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Prenatal solid tumor volume index: novel prenatal predictor of adverse outcome in sacrococcygeal teratoma

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ABSTRACT

Background: Sacrococcygeal teratoma is the most common neonatal tumor. Fetuses with large tumors may develop hydrops from a high cardiac output state (HCOS) and progress rapidly to fetal demise. We postulate that the prenatal solid tumor volume index (STVI), or the ratio of solid tumor volume to the estimated fetal weight (EFW), has greater impact than the total tumor volume in outcome prediction.

Methods: A retrospective chart review of all sacrococcygeal teratoma patients ($n = 38$) between 2005 and 2012 was conducted. Total tumor volume and percent of solid component were calculated by magnetic resonance imaging and then normalized by dividing them by either head circumference or EFW. Outcomes measured were survival, hydrops or high cardiac output state, defined as a combined ventricular output of >625 mL/min/kg with abnormal Doppler or echocardiogram findings.

Results: Thirty-one patients were included in the study. All deaths ($n = 7$) had either high cardiac output state or hydrops. At a total tumor volume/EFW >0.16, the patient was 17 times more likely to develop HCOS/hydrops ($P = 0.001$) with 81.25% sensitivity and 86.67% specificity. At a STVI >0.09, the patient was 120 times more likely to develop HCOS/hydrops ($P < 0.0001$) with 81.25% sensitivity and 100% specificity.

Conclusions: While total tumor volume aids in stratifying patients into high risk categories, STVI (solid tumor volume/EFW) is a better predictor of adverse outcomes. This data will allow us to identify patients who are high risk for cardiac compromise and guide appropriate therapy.

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1. Introduction

Sacrococcygeal teratoma (SCT) is the most common congenital tumor in neonates with an incidence of 1 in 23,000 to 40,000 births [1]. A majority of the tumors are detected during routine prenatal screening, which allows for enhanced maternal counseling, more intensive monitoring, and appropriate intervention when necessary. Despite the improvements in prenatal diagnosis, mortality still approaches 50% during the prenatal period secondary to maternal and fetal complications from the possible high flow vascular tumor pathophysiology [2,3].

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The high prenatal mortality stems from its unpredictable nature in terms of growth and vascularization [3,4]. Tumors become large and vascular, resulting in internal tumor arteriovenous shunting. Venous overload leads to high output cardiac failure in the fetus and sequelae such as cardiac failure, hydrops, maternal mirror syndrome, and fetal demise can ensue [5–7]. This high output cardiac pathophysiology then becomes one of the relative indications that requires urgent prenatal intervention [2]. Attempts have been made to calculate how the tumor will behave but only a few characteristics have been correlated with poor outcomes, including large size and vascularity [8–10].

Radiological advances in high resolution ultrasound and ultra-fast magnetic resonance imaging (MRI) has increased the ability to diagnose many teratomas early during the prenatal course. The focus of care then becomes stratification of patients into low and high risk groups, which facilitates appropriate counseling and interval monitoring. Frequent cardiac, ultrasound, and MRI assessments for patients with worrisome tumor characteristics, such as tumor growth and signs of high output cardiac failure, permits earlier detection of complications that can be managed with measures such as intensive inpatient monitoring, open fetal surgery, early delivery, and *ex utero intra partum* therapy to resection [2,4,11,12]. However, the risk-benefit ratio in regards to management can be difficult to assess. Early delivery is hindered by the mortality and morbidity associated with prematurity. Expectant management with closer monitoring can be disastrous as hydrops can manifest precipitously and rapidly progress to intrauterine fetal demise. Finally, fetal surgery can be a lifesaving intervention but may incur its own complications to both the mother and the baby. For the most part, the decision tree has been based on clinical expertise utilizing minimal objective indices in an algorithm [13].

The purpose of this study is to investigate the predictive value of solid tumor volume on outcome, specifically development of a high cardiac output state and hydrops. We aimed to develop a solid tumor volume index (STVI) that could be used to stratify patients into high risk groups and assist in their management algorithm, with the goal of optimizing the risk-benefit ratio for both mother and child.

2. Materials and methods

2.1. Data collection

A retrospective review of all SCT patients prenatally evaluated at our fetal care center between the 2005 and 2012 was conducted. Approval was obtained from the Institutional Review Board of Cincinnati Children's Hospital Medical Center (IRB #2011-2078). Patients were excluded from the study if pregnancy was voluntarily terminated prior to delivery, adequate postnatal data was not available, or if multiple tumors were present. Data collected included gestational age at evaluation, time of imaging and delivery, tumor dimensions and characteristics, estimated fetal weight (EFW), and maternal and fetal outcome. Outcomes evaluated were survival and development of a high cardiac output state or frank fetal hydrops.

2.2. Ultrasound imaging

Prenatal ultrasound was used to obtain fetal status, EFW using the Hadlock method, head circumference (HC), and Doppler indices [14]. The type of SCT was also obtained using the American Academy of Pediatrics, Surgical Section (AAPSS) classification system [15]. Findings of placentomegaly, reversal of diastolic blood flow in the umbilical arteries, and evidence for third space fluid status contributed to the diagnosis of impending fetal hydrops [12]. Fetal hydrops was defined as two or more fetal body cavities containing effusion or abnormal fluid collection with some evidence of cardiac compromise.

2.3. Tumor volumes

Fetal MRI was performed on 38 pregnancies complicated by fetal SCT. MRI studies were obtained utilizing a phased array body coil in a 1.5-T scanner (Horizon; GE Healthcare Milwaukee, WI). A field-of-view of 30 cm and 3- to 4-mm thick contiguous slices were performed in three orthogonal planes with T2-W, single-shot fast spin-echo and supplemented with additional, 2-D fast imaging employing steady-state acquisition. Fast spoiled gradient-echo T1-W sequences were obtained in 1–2 planes at a slice thickness of 5 mm. Anatomical imaging was utilized to grade tumor extent. A single radiologist (B.K.F.) retrospectively obtained total tumor volume by performing maximum tumor measurements in craniocaudal, transverse, and anterior-posterior dimensions. Volume was calculated using a formula for obtaining a prolate ellipsoid [16]. The same radiologist also ascertained the percentage of solid tumor component *versus* cystic portion. The maximum craniocaudal, transverse, and anterior posterior dimensions of the solid component of the tumor were utilized to calculate solid tumor volume and then divided by total tumor volume to determine the percentage of solid component of the tumor. In 10 cases, the tumor was significantly mixed such that solid and cystic components could not be separated. In these cases, the solid component percentage was subjectively designated. In order to adjust for differences in gestational age, the volumes were also divided by either HC or EFW. The STVI was specifically calculated by dividing the solid tumor volume by the EFW. Although using the Hadlock method does not theoretically augment the tumor size and/or weight with the EFW, we nevertheless also used HC as a secondary reference to validate our results.

2.4. High cardiac output state

Fetal echocardiogram studies were used to assess cardiac status and the high cardiac output state (HCOS). They were performed at the initial evaluation and at subsequent intermittent time points throughout the prenatal period as clinically indicated. HCOS was defined as an elevated combined cardiac output that was persistent on two or more echocardiograms, displayed a gradual increase over time, or in the presence of abnormal Doppler or echocardiogram findings. We used two SD above the normal biventricular combined cardiac output or 625 mL/min/kg. The normal reference range is 425 ± 100 mL/min/kg [17]. Abnormal findings used in interpreting impending cardiac failure included a cardiac-

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