Urologic and anorectal complications of sacrococcygeal teratomas: Prenatal and postnatal predictors

Emily A. Partridge a, Douglas Canning b, Christopher Long b, William H. Peranteau a, Holly L. Hedrick a, N. Scott Adzick a, Alan W. Flake a,⁎

a The Center for Fetal Diagnosis and Treatment, Children’s Hospital of Philadelphia, Philadelphia PA
b Division of Urology, Children’s Hospital of Philadelphia, Philadelphia PA

A R T I C L E   I N F O
Article history:
Received 21 September 2013
Accepted 30 September 2013

Key words:
Sacrococcygeal teratoma
Urologic complications
Anorectal complications
Prenatal imaging

A B S T R A C T

Purpose: Anorectal and urologic sequelae are observed in long-term survivors of sacrococcygeal teratoma (SCT). In this study we evaluate the incidence and predictors of anorectal and urologic complications in SCT.

Methods: A retrospective review was performed for all SCT patients who underwent resection at a single institution between 2000 and 2012. Enrollment criteria included a minimum of 12 months follow-up. Categorical variables were analyzed by Fisher’s exact test and continuous variables by Mann Whitney test (p < 0.05).

Results: Forty-five patients were studied. Anorectal complications occurred in 29%, including severe chronic constipation (n = 13) and fecal incontinence (n = 4). Urologic complications occurred in 33%, including neurogenic bladder (n = 12), vesicoureteral reflux (n = 5), and urinary incontinence (n = 7). Prenatal imaging by fetal MRI demonstrated mass effect with obstruction of the bowel (n = 4) or bladder and collecting system (n = 7) in a subset of patients with postnatal complications (anorectal 4/4, PPV 100%; urologic 6/7, PPV 86%). Postnatal complications were associated with obstructive findings on prenatal imaging, prenatal therapeutic interventions, Altman classification, perineal reconstruction, and tumor recurrence. No anorectal or urologic complications occurred in patients with Altman type I tumors.

Conclusions: Urologic and anorectal complications are common in patients with SCT. Higher Altman classification and prenatal imaging suggestive of intestinal or urologic obstruction should prompt focused prenatal counseling and postnatal screening for anorectal and urologic dysfunction.

© 2014 Elsevier Inc. All rights reserved.
1. Methods

Medical records of all patients who underwent SCT resection at our institution between 2000 and 2012 were reviewed. Recorded data on patient demographics, prenatal course and imaging, preoperative imaging, surgical resection and pathology, postoperative complications during admission, and late sequelae during regular outpatient follow-up were analyzed.

Functional sequelae were evaluated at regular follow-up appointments and were assessed by detailed history and physical examination, including digital rectal examination, and imaging including ultrasonography and videourodynamics when indicated. Urologic complications included hydronephrosis and vesicoureteral reflux (graded by standard radiologic criteria), neurogenic bladder (defined as a failure to either store or hold an adequate amount of urine based on expected bladder capacity as assessed by formal urodynamics), and sequelae of impaired urologic function including the requirement for chronic intermittent catheterization, urinary tract infection prophylaxis, and incontinence (defined as wet episodes regularly observed by a parent or caregiver). Anorectal complications included constipation (defined as the requirement for oral laxative therapy for a minimum of six months), incontinence (defined as soiling episodes regularly observed by a parent or caregiver), stenosis (defined by requirement for regular rectal dilations), and procedures related to severe chronic constipation (requirement for colonic irrigations and/or fecal disimpaction).

Statistical analysis was performed using Fisher’s exact test for categorical variables and Mann-Whitney test for continuous variables, with p-values < 0.05 considered significant. All data analysis was conducted using GraphPad Prism 6.0 (La Jolla, CA).

2. Results

A total of 60 patients underwent SCT resection during the study period. 45 patients met criteria for inclusion in the study including a minimum of 12 months follow-up. 15 patients were excluded: 7 died during the neonatal period, and 8 were lost to follow-up or discharged with follow-up care arranged at outside centers. 26 of the 45 patients (58%) had no impairment of bowel or bladder function after a median follow-up period of 41.5 months (range 12–124 months), while functional sequelae were noted in a total of 19 patients (42%).

Table 1 displays the characteristics of the 45 patients. Tumors were classified according to the criteria proposed by the Surgical Section of the American Academy of Pediatrics (Altman et al. 1973) [11]. 9 patients had type I (predominantly external tumor), 24 had type II (predominantly external with intrapelvic component), 8 had type III (predominantly internal with abdominal extension), and 4 had type IV (intrapelvic tumor with no external component). Altman classification of II or greater was significantly associated with functional outcomes (p = 0.0058). There were no differences in gender, timing of SCT diagnosis, mode of delivery, gestational age at delivery, birth weight, length of NICU admission, or duration of mechanical ventilation between the functional cohorts.

SCT was prenatally diagnosed in 40 of the 45 patients, and prenatal intervention was performed in a total of 6 pregnancies (tumor aspiration, n = 4, amniotic fluid reduction, n = 2, open fetal surgery for tumor debulking, n = 2, and ex-utero intrapartum therapy with tumor debulking, n = 1). Prenatal intervention was significantly associated with functional outcomes (p = 0.0023). 4 patients required extensive reconstructive procedures to restore normal perineal anatomy, including posterior sagittal anorectoplasty (n = 1), anoplasty (n = 2) or vaginoplasty (n = 1), and perineal reconstruction was significantly associated with impaired functional outcomes (p = 0.0260). Five patients had a benign local recurrence after initial definitive resection requiring re-excision, and recurrence was also found to be significantly associated with functional sequelae (p = 0.0095).

Fetal MRI and ultrasonography were reviewed for radiographic evidence of obstruction of the gastrointestinal tract or urinary collecting systems in all prenatally diagnosed cases of SCT. Hydronephrosis was observed in a total of 8 studies, while large bowel dilation suggestive of gastrointestinal obstruction was noted in 4 cases. Obstructive radiographic findings were significantly associated with functional outcomes for both the gastrointestinal (p = 0.0260) and urinary collecting systems (p = 0.0064).

Table 2 details the specific anomalies of the urinary collecting system identified on follow-up examinations and imaging studies. Urologic sequelae occurred in a total of 15 patients (33%). Neurogenic bladder was the most common complication observed, followed by hydronephrosis, vesicoureteral reflux (VUR) and incontinence. Requirements for intermittent catheterization (n = 10) and antibiotic prophylaxis therapy (n = 9) occurred at high rates in this patient cohort.

Table 3 details the complications affecting anorectal function encountered, with a total of 13 patients affected (29%). Constipation was the most common occurrence, followed by incontinence and rectal stenosis. Colonic irrigation or fecal disimpaction was required for management of severe constipation in a minority of patients.

Table 1
Patient demographics.

<table>
<thead>
<tr>
<th>Description</th>
<th>No functional sequelae (n = 26)</th>
<th>Urologic and/or anorectal sequelae (n = 19)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>n = 22 (85%)</td>
<td>n = 17 (89%)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Prenatal Diagnosis of SCT</td>
<td>n = 24 (92%)</td>
<td>n = 16 (84%)</td>
<td>0.6361</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>C-section (n = 19, 73%)</td>
<td>C-section (n = 15, 79%)</td>
<td>0.1761</td>
</tr>
<tr>
<td>Vaginal (n = 7, 27%)</td>
<td>Vaginal (n = 3, 16%)</td>
<td>EXIT (n = 0)</td>
<td>EXIT (n = 1, 5%)</td>
</tr>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td>35.85 (range 28–38)</td>
<td>34.11 (range: 27–40)</td>
<td>0.3623</td>
</tr>
<tr>
<td>Weight at delivery (g)</td>
<td>2845 +/- 814.11</td>
<td>2700.29 +/- 1041.64</td>
<td>0.9595</td>
</tr>
<tr>
<td>Length of stay post-resection (days)</td>
<td>19.36 +/- 22.11</td>
<td>42.77 +/- 57.50</td>
<td>0.1053</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (days)</td>
<td>2.44 +/- 7.75</td>
<td>7.22 +/- 9.68</td>
<td>0.0796</td>
</tr>
<tr>
<td>Prenatal intervention</td>
<td>SCT debulking (n = 1, 4%)</td>
<td>Amniotic fluid reduction (n = 2, 11%)</td>
<td>0.0023</td>
</tr>
<tr>
<td>Altman Classification</td>
<td>Type I: 9 (35%)</td>
<td>Type I: 0 (0%)</td>
<td>0.0058</td>
</tr>
<tr>
<td>Type II-IV: 17 (65%)</td>
<td>Type II-IV: 19 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perineal reconstruction</td>
<td>n = 0 (0%)</td>
<td>n = 4 (21%)</td>
<td>0.0260</td>
</tr>
<tr>
<td>n = 0 (0%)</td>
<td>n = 5 (26%)</td>
<td>0.0095</td>
<td></td>
</tr>
<tr>
<td>n = 1 (4%)</td>
<td>n = 7 (37%)</td>
<td>0.0064</td>
<td></td>
</tr>
<tr>
<td>n = 0 (0%)</td>
<td>n = 4 (21%)</td>
<td>0.0260</td>
<td></td>
</tr>
</tbody>
</table>

* Indicates parameters found to be statistically significant (P < 0.05).
Fig. 1 depicts the proportion of patients with abnormal prenatal imaging of the collecting and gastrointestinal systems who subsequently developed urologic or anorectal sequelae. Evidence of obstruction on fetal MRI or ultrasonography was significantly associated with functional outcomes, with positive findings in 7 patients with postnatal urologic dysfunction and 4 patients with anorectal sequelae. One patient with prenatal evidence of hydronephrosis had normal postnatal function, and no false positives were associated with prenatal findings of bowel obstruction. Prenatal imaging represents a prognostic tool with good predictive value for urologic (sensitivity 47%, specificity 96%, PPV88%, NPV75%) and anorectal (sensitivity 31%, specificity 100%, PPV 100%, NPV74%) complications following SCT resection.

3. Discussion

There is significant variability in the literature with respect to the incidence of functional sequelae after SCT resection. Urologic complications have been more widely reported, while comparatively fewer studies address anorectal function in these patients (Table 4). Variability in sample size may account for some discordance in the rates of complications observed, with the majority of studies limited to relatively small patient cohorts (n = 10–30). Additionally, while some studies limited diagnosis of functional sequelae to patients seen in standardized outpatient follow-up, others relied on patient or caregiver surveys to assess for long-term functional outcomes, with recall bias posing a significant potential confounding factor in such series [14,15]. In this retrospective review of 45 patients, we observed rates of urologic and anorectal complications in 33% and 29% respectively, with sequelae diagnosed by clinical examination and radiologic imaging in patients undergoing standardized follow-up at a single institution.

Controversy exists in the literature with respect to the postulated mechanism of injury to pelvic structures observed in SCT, with arguments in support of tumor invasion and extent of resection versus local mass effect with compression injury hypothesized to account for functional sequelae. High rates of urinary dysfunction have been observed following SCT resection, but characterization of the mechanism of incontinence is not uniformly reported in the literature. However, several studies have reported radiologic and urodynamic findings consistent with neurogenic bladder in a high proportion of SCT patients with urologic dysfunction. In a series of 14 patients with diagnosed impairments in bladder emptying or urinary infection after SCT resection, Ozkan et al. [8] reported high rates of hydronephrosis (43%), vesicoureteral reflux (50%), and neurogenic bladder (86%). These findings support a role for direct injury to neural structures supplying the bladder and/or sphincter. In our series, evidence of direct compression-induced structural injury to the pelvic organs was observed in some patients requiring genitourinary and anorectal reconstructive procedures including posterior sagittal anorectoplasty (n = 1), anoplasty (n = 2) or vaginoplasty (n = 1), and was significantly associated with urologic and anorectal dysfunction in our series (p = 0.0260).

To further explore the role for tumor mass effect in the etiology of postnatal complications, a number of studies have examined the role of intrapelvic extension of the lesion as defined by the Altman classification. Malone et al. demonstrated an association between Altman type IV tumors and both urologic and GI dysfunction, and Le et
al. demonstrated significantly higher rates of neurogenic bladder and renal injury in patients with higher-grade Altman lesions. However, a number of other studies failed to support an association with Altman type and postnatal sequelae [11,13,9,15], leading to controversy over the acceptance of mass effect as a causative factor in postnatal complications in SCT. In the present study, we show that Altman type strongly correlates with both urologic and anorectal dysfunction ($p = 0.0058$), further supporting this association. We also observe an association of sequelae with the requirement for prenatal therapeutic intervention ($p = 0.0023$). Although tumor volumes were not formally analyzed in this study, fetal intervention is generally reserved for large-volume lesions with higher likelihood of associated mass effect. Additional support for the role of mass effect in postnatal complications is found by the observation that prenatal imaging suggestive of obstruction of the urologic or gastrointestinal tract is statistically correlated with postnatal complications. To the authors' knowledge, this is the first study to demonstrate the significance of prenatal imaging as a predictor of postnatal urologic and/or anorectal dysfunction, supporting the use of detailed imaging including fetal MRI in the assessment of pregnancies affected by SCT.

Early identification of VUR and neurogenic bladder is of particular importance in the prevention of long-term renal injury, with early introduction of prophylactic antibiotics, anticholinergics and intermittent catheterization as key management tools to optimize outcomes in these patients. Of the 14 patients with identified neurogenic bladder or reflux in our study, 10 received an initial diagnosis of neurogenic bladder or VUR during their NICU admission, with early introduction of intermittent catheterization and no long-term renal injury observed. Recognition of functional constipation is also essential to improve long-term bowel function, with implementation of stool softeners, disimpaction and irrigation as needed to achieve regular toileting. Early intervention to achieve symptom control and continence reduces the psychological and social burden of urinary and fecal incontinence, improving quality of life for patients and caregivers.

The results of this single-center retrospective study support a high incidence of urologic and anorectal dysfunction in survivors of SCT, and identifies several risk factors with significant predictive value of postnatal sequelae. The observed association of Altman classification and prenatal intervention with postnatal outcomes supports a role for mass effect with direct injury to pelvic structures as a mechanism for the observed complications, while the finding that prenatal evidence of urologic and/or GI obstruction correlates with postnatal function provides a novel predictive tool to identify at-risk patients. Focused prenatal counseling and postnatal screening for anorectal and urologic dysfunction should be undertaken in all high-risk patients to prevent end-organ damage and improve functional outcomes in these patients.

References


Discussion

Unidentified Speaker: When you looked at your prenatal imaging in the patients, did you also look at the prenatal imaging in the patients that didn’t have these symptoms?

Response: Dr. Emily Partridge: Yes we did. It is an excellent question. In the interest of trimming the number of slides, I did not present that data, but in fact we had only one false-positive, so there was one patient with evidence of moderate pelviectasis who went on to have normal postnatal urologic function. That was the only false-
positive for the urologic patients, and for the GI patients there were no patients with evidence of obstruction of the gastrointestinal tract who went on to have complications.

Unidentified Speaker: How did you assess the constipation and how far out did you assess the constipation?

Response: Dr. Partridge: That is a great question because the existing literature varies significantly with respect to how this data is collected varying from patient and caregiver surveys all the way to a more real-time clinical collection in the clinic. All of our patients’ data was collected during their regular follow-up period, so they were seen by the surgeon who performed the primary resection and a detailed history was taken regarding the incidence and severity of all of the functional anomalies that we characterized. Chronic constipation was defined as the need for laxative therapy for greater than six months and our mean follow-up period was 42.5 months.

Unidentified Speaker: I may have missed this in your presentation but were these urinary tract issues and constipation associated with intra-abdominal tumors or were these — did you find the same rate of occurrence in the extra-abdominal tumors, because it doesn’t make any sense why you would have those kinds of things. You clearly see often times pelviectasis with the patients with intra-abdominal tumors simply because of mass.

Response: Dr. Emily Partridge: We saw a strong correlation with the Altman classification so that speaks to some extent to the internal component of the tumor. Interestingly, we did not see any correlation with tumor recurrence. The other independent predictors or postnatal dysfunction were the requirement for extensive reconstruction of the perineum and the requirement for prenatal intervention such as shunting, open fetal debulking, etc., but we did not see a correlation with recurrence. The Altman classification is the only indicator that we have of the internal component being a contributor.