Journal of Pediatric Surgery xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

The incidence of associated abnormalities in patients with sacrococcygeal teratoma

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ARTICLE INFO

Article history:
Received 17 August 2017
Received in revised form 14 January 2018
Accepted 16 January 2018
Available online xxxx

Key words:
Germ cell tumor
Sacrococcygeal teratoma
Congenital anomalies

ABSTRACT

Background: Gross genetic causes for SCT are unknown; however, it might be associated with other abnormalities. We assessed the incidence of associated abnormalities in a large national cohort of neonates with SCT and aimed to identify predictive risk factors.
Procedure: The medical records were reviewed of 235 consecutive neonates with SCT treated at the six pediatric surgical centers in the Netherlands from 1970 to 2010. Potential risk factors for associated abnormalities analyzed included sex, gestational age, tumor-volume/histology and Altman-classification.
Results: In 76 patients (32.3%) at least one associated abnormality was diagnosed, with hydronephrosis as the most common (16.2%) and hip dysplasia in 4.3%. Multiple abnormalities were documented for 21 (9.0%). Prematurity and Altman type IV SCT were associated with an increased risk of any associated abnormality. No association between increased tumor-volume and hydronephrosis or hip dysplasia was found. Patients with type IV Altman SCT had a fourfold risk of suffering from hydronephrosis compared to Altman type I SCT.
Conclusions: SCT was associated with other abnormalities in one-third of children. Some were tumor-related while others were related to prematurity or occurred sporadically. In contrast to clinically obvious anomalies, hip dysplasia or hydronephrosis might be latently present with more subtle clinical presentation. We therefore suggest renal- and hip-ultrasound in all patients, certainly those with Altman type IV SCT.
Level of evidence rating: Level II (retrospective study)

Sacrococcygeal teratoma (SCT) is the most common neoplasm in neonates with a reported female to male predominance of 4:1. However, with a live birth incidence of one in 15,000–40,000 live births it is still rare. [1–4] According to the classification by Altman and colleagues four anatomical types are distinguished. Type I is localized predominantly externally; type II also has an intrapelvic tumor component; type III predominantly extends in the abdominal cavity; and type IV is entirely localized presacrally without an obvious external component. [5].

Gross cytogenetic or chromosomal changes have not yet been identified in patients with SCT. The exception is a presacral teratoma as part of the Currarino triad. The Currarino triad is a very rare hereditary disorder characterized by the occurrence of an anorectal malformation in combination with a defect of the sacral bone and a presacral mass that is mostly a meningocele or a presacral teratoma. [6,7] Other than the stand-alone SCT, the Currarino triad is an autosomal dominant defect apparently linked to mutation of the HLXB9 gene on chromosome 7q36. [8] Presacral teratomas diagnosed as part of the Currarino triad furthermore differ from SCT in their very low risk of malignant transformation even if containing immature tissue. [9,10].

Gross genetic causes for SCT are unknown, but previous studies secondarily mentioned associated abnormalities in 12%–30% of patients with SCT. [1,11,12] A Finnish study on the prevalence of SCT and pregnancy outcomes in Finland found congenital abnormalities in 30% of the children. (1) A Japanese study on outcomes of prenatally diagnosed SCT found various associated abnormalities in 12% of the 97 children.

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https://doi.org/10.1016/j.jpedsurg.2018.01.013
0022-3468/

[12] However, both studies did not further evaluate risk factors associated with those abnormalities.

Urologic abnormalities such as hydronephrosis or vesicoureteral reflux have been reported in 36%–46% of the postoperative patients treated for SCT with variable degrees of chronic kidney disease. [13] Urological abnormalities are often seen as tumor-pressure related conditions and a higher Altman type is considered a risk factor for the occurrence of urological abnormalities. [13] Furthermore, musculoskeletal abnormalities including hip dysplasia and clubfoot as well as cardiopulmonary defects including ventricular septal defect, pulmonary hypoplasia and thoracic dystrophy have been reported with varying incidences. Some of these associated abnormalities might have consequences for preoperative screening, surgical treatment and follow-up.

The objective of this nationwide retrospective study was to determine the incidence of abnormalities associated with SCT and to identify possible disease- and patient-related risk factors predicting the occurrence of theses abnormalities.

1. Methods

1.1. Patients and study design

We included patients born between January 1970 and December 2010 with a SCT and treated in one of the six pediatric surgical centers in the Netherlands (Emma Children's Hospital University Medical Centre and VU University Medical Centre Amsterdam; University Medical Centre Groningen; Maastricht University Medical Centre; Sophia Children's Hospital Rotterdam; University Medical Centre Nijmegen; and Wilhelmina Children's Hospital Utrecht). The medical records were retrospectively reviewed for patient characteristics (sex, gestational age, birth weight, mode of delivery, comorbidities and time of diagnosis) and disease-related characteristics (Altman classification [5], tumor histology and tumor volume, age at operation, surgical approach, radical or nonradical resection, complications and metastases). In particular, information on associated abnormalities was retrieved, including genitourinary abnormalities (i.e. hydronephrosis with or without ureteral dilatation, vesicoureteral reflux, strictures, and fistulas), musculoskeletal abnormalities (i.e. hip dysplasia or clubfeet), neural defects (i.e. neurological deficits or paraplegia), pulmonary disorders, cardiovascular anomalies, anorectal malformations and fistulas, chromosomal aberrations and other congenital anomalies (i.e. esophageal atresia). Patients in whom the teratoma was part of the Currarino triad were excluded. The medical ethical committee of the Maastricht University Medical Centre approved the study.

1.2. Statistical analysis

Statistical analysis was performed using Graph Pad Prism 6 (GraphPad Software, Inc., La Jolla, CA, USA). Normal distribution of data was assessed with the D'Agostino–Pearson omnibus normality test. Logistic regression analysis was used to calculate odds ratios with 95% confidence intervals to determine risk factors (sex, Altman type, tumor volume, tumor histology and prematurity) for associated abnormalities. Statistical significance was defined as p-values of ≤0.05. Values are given as mean with standard deviation or as median with interquartile range (IQR).

2. Results

2.1. General patient characteristics

In the study period, 235 children (186 girls and 49 boys) were born alive and treated for SCT in the participating centers. Table 1 gives the detailed patient- and disease-related characteristics. The majority had been born term by vaginal delivery and had a type I SCT (34.5%) of mature histology. Fifty-four infants had an Altman type IV SCT, which in 44 was discovered after birth (median age at diagnosis 120 days, IQR 3–365 days). Histopathological examination showed that 15 of the Altman type IV tumors were malignant with endodermal sinus tumor in 14 and embryonal cell carcinoma in one. The other tumors were of mature ($n = 33$) or immature histology ($n = 5$). In one patient with an Altman IV tumor the histopathology was unknown. Six of the patients with malignant Altman IV SCT were treated with chemotherapy.

Table 1
Patient and disease related baseline characteristics.

	n (%)
Gestational age	
Mean gestational age in weeks (SD)	37.5 (±2.9 weeks)
Birth weight	
Mean birth weight in kilogram (SD)	3.2 kg (±0.68 kg)
Prematurity	
Premature (≤37 weeks of gestation)	43 (18.3%)
Term (>37 weeks of gestation)	143 (60.9%)
Unknown	49 (20.9%)
Time of diagnosis	
Prenatally	69 (29.4%)
At birth	90 (38.3%)
Postpartum	75 (31.9%)
Unknown	1 (0.4%)
Mode of delivery	
Vaginal	118 (50.2%)
Cesarean section	64 (27.2%)
Unknown	53 (22.6%)
Age at surgery	
Median age in days (IQR)	8 days (IQR 3–174.5 days)
Surgical approach	
Sacral	172 (73.2%)
Abdominosacral	43 (18.3%)
Abdominal	7 (3.0%)
Unknown	13 (5.5%)
Altman type	
Type I	81 (34.5%)
Type II	57 (24.3%)
Type III	36 (15.3%)
Type IV	54 (23.0%)
Unknown	7 (3.0%)
Tumor histology	
Mature	151 (64.3%)
Immature	42 (17.9%)
Malignant	35 (14.9%)
Yolk sac	30 (12.8%)
Embryonic cell carcinoma	2 (0.9%)
Unknown	7 (3.0%)

A total of 17 patients died owing to disease progression, circulatory failure shortly after birth or postoperative infectious complications. One neonate died as life-sustaining treatment was discontinued immediately after birth because of multiple anomalies including omphalocele, thoracolumbar spina bifida, anorectal malformation, genital malformation and renal agenesis. Associated abnormalities of all patients were included in the analysis.

At least one associated abnormality had been diagnosed in 76 patients (32.3%), with more than one in 21 patients (9%) of the whole cohort. Excluding pulmonary anomalies and a patent ductus arteriosus, still 70 patients had any associated abnormality. The total number of associated abnormalities in the whole cohort was 108. Hydronephrosis was the most frequent one (in 16.2% of the patients) followed by musculoskeletal anomalies (6.4%) and neurological defects (6%) (Table 2). Four of the five patients with pulmonary anomalies as well as the two in whom an open ductus arteriosus was detected were born prematurely.

2.2. Risk factor analysis

Patient's sex, Altman type, tumor volume, tumor histology, and prematurity were analyzed to determine a possible association of

Please cite this article as: Kremer MEB, et al, The incidence of associated abnormalities in patients with sacrococcygeal teratoma, J Pediatr Surg (2018), https://doi.org/10.1016/j.jpedsurg.2018.01.013