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Sacrococcygeal teratoma growth rate predicts adverse outcomes

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ABSTRACT

Purpose: The purpose of this study was to characterize the growth rate of sacrococcygeal teratomas (SCTs) and determine its relationship to adverse outcomes.
Methods: A retrospective review of all pathology-confirmed isolated SCT patients evaluated with at least two documented ultrasounds and followed through hospital discharge between 2005 and 2012 was conducted. SCT growth rate was calculated as the difference between tumor volumes on a late- and early-gestation ultrasound divided by the difference in time. Outcomes were death, high-output cardiac failure (HOCF), hydrops, and preterm delivery. Student's *t*-test, receiver operator characteristics, Fisher's Exact test, and Pearson's correlation were performed.
Results: Of the 28 study subjects, there were 3 in utero demises and 2 neonatal deaths. Significantly faster SCT growth rates were seen in all adverse outcomes, including death ($p < 0.0001$), HOCF ($p = 0.005$), and preterm delivery ($p = 0.009$). There was a significant association with adverse outcomes at >61 cm^3/week (AUC = 0.87, $p = 0.001$, LR = 4.52). Furthermore, there was an even greater association with death at >165 cm^3/week (AUC = 0.93, $p = 0.003$, LR = 18.42). Growth rate was directly correlated with the percent of solid tumor ($r = 0.60$, $p = 0.0008$).
Conclusion: Faster SCT growth is associated with adverse outcomes. SCT growth rate determined by ultrasound is an effective prognostic indicator for adverse outcomes and easily applied to patient management.

Sacrococcygeal teratoma (SCT) can grow to very large dimensions causing complications related to mass effect such as distortion of pelvic and sacral anatomy, bladder obstruction, and dystocia [1]. Additionally, its accelerated growth can lead to significant arteriovenous shunting with subsequent high-output cardiac failure, polyhydramnios, preterm labor, hydrops, and maternal mirror syndrome [2,3]. Many of these complications contribute to in utero mortality rates upward of 50% [2,4]. Comprehensive prenatal evaluation allows for appropriate counseling and management for the expecting parents and has the potential to identify high-risk fetuses that may benefit from in utero therapy or alternative delivery strategies.

The mainstay of prenatal management for SCT is serial evaluation using imaging modalities such as ultrasound and echocardiography to continually monitor fetal well-being, tumor growth, and signs of cardiac failure [2,5]. Tumor growth is believed to have a variable course and directly related to outcomes. Several reports have commented on rapid SCT growth to be more of an independent risk factor for adverse outcomes than tumor size alone [3,6]. Changes in the hemodynamic stability of the fetus can be precipitous with little time to intervene if not monitored frequently. If frank hydrops is discovered, the outcome is associated with a much higher mortality [1]. Therefore, ultrasound evaluations are conducted at regular intervals and their frequency is adjusted depending on concerns for fetuses that are at high risk for adverse outcomes.

An SCT that demonstrates a rapid growth over a short period of time is potentially at high risk for adverse outcomes. The purpose of this study was to determine if increased growth rates of SCT are associated with adverse outcomes. Furthermore, we will determine if tumor growth rates correlate with tumor composition (solid versus cystic) and be useful in initially stratifying patients into risk categories.

1. Methods

1.1. Data collection

A retrospective review of all SCT patients prenatally evaluated at our fetal care center between the May 2005 and October 2012 ($n = 40$) was conducted. Approval was obtained from the Institutional Review Board of Cincinnati Children's Hospital Medical Center (IRB #2011-2626). Only patients with at least two prenatal ultrasounds done at our institution and follow-up through hospital discharge were included in the study. Data collected included maternal age, gestational age at evaluation, time of imaging and delivery, tumor characteristics, and maternal and fetal outcome.

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1.2. Prenatal imaging

Prenatal ultrasound was used to obtain fetal status, estimated fetal weight (EFW) using the Hadlock method [7], head circumference (HC), and Doppler indices. The type of SCT was also determined using the American Academy of Pediatrics, Surgical Section (AAPSS) classification system [8]. Amniotic fluid status, signs of hydrops, and changes in tumor size were recorded.

Prenatal magnetic resonance imaging (MRI) was also performed on all included patients utilizing a phased array body coil in a 1.5-Tesla scanner (Horizon, GE Healthcare Milwaukee, WI). MRI was useful in determination of additional fetal malformations, tumor composition, and as a comparison of tumor measurements to those obtained by ultrasound.

Fetal echocardiogram studies were used to assess cardiac status and to measure combined cardiac output, cardiothoracic ratio, inferior vena cava diameter, and descending aorta peak systolic velocity. Doppler findings were also noted and abnormalities were further used to determine high-output cardiac failure.

1.3. Tumor characteristics and growth

SCT tumor volumes were calculated using a formula for obtaining a prolate ellipsoid using three orthogonal planes measured on ultrasound—craniocaudal, transverse, and anterior–posterior [9]. Volumes were calculated similarly using MRI in addition to assigning composition percentages related to cystic and solid components. SCT growth rate was calculated as the difference between tumor volumes on a late- and early-gestation ultrasound divided by the difference in time between the two evaluations. Furthermore, volumes were plotted for each patient at each recorded time point to determine patterns of growth and the relationship to outcomes.

1.4. Outcomes

Outcomes evaluated were survival, high-output cardiac failure (HOCF), hydrops, maternal mirror syndrome, and preterm delivery. HOCF was defined as an adjusted combined cardiac output of >625 ml/min/kg concurrent with abnormal Doppler findings, impending fetal hydrops, or as clinically documented as an indication for fetal intervention [10]. Fetal hydrops was defined as two or more fetal body cavities containing fluid. Preterm delivery was defined as live delivery prior to 37 weeks of gestation. Patients were grouped into those who had good outcomes and those who had adverse outcomes (i.e. any complication of death, HOCF, hydrops, or preterm labor during pregnancy) for simplicity of analysis. Good outcomes were defined as full-term delivery with no fetal cardiac compromise and survival to 60 days of life.

1.5. Statistical analysis

Variables were evaluated using Student's *t*-test and chi-squared tests with respect to outcome where appropriate. Variables were analyzed using receiver operator characteristics (ROC) to determine the area under the curve (AUC) or its predictive value. A cutoff value based on optimal sensitivity and specificity was selected. Patients were then stratified based on these values and their outcomes were analyzed with Fisher's Exact test. Pearson's correlation test was used to determine significant relationships between composition and tumor growth rate. Statistical analysis was performed using Prism 6.0 (GraphPad software, La Jolla, CA). Values were reported as mean ± standard error of the mean unless otherwise indicated. A p-value of <0.05 was considered statistically significant.

2. Results

During the study period a total of 40 patients were evaluated for SCT at the fetal care center. Twelve patients were excluded from the study: three patients voluntarily terminated their pregnancy, one patient had multiple tumors in addition to the SCT, one patient had a final pathologic diagnosis of kaposiform endothelioma, one patient with dichorionic diamniotic twin gestation was found to have in utero demise of the affected twin at the initial evaluation, and two patients had urgent open fetal surgery for HOCF shortly after their initial evaluation. The remaining four excluded patients were found to have favorable parameters, i.e. small size and/or predominately cystic tumors, during their evaluation went back to their local facility for their care and management. As expected, these four favorable patients had uncomplicated deliveries and hospital courses with 100% survival beyond 6 months old.

Of the 28 patients who met the criteria for analysis, the mean maternal age was 27 years (SD = 4.8, range 15–34 years) with a mean gestational age at initial evaluation of 24.18 weeks (SD = 4.51, range 18.43–36 weeks). Three of the four patients with hydrops died in utero (75% mortality). The mean gestational age at delivery of live births ($n = 25$) was 33.95 weeks (SD = 4.15, range 26.57–39.29 weeks). Two patients died soon after birth: one from premature delivery at 26.57 weeks' gestation and the other from in utero tumor rupture and significant hemorrhage.

Table 1
Tumor volumes and growth rates stratified by outcome.

	Initial tumor volume (cm^3)	Late tumor volume (cm^3)	Tumor growth rate (cm^3/week)
Survival ($n = 23$)	64.21 ± 19.07	604.06 ± 108.94	68.47 ± 12.32
Death ($n = 5$)	164.33 ± 55.47	673.85 ± 152.65	258.90 ± 67.23
p-Value	0.05*	0.78	<0.0001*
No HOCF ($n = 15$)	78.32 ± 28.09	520.52 ± 136.84	51.64 ± 14.02
HOCF ($n = 4$)	86.44 ± 27.81	727.28 ± 120.39	161.13 ± 35.02
p-Value	0.84	0.27	0.005*
No hydrops ($n = 24$)	66.21 ± 18.34	641.55 ± 108.33	78.01 ± 12.76
Hydrops ($n = 4$)	177.37 ± 70.01	466.33 ± 208.34	249.26 ± 102.37
p-Value	0.04*	0.52	0.002*
Full-term ($n = 11$)	90.63 ± 37.20	413.03 ± 172.75	36.86 ± 15.00
Preterm ($n = 14$)	67.71 ± 26.08	805.55 ± 105.35	114.69 ± 20.82
p-Value	0.61	0.05	0.0009*
Good outcomes ($n = 11$)	90.63 ± 37.20	413.03 ± 172.75	36.86 ± 15.00
Adverse outcomes ($n = 17$)	76.56 ± 22.13	748.19 ± 95.06	144.93 ± 28.01
p-Value	0.73	0.08	0.007*

HOCF, high-output cardiac failure.
All values are expressed as mean ± standard error of mean.
* Indicates statistical significance.