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Systemic hypertension in giant omphalocele: An underappreciated association

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ABSTRACT

Purpose: To evaluate the incidence, severity and duration of systemic hypertension in infants born with giant omphalocele (GO).
Methods: A retrospective review of patients born from 2003 through 2013 with a GO or intestinal atresia (control population) and managed at a single institution was performed. The hospital course was reviewed including all blood pressures, method of omphalocele repair, requirement for antihypertensive medications and renal function.
Results: Forty-five GO and 20 control patients met criteria for the study. Thirty-three GO patients underwent Schuster repair and 12 GO patients underwent delayed repair after epithelialization. Overall, 78% of GO patients had episodes of hypertension (82% Schuster and 67% delayed repair) compared to 15% of control patients ($P < 0.001$). The majority of episodes were transient and occurred in the postoperative period (97%). Hypertension was persistent in 4 GO patients. These patients required antihypertensive medication at discharge, which was discontinued as an outpatient. No patient demonstrated significant evidence of renal abnormalities as indicated by renal ultrasound, urinalysis and/or serum creatinine level at the time of hypertension.
Conclusion: Episodes of systemic hypertension are frequent in patients with GO. Episodes are often post-operative, transient and can be present in patients undergoing either a delayed or Schuster repair. A small subset of patients will have persistent hypertension requiring antihypertensive medication that can be weaned off in an outpatient setting.

Omphaloceles are frequently classified as small or giant. A giant omphalocele (GO) is defined as one in which a majority of the liver is contained in the defect [1,2]. Surgical repair is ultimately required but the method of repair is dependent on surgeon preference, size of the omphalocele defect, associated anomalies and the infant's clinical condition. Options for surgical repair include a primary repair for small omphaloceles in stable infants; a staged closure, such as the Schuster procedure, for stable infants (near term, no respiratory distress) with larger defects assessed to be able to tolerate closure; or escharotic therapy followed by a delayed closure secondary to surgeon preference or in infants that are unstable or with large defects that are assessed to be unable to tolerate a staged procedure in a reasonable length of time [3–5].

Despite the many known comorbidities associated with GOs, little attention has been given to presence of systemic arterial hypertension and/or renal dysfunction in infants with GOs. Limited reports exist in the literature describing episodes of transient systemic arterial hypertension after surgical closure of omphaloceles [6–8]. The majority of patients evaluated in these reports have small omphaloceles (23 patients) with a minority presenting with GOs (9 patients). In the current study we present our experience at a single institution with the postnatal management of infants diagnosed with a GO. We focus on the surgical management of these infants with particular attention to the development of systemic arterial hypertension and/or evidence of renal insufficiency as it relates to the method and timing of surgical repair.

1. Materials and methods

This is a retrospective review of patients born from 2003 through 2013 who were prenatally diagnosed with a GO and who had their neonatal and surgical management at our institution. This study was approved by the CHOP Institutional Review Board, Committee for the Protection of Human Subjects (IRB 06-003779). Infants with a GO were defined as those that contained the majority of the liver herniated through the abdominal wall defect as seen on prenatal ultrasound and physical examination at birth. The hospital records of all infants in the study were reviewed to assess for gestational age (GA) and weight at birth, timing of surgical repair and method of surgical repair. All surgical repairs were categorized as either a staged closure using the Schuster

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technique [4] or a delayed repair ("paint and wait"). The Schuster procedure involved the sequential tightening of polytetrafluoroethylene (PTFE) mesh (C. R. Bard Inc.; Cranston, RI), which had been sutured to the abdominal wall fascia to enclose the omphalocele with the membranes intact. The fascia was subsequently closed when the contents of the omphalocele are level with the abdominal wall. The delayed repair was performed beyond the immediate neonatal period after topical escharotic dressing with Silvadene® cream 1% (silver sulfadiazine) or Xeroform® (gauze infused with petrolatum and 3% bismuth tribromophenateis) had been performed and epithelialization of the omphalocele sac occurred. Since this review included only patients with GOs, there were no patients who underwent primary closure of the omphalocele defect. The daily hospital records of all patients were reviewed for their entire pre and postoperative admission with particular attention to all systolic and diastolic blood pressure measurements and pain and/or narcotic withdrawal assessments at the time of the blood pressure measurements. Systolic and diastolic blood pressures ≥ the 95th percentile according to GA at birth, age at blood pressure measurement and birth weight were defined as hypertensive [8,9]. Blood pressure readings taken at a time when the infant was assessed to be in pain or withdrawing from narcotics were discarded. Pain was assessed according to the Face Legs Activity Cry and Consolability (FLACC) behavioral pain assessment tool [10,11]. Narcotics withdrawal was assessed using the Withdrawal Assessment Tool-1 (WAT-1), which is a scale based on the presence of the following signs: loose stools, vomiting/retching, elevated temperature, tremor, sweating, uncoordinated/repetitive movement, yawning/sneezing and startle to touch [12,13]. Additionally, the need for antihypertensive medication [Capoten® (captopril), Vasotec® (enalapril) or Apresoline® (hydralazine)] as well as diuretics [Lasix® (furosemide) or Diuril® (chlorothiazide)] was noted. Neonates diagnosed with and undergoing a laparotomy and surgical repair of an intestinal atresia and without additional congenital anomalies were included as an age-matched control population to assess the contribution of an abdominal procedure and hospitalization in the neonatal intensive care unit (NICU) to the etiology of systemic hypertension. Poor renal perfusion can contribute to the etiology of hypertension. Alternatively, impaired renal function may be caused by hypertension or associated with other physiologic derangements in patients with GO such as pulmonary hypertension [14–19]. Thus we reviewed findings on renal ultrasound, serum creatinine levels and urinalysis results as an indication of renal function in our patients. Statistical significance was calculated using the Fisher exact test and Student *t* test. $P \leq 0.05$ was considered significant.

2. Results

2.1. Patients

A total of 45 GO patients and 20 control patients met study criteria and were included in this review. Neonatal and surgical data are summarized in Table 1. There was no significant difference between the GA at birth and the birth weight between all patients with GO and the control population as well as between infants undergoing a Schuster repair compared to a delayed repair. Infants undergoing the Schuster procedure required an average of 5 ± 2 (median: 4.5) sequential reductions until complete closure of the abdominal wall fascia was obtained. There were 5 patients who required conversion to either a delayed closure (N = 2) or closure of the abdominal wall fascia with vicryl mesh (N = 3) after a failed Schuster procedure. The reasons for a failed Schuster procedure included a significant liver bleed, mesh infection, dehiscence of the abdominal fascia and dislodgement of the mesh from the fascia. Patients born with GO had a prolonged NICU stay independent of the mode of surgical repair. Infants undergoing a delayed repair were discharged from the hospital after the initial NICU stay with subsequent readmission for final abdominal fascia closure. The length of hospital stay at the time of final abdominal fascia closure in infants undergoing a delayed repair was significantly shorter than that required in the immediate newborn period for both delayed repair and Schuster patients.

2.2. The association of GO with systemic arterial hypertension

Seventy-eight percent of GO patients compared to 15% of control patients ($P < 0.001$) met criteria for systemic hypertension (Table 2). Both systolic and diastolic hypertensive events occurred in GO patients with a higher percentage of systolic episodes. Hypertensive events occurred more frequently in the postoperative period especially in patients undergoing a Schuster procedure in which 100% of events occurred postoperatively and no hypertensive events occurred preoperatively. Hypertensive events occurred throughout the hospital course ranging from immediately post-operative to just prior to discharge in Schuster patients and as early as day of life 9 in delayed repair patients. The hypertensive events were transient in GO and control patients. Of those GO patients categorized as hypertensive, only 21% and 8% of the days during their hospital stay had an episode of systolic and diastolic hypertension respectively. In addition to being transient, most hypertensive episodes were mild, not requiring pharmacologic treatment. No control patients required pharmacologic management of the hypertensive episodes. There were, however, 5 GO patients that required either captopril, enalapril or hydralazine to manage their hypertension preoperatively (N = 1, patient undergoing delayed repair) or after repair by the Schuster procedure (N = 4) (Table 3). The 4 Schuster patients requiring anti-hypertensive medication post-operatively were discharged on the medication, which was discontinued as an outpatient by 3 months to 7 years post discharge.

Of note, a significant number of patients were treated with a diuretic principally for respiratory symptoms. However, this also could affect the patients' blood pressure.

Table 1
Patient population.

	N	GA @ birth[*#] (weeks)	birth weight[*#] (grams)	age @ surgery (days)		NICU LOS[*&] (days)	LOS @ delayed repair (days)
Schuster	33	36.6 ± 2 [37]	2771 ± 619 [2705]	4.8 ± 4 [3] Initial stage	16.6 ± 12 [11] Final closure	83 ± 63 [69]	–
Delayed	12	35.1 ± 2.8 [35.5]	2380 ± 717 [2500]	639 ± 567 [425]		63 ± 45 [45.5]	14 ± 14 [7]
All GOs	45	36.2 ± 2.4 [37]	2667 ± 669 [2680]	–		77 ± 60 [58]	–
Control	20	35.7 ± 2.7 [36]	2527 ± 705 [2447]	3.9 ± 7 [2]		32 ± 24 [23]	

Associated anomalies for GO patients (28% of patients): vertebral, shortened long bones, hemangioma, TEF, kyphoscoliosis, bronchopulmonary sequestration, coarctation of aorta, CDH, pentology of cantrell, duodenal atresia, BWS, heterotaxy/asplenia, Morgagni hernia, TOF, VSD.
Control patients: duodenal atresia, N = 10; jejunoileal atresia, N = 9; colonic atresia, N = 1.
LOS, length of stay; TEF, tracheoesophageal fistula; CDH, congenital diaphragmatic hernia; BWS, Beckwith–Wiedemann syndrome; TOF, Tetralogy of Fallot; VSD, ventricular septal defect.
LOS @ delayed repair indicates the hospital stay at time of delayed repair.
Median values are presented in brackets "[ ]".
[*] $P > 0.12$ when comparing Schuster to delayed repair.
[#] $P > 0.4$ when comparing all GO to control.
[&] $P < 0.05$ when comparing all GO to control.