetic resonance imaging, which revealed the conus medullaris below the L2 vertebra. Presacral masses and anorectal malformations, when present, were treated by posterior sagittal anorectoplasty (PSARP) as described by Peña in 1982 [14] (Fig. 1). To reduce the risk of recurrence of presacral masses, excision of the coccyx was always performed.

The surgical timing was decided by the two surgical teams. In case of neurosurgical treatment, this was the first to be performed, followed by PSARP in case of presence of ARM and, finally, excision of presacral mass.

All the patients have been operated by the same two surgical teams: spinal cord surgery was performed by neurosurgical team, anorectal and presacral mass surgery by the general surgeon team.

After surgery, patients were followed by a multidisciplinary team including neurosurgeons, pediatric surgeons and urologists at regular intervals (at least 3, 6, and 12 months after each surgery and then once per year, more often in case of symptoms).

To evaluate postsurgical urinary outcomes, we considered: renal function, presence of urinary infections, vesicoureteral reflux, ultrasound pattern, voiding pattern. All patients were evaluated clinically, by ultrasound, renal function using Schwartz creatinine clearance formula [15] and urinalysis, in case of anomalies cystogram, nuclear scan and/or urodynamic testing were performed.

Regarding voiding pattern, each patient was categorized as continent, intermittently incontinent, or continuously incontinent, according to the Report from the Standardisation Committee of the International Children’s Continence Society [16]. Bladder was defined neuropathic if the patient had clinical or urodynamic signs of voiding disorder or trouble of urinary continence.

Fisher exact test was used for statistical analysis to evaluate the correlation between neuropathic bladder and the associated spinal abnormalities, age at presentation, age at surgery, type of mass resected, type of ARM, type of neural tube defect and number of surgical treatment. A p < 0.05 was considered statistically significant.

Table 1

Patients collected data.

<table>
<thead>
<tr>
<th>ID</th>
<th>Gender</th>
<th>Age at presentation (months)</th>
<th>Genetics</th>
<th>Neural tube defect</th>
<th>Age at NST (months)</th>
<th>Presacral mass</th>
<th>Age at OST (months)</th>
<th>ARM</th>
<th>Age at GIT (months)</th>
<th>Number of surgical intervention</th>
<th>Bowel outcome</th>
<th>Urological outcome</th>
<th>Follow-up (months)</th>
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<td>1</td>
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<td>42</td>
<td>Lipoma</td>
<td>42</td>
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<td>Constipation</td>
<td>Neurogenic bladder, VUR</td>
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<td>Sacral dermoid</td>
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<td>Constipation</td>
<td>Neuropathic bladder Detrusor overactivity</td>
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<td>74</td>
<td>55</td>
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</table>

NST: Neurosurgical treatment; OST: Oncological surgical treatment; ARM: Anorectal malformation; GIT: Gastrointestinal treatment; VUR: Vesicoureteral reflux; UTI: Urinary tract infection.
2. Results

Of 20 patients, we could evaluate the urological outcome in 16 (13 girls, 3 boys) for incomplete data of 3 patient and a death of a patient owing to a malignant teratoma.

Median age at diagnosis was 24 months (range 1–144 months).

All of 16 patients studied had a sacral defect, fourteen presenting a presacral mass (87.5%), eight (50%) a tethered cord, and seven (43.7%) ano-rectal malformations (Table 1). Among 16 cases, two showed a cytogenetic rearrangements including also 7q36 region, the locus of MNX1 gene, and four patients (Patient ID 7, 10, 15, and 16) carried a pathogenic mutation in MNX1 gene (of which 2 familiar cases). We could perform MLPA analysis to exclude the loss of one or more exons, only in seven of patients resulting MNX1-negative, and we did not detect any deletion.

Neurosurgical treatment was performed in 8 patients, with a prevalence of tethered cord (8 cases), and lipomyelocoele (2 cases). Median age at neurosurgical intervention was 36 months (range 13–135 months).

In 14 patients, the presacral mass was resected, with a prevalence of anterior meningocele (5 cases), sacral dermoid (2 cases), followed by teratoma (5 cases) and lipoma (2 cases). Median age at excision was 32 months (range 2–135 months). In 8 cases the presacral mass was resected as a single procedure, in 6 cases it was resected during another procedure: in 2 patients at the same time as neurosurgical procedure (one of these patients resulted with neuropathic bladder), in 4 patients during ARM correction (one of these resulted with fecal incontinence).

ARM was treated in a single stage without colostomy in all 7 patients and consisted in 6 rectoperineal fistula and 1 rectal stenosis. Median age at gastrointestinal surgery was 22 months (range 2–38 months). ARM correction was never performed in combination with neurosurgical treatment.

The only postoperative complication occurred in patient number 15 firstly treated for anterior meningocele and rectoperineal fistula with recurrent perineal abscess after ARM correction that required multiple drainage with abscess resolution and constipation at 98 months follow-up.

The follow-up ranged from 18 to 220 months, with a median of 78 months.

Two cases had a history of urinary tract infection resolved with medical treatments, and two other patients had a diagnosis of vesicoureteral reflux. One of them presented with a grade 1 vesicoureteral reflux which resolved without any surgical treatment, and the other one presented with a grade 3 vesicoureteral reflux treated successfully with antibiotic prophylaxis. None of these patients had positive urinary culture tests at follow-up.

One patient with tethered cord and rectoperineal fistula presented detrusor overactivity, but he was clean on daytime and at night with a normal voiding pattern.

Both patients with lipomyelocoeles were continuously incontinent and performed CIC and oxybutynin. The other 14 were continent without anticholinergic therapy. All these could void the bladder spontaneously and renal function was normal in all.

On statistical analysis there was no significant association between urological sequelae and age at presentation, type of tumor, type of ARM, age at surgery and number of surgical procedures (p > 0.05). No significant urological worse outcome in patients with mutation of the MNX1 was observed.

Regarding type of neural tube defect, there was a statistically significant association between the two lipomyelocoeles and the two neuropathic bladders using Fisher exact test (p = 0.008).

Renal function was normal in all 16 patients.

Nine patients of our cohort (56%) presented with constipation, and one patient required treatment with Macrogol at time of follow-up.

Two patients presented with fecal incontinence and one of this required treatment with transanal irrigation.

3. Discussion

CS is a relative recent syndrome, first described in 1981, with a variable phenotype that request variable surgical treatments.

The surgical approach of CS must take into account a variable outcome, the constipation and urological disorders that were the major sequela described in the literature. As CS is uncommon, the series described in the literature are little and not always complete clinical data and long follow-up are available. Our series is composed of children treated and followed for many years in a single institution. We focused our attention on the long term urological outcome of these patients, notably renal and bladder function.

We tried to elucidate if bad urological outcome could be owing to the neural tube defect or to some other factor.

Possible causes of neuropathic bladder and/or urinary incontinence include tethering of the spinal cord, sacral agenesis, presence of a presacral mass, injury to parasympathetic nerves during surgery for dysraphism, ARM or presacral mass. Every surgical treatment may be potentially dangerous for urological outcome of these patients.

Of 16 patients studied, the only 2 neuropathic bladders (12.5%) were observed in the only two patients affected by lipomyelocele. Although it is not possible to demonstrate that in these patients lipomyelocele was the cause of neuropathic bladder, this result is in our opinion very suggestive of it. Constipation may be related to presacral mass or anorectal malformation; some authors described an association between CS and Hirschsprung disease and recommended to perform rectal biopsy to exclude aganglionosis [17–19].

Lipomyelocele is characterized by a subcutaneous fatty mass located above the intergluteal crease and usually extending asymmetrically into one buttock (Fig. 2). Histologically, the mass is composed of clusters of mature adipocytes separated by collagenous bands, usually associated with other tissues such as striated muscle, cartilage, bone, nerve cells, ependyma, and aberrant neuralglial tissue. In the lipomyelocele the placode-lipoma interface lies within the spinal canal and may extend over several vertebral levels. Intraspinal lipoma is characterized by a strict contact with the subcutaneous fat tissues through a posterior spina bifida [20]. These features explain the association of lipomyelocele with urological incontinence in 20.1% and urinary retention in 19.5%.
according to the literature [21]. In our published series of 502 patients treated for spinal dysraphism, neuropathic bladder was observed in 39% of lipomyeloceles [22].

The present study has three major limitations, namely our series is small owing to the rarity of CS, the short follow-up considering the long evolution of CS and the patients have been studied retrospectively after repeated different treatments (neurosurgical treatment, presacral mass treatment or ARM correction).

A prospective multicentric study with urodynamic study performed before and after each single surgery could provide more information about the role of the congenital anomaly versus surgical procedures in determining the urological outcome.

4. Conclusions

CS is a rare pediatric disorder with a variable phenotype. Neuropathic bladder can be present, but in our series it was associated with the presence of lipomyeloceles. This emphasizes the usefulness of magnetic resonance to help the clinicians to make a precise diagnosis of neural tube defect and select the cases at risk of urological dysfunction, however considering our short follow-up and the small series of patients, further prospective studies are necessary to confirm our results.

Conflict of interest

None declared.

References