

Targeted Neonatal Echocardiography-Guided Therapy in Vein of Galen Aneurysmal Malformation: A Report of Two Cases with a Review of Physiology and Approach to Management

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Abstract

Vein of Galen malformation results in predictable changes in physiology which exist on a continuum. Severe pulmonary hypertension may present as hypoxemia; however, excessive reduction in pulmonary vascular resistance may precipitate progressive pulmonary overcirculation and impaired systemic blood flow. Right ventricular performance and the patency and direction of the ductus arteriosus may play a crucial role in postductal organ perfusion. Physiological stabilization may be complex and variable over time. The utilization of targeted neonatal echocardiography to guide treatment decisions may improve the ability to provide therapy tailored to the specific disease pathophysiology and monitor serially as conditions change. An enhanced approach to physiological stabilization may reduce the risk of unexpected decompensation and allow for thoughtful, controlled endovascular embolization in appropriate candidates.

Keywords

- ▶ vein of Galen malformation
- ▶ targeted neonatal echocardiography
- ▶ hemodynamics

Neonates with vein of Galen aneurysmal malformation (VGAM) present with a variety of systemic and pulmonary cardiovascular manifestations due to high-volume preductal left-to-right shunt. In utero maldevelopment of the pulmonary vascular bed due to overcirculation may lead to severe pulmonary hypertension (PH),¹ presenting at birth as hypoxic respiratory failure. The postnatal cardiovascular course represents a pathophysiologic continuum from asymptomatic to the progressive development of hypotension, and impaired organ perfusion. Studies have shown that early neonatal cardiovas-

cular decompensation is a marker of poor outcome with a high mortality rate without treatment.² Treatment using staged endovascular embolization requires admission to a specialized center; however, attaining cardiovascular stability prior to embolization may be challenging.³ These patients represent a unique population, rarely seen by most neonatologists. The clinical presentation and degree of hemodynamic compromise may be variable meriting standardization of the approach to assessment and therapeutic intervention. Targeted neonatal echocardiography (TnECHO) by trained neonatologists is used

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in many centers across the world to manage pulmonary and systemic hemodynamics.⁴⁻⁸ Most neonatologists with this advanced skill and fundamental knowledge of cardiovascular physiology will see a large volume of critically ill newborns with acute PH, right ventricular dysfunction, and hemodynamic compromise where the range of physiologic derangement may be comparable with that of neonates with VGAM. In this report of two representative but complex cases, we describe the value of novel physiological insights gained from comprehensive TnECHO assessment and provide a systematic approach to preoperative stabilization.

Case 1

A male infant was born at 38 weeks by emergency cesarean section for poor biophysical profile at a rural hospital. Fetal assessment performed on the day of delivery revealed a large brain vascular malformation. Postnatal adaptation was good apart from mild respiratory depression that responded to routine resuscitation and birth weight was 3.9 kg. The infant was transferred to the regional tertiary neonatal intensive care unit (NICU) on continuous positive airway pressure (CPAP). Magnetic resonance imaging (MRI) of the brain on postnatal day 1 confirmed a large vein of Galen aneurysmal malformation (VGAM). An anatomic echocardiogram demonstrated right-to-left shunt at both the ductal and foraminal levels and a dilated right ventricle (RV) with RV

systolic dysfunction. A diagnosis of PH was made. The fraction of inspired oxygen (FiO₂) administered had increased from room air at transfer to 1.0 on CPAP 7 cmH₂O; therefore, 20 ppm of inhaled nitric oxide (iNO) was initiated noninvasively. Immediate reduction in FiO₂ to 0.3 was observed. On postnatal day 2, he developed evidence of end-organ compromise and a TnECHO consultation was requested. Bidirectional ductal shunt, normal RV systolic performance, and high biventricular output with a ratio of right ventricular output (RVO) to left ventricular output (LVO) of 1.5 were identified (► **Table 1**). An intravenous infusion of dobutamine was initiated and then escalated to a dose of 10 µg/kg/min. The patient subsequently developed oliguria and significant lactic acidosis on postnatal day 3. Repeat TnECHO demonstrated a closing ductus arteriosus (DA) with bidirectional flow, severe RV dysfunction, and reduced RVO with an RVO:LVO of 0.42. Mechanical ventilation and prostaglandin E₁ were started and transfer to an embolization center was arranged. At the time of transfer, despite stable ventilation with FiO₂ 0.28 and iNO 20 ppm, and treatment with dobutamine and prostaglandin, lactic acidosis and severe oliguria recurred. TnECHO assessment demonstrated a large, predominantly left-to-right DA with normal RV systolic performance. iNO was discontinued and respiratory support modified to encourage right-to-left DA flow, which was temporally related to normalization of both the lactic acidosis and urine output. Follow-up TnECHO demonstrated a

Table 1 Clinical and echocardiography course of case 1

Postnatal age (d)	2	3	4	4	7
Clinical condition					
Preductal arterial pressure (mm Hg)	55/34	65/36	68/22	66/40	52/44
Urine output (mL/kg/h)	0	1.8	0	3.6	0.7
Lactate (mmol/L)		8.0	5.1	1.3	4.4
Preductal SpO ₂ (%)	95	93	92	92	92
FiO ₂	0.5	0.35	0.28	0.26	0.21
Ventilation (cmH ₂ O)	CPAP 7	VG 4.5 mL/kg, PEEP 7	VG 4.5 mL/kg, PEEP 7	VG 4.5 mL/kg, PEEP 7	VG 4.5 mL/kg, PEEP 7
Adjunct therapy	iNO	iNO, dobutamine	iNO, dobutamine, PGE	Dobutamine, PGE	
TnECHO findings					
Ductal shunt direction and pattern	Bidirectional unrestrictive	Small restrictive	Mainly L→R unrestrictive	R→L large unrestrictive	R→L small, unrestrictive
TAPSE (mm)	11.8	5.1	10.2	11.1	4.7
RVO (mL/min/kg)	550	190	320	460	210
Ejection fraction (%)	54	62	63	56	62
LVO (mL/min/kg)	365	454	360	330	340
RVO:LVO ratio	1.5	0.42	0.89	1.4	0.62
Recommendations and response					
Therapy	Dobutamine	Prostaglandin	Stop iNO	↓ PGE and dobutamine	Dobutamine restarted
Response	↑ Urine output	↓ Lactate to 3.0 mmol/L	↓ Lactate to 2.0 mmol/L ↑ Urine output	Gradual ↑ Lactate ↓ Urine output	↓ Lactate to 1.6 mmol/L ↑ Urine output

Abbreviations: CPAP, continuous positive airway pressure; FiO₂, fraction of inspired oxygen; iNO, inhaled nitric oxide; LVO, left ventricular output; PEEP, positive end-expiratory pressure; PGE, prostaglandin E; RVO, right ventricular output; SpO₂, oxygen saturation; TAPSE, tricuspid annulus plane systolic excursion; TnECHO, targeted neonatal echocardiography; VG, volume guarantee.

large right-to-left DA with normal RV performance and RVO:LVO of 1.4. Once stable, weaning cardiovascular support was attempted but due to recurrence of poor perfusion and severe RV dysfunction, he underwent successful VGAM embolization with symptomatic improvement.

Case 2

A female infant was born by vaginal delivery following an uncomplicated pregnancy at 37 weeks with a birth weight of 2.4 kg. Shortly after delivery, she was noticed to be visibly cyanotic with right hand oxygen saturation (SpO₂) of 70%. She required 3 L of flow via nasal canula in FiO₂ of 1.0 to achieve a preductal SpO₂ of 90%. Pre- and postductal arterial pressures were 52/29 (37), right arm and right leg were 41/35 (37), respectively. She was transferred to the local tertiary NICU at 4 hours postnatal age where she was placed on CPAP in FiO₂ of 0.5. An anatomic echocardiogram was done due to suspicion of congenital heart disease. A large DA with right-to-left shunt and a dilated right heart with normal biventricular systolic performance was thought to be in keeping with transitional circulation. On postnatal day 2, a head ultrasound, done to evaluate decreased tone, was suggestive of VGAM. Despite initiation of furosemide, she remained oliguric and a capillary blood gas demonstrated evidence of metabolic acidosis (pH of

7.14, CO₂ of 48, and HCO₃ of 15). She was electively intubated for transport to an embolization center. Upon arrival to our center, she was noted to be critically unwell; specifically, she remained ventilated on moderate settings in FiO₂ of 0.65 and had low preductal systolic arterial pressure, oliguria, and elevated lactate (►Table 2). TnECHO evaluation demonstrated a small, restrictive right-to-left DA with moderate-to-severe RV dysfunction and RVO:LVO ratio of 1.5 (►Table 2). An intravenous infusion of dobutamine was initiated at a dose of 5 µg/kg/min and increased to 10 µg/kg/min, but only with modest improvement after 4 hours; therefore, prostaglandin E₁ was added. FiO₂ subsequently declined to 0.45 with concomitant improvement in arterial pressure, urine output, and lactate. On postnatal day 3, she was transferred to the radiology department for MRI of the brain. During the procedure, she acutely desaturated to preductal SpO₂ of 75%, despite FiO₂ of 1.0 and iNO which had been started empirically a priori. Subsequent TnECHO demonstrated a large, exclusively right-to-left DA with normal RV systolic performance and high RVO with an RVO:LVO of 2.4 (►Table 2). Despite attaining clinical stability, the multidisciplinary team of a neonatologist, neurologist, neurosurgeon, and neurointerventionalist recommended withdrawal of intensive care based on severe white matter disease and poor neurological prognosis.

Table 2 Clinical and echocardiography course of case 2

Postnatal age (d)	2	2 ^{+4 h}	2 ^{+4 h}	3
Clinical condition				
Preductal arterial pressure (mm Hg)	49/37	53/36	64/36	60/43
Urine output (mL/kg/h)	0.1	0.3	1.2	4.9
Lactate (mmol/L)	5.5	5	2.5	1.3
Preductal SpO ₂ (%)	90	93	92	92
FiO ₂	0.65	0.65	0.45	0.47
Ventilation (cmH ₂ O)	VG 5 mL/kg, PEEP 7	VG 5 mL/kg, PEEP 7	VG 5 mL/kg, PEEP 7	VG 5 mL/kg, PEEP 7
Adjunct therapy		Dobutamine 10 µg/kg/min	Dobutamine, PGE ₁	iNO, dobutamine, PGE ₁
TnECHO findings				
Ductal shunt direction and pattern	R→L moderate, restrictive	R→L moderate, restrictive	R→L large unrestrictive	R→L large unrestrictive
TAPSE (mm)	6.4	7.2	8.8	11.1
RVO (mL/min/kg)	330	350	400	560
Ejection fraction (%)	57	60	62	56
LVO (mL/min/kg)	220	215	218	230
RVO:LVO ratio	1.5	1.6	1.8	2.4
Recommendations and response				
Therapy	Dobutamine	Prostaglandin	iNO if ↑ FiO ₂ > 0.6	
Response		↓ Lactate to 3.4 mmol/L ↑ Urine output		

Abbreviations: FiO₂, fraction of inspired oxygen; iNO, inhaled nitric oxide; LVO, left ventricular output; PEEP, positive end-expiratory pressure; PGE₁, prostaglandin E₁; RVO, right ventricular output; SpO₂, oxygen saturation; TAPSE, tricuspid annulus plane systolic excursion; TnECHO, targeted neonatal echocardiography.

Table 3 Suggested medical management based on pathophysiological phenotype

	Right ventricular dysfunction	High PVR ∴ low PBF	Pseudocoarctation ∴ low SBF
Clinical	FiO ₂ > 0.6 ↓ Urine output ↓ Systolic arterial pressure ↑ Lactate/metabolic acidosis	FiO ₂ > 0.6 ↓ Urine output ↓ Systolic arterial pressure ↑ Lactate/metabolic acidosis	FiO ₂ < 0.6 ↓ Urine output ↓ Diastolic arterial pressure ↑ Lactate/metabolic acidosis
Echocardiography	RVOLVO ↓ TAPSE; ↓ FAC	RVOLVO Ductal shunt more L→R	
Desired physiologic effect	Augment heart function and reduce afterload	Lower PVR to promote PBF	Facilitate right-to-left ductal shunt
Therapeutic approach	1. Dobutamine or low dose epinephrine 2. iNO and/or PGE	1. Optimize CO ₂ , FiO ₂ 2. Sedation/muscle relaxation 3. iNO to reduce PVR	1. Prostaglandin 2. Permissive hypercapnia, lower target SpO ₂ 3. Dobutamine

Abbreviations: CO₂, carbon dioxide; FiO₂, fraction of inspired oxygen; iNO, inhaled nitric oxide; LVO, left ventricular output; PBF, pulmonary blood flow; PGE, prostaglandin E; PVR, pulmonary vascular resistance; RVO, right ventricular output; SBF, systemic blood flow; TAPSE, tricuspid annulus plane systolic excursion.

Discussion

The immediate postnatal period is a time of physiological metamorphosis when changing pulmonary and systemic vascular resistance (SVR) are essential adaptations. The clinical presentation of VGAM in newborns represents a

spectrum with multiple pathophysiological changes which may contribute to poor tissue oxygen delivery.

The approach to treatment of these patients requires careful physiologic delineation. Possible contributors to instability include impaired RV performance, low pulmonary blood flow due to high pulmonary vascular resistance, and

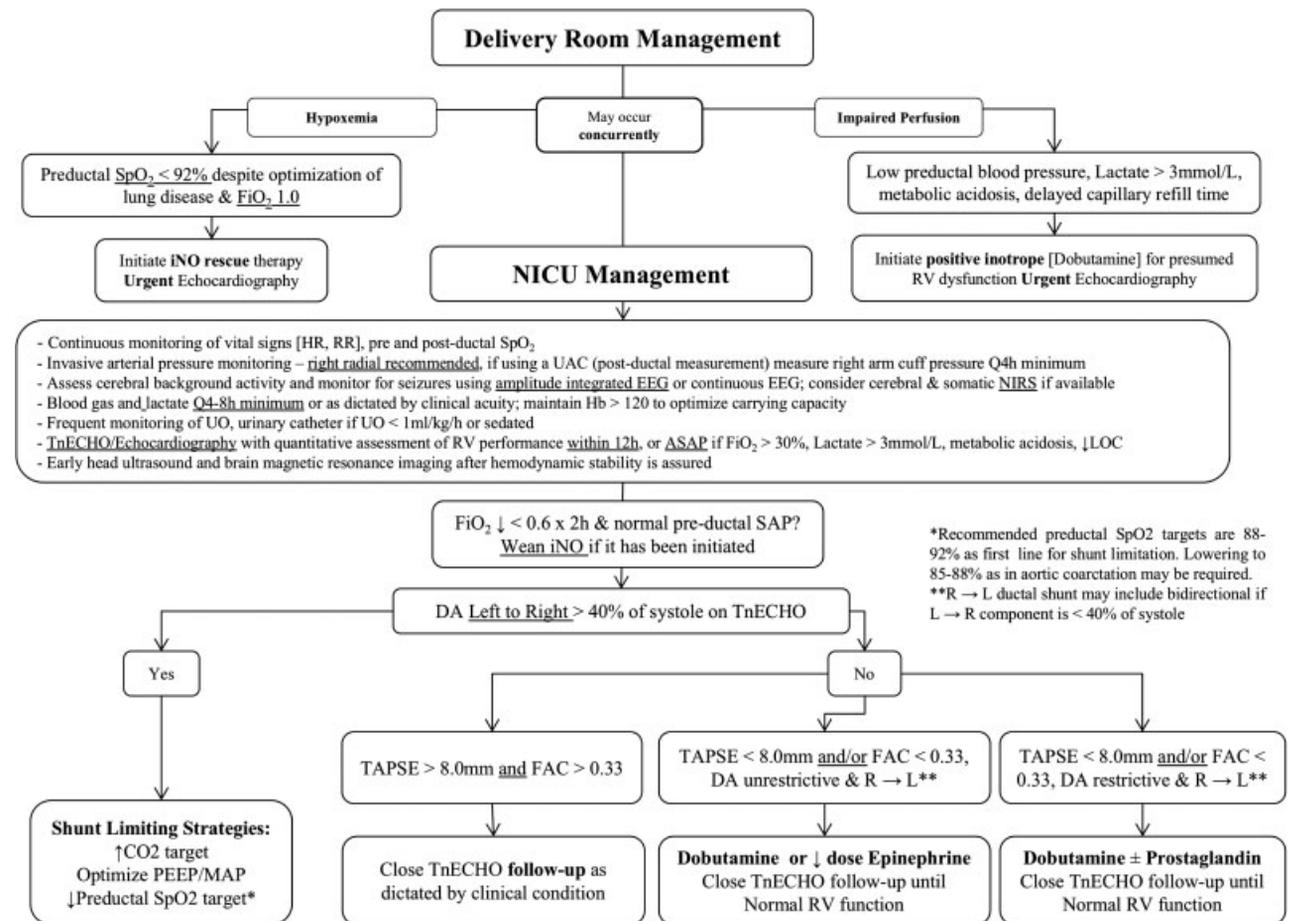


Fig. 1 Suggested management algorithm for the cardiovascular stabilization of neonates with vein of Galen aneurysmal malformation. CO₂, carbon dioxide; DA, ductus arteriosus; EEG, electroencephalogram; FAC, fractional area change; FiO₂, fraction of inspired oxygen; HR, heart rate; iNO, inhaled nitric oxide; L, left; LOC, level of consciousness; MAP, mean airway pressure; NICU, neonatal intensive care unit; NIRS, near-infrared spectroscopy; PEEP, positive end-expiratory pressure; R, right; RR, respiratory rate; RV, right ventricle; SpO₂, oxygen saturation; TAPSE, tricuspid annulus plane systolic excursion; TnECHO, targeted neonatal echocardiography; UO, urinary output.

pseudocoarctation physiology (→Table 3). First, both high pulmonary blood flow with subsequent pulmonary vascular muscularization^{9,10} with associated vascular hyperreactivity¹¹ contribute to high pulmonary pressure. Second, chronic volume loading leads to RV dilation and therefore increased susceptibility to afterload mediated dysfunction¹² and elevated energy demand.¹³ Finally, intracranial steal may contribute to heart dysfunction via low coronary root pressure and is associated with retrograde descending aortic flow which may cause pseudocoarctation physiology. Balancing the VGAM circulation requires pulmonary pressure to be sufficiently low to avoid RV decompensation and impaired cardiac output but not so low as to exacerbate systemic steal either via the VGAM or via left-to-right ductal shunt. Changing pulmonary pressure may precipitate dramatic changes in cardiovascular physiology which are difficult to piece together clinically. The use of iNO to improve oxygenation, therefore, requires careful consideration of timing and frequent reassessment to avoid precipitating pseudocoarctation as in our first case. In contrast, the combination of highly reactive pulmonary vasculature and a vulnerable RV may precipitate dramatic pulmonary hypertensive crisis in which iNO may be invaluable as in our second case. Documentation of normal RV systolic performance prior to any noxious stimulus is recommended.

We have developed an algorithm which recognizes the variance in phenotypic presentation and incorporates an approach to therapeutic intervention based on enhanced physiologic precision (→Fig. 1). Dobutamine has favorable properties as a relatively pure inotrope.¹⁴ The avoidance of potent systemic vasoconstrictors (e.g., dopamine, epinephrine, norepinephrine, vasopressin) is recommended, unless there is an additional illness with low SVR such as sepsis.¹⁵ Milrinone, a nonselective vasodilator, may cause dangerously low diastolic arterial pressure and compromise coronary and organ perfusion pressure. It may be considered cautiously, however, in the setting of increased LV exposed afterload following embolization to support myocardial performance. Prostaglandin has a dual role including RV afterload reduction and postductal delivery of systemic blood flow which may be relatively protected from the impact of intracranial steal. The ability to provide longitudinal assessment makes TnECHO an important tool in the acute management of these infants and may also provide insights into disease prognosis. It has been suggested that high combined cardiac output is associated with mortality in fetuses with VGAM,¹⁶ and therefore, postnatal cardiac output may provide useful insight. Interestingly, both a higher ratio of RVO:LVO to achieve stable systemic blood flow and severe white matter injury were identified in the second case indicating a greater shunt magnitude. The complexity and delicate balance of disease pathophysiology illustrated in these cases highlight the importance of management of this rare disorder in centers with both the neurointerventional and neonatal hemodynamic experience to optimize their care.

Conflict of Interest

None.

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