BMC Pediatrics

CASE REPORT Open Access

Circulatory collapse requiring mechanical circulatory support in a child with autoimmune adrenal insufficiency: a case report

Yahia Hejazi[1,3*], Ken Tegtmeyer[2,3], Meghan Chlebowski[1,3] and Katja M. Gist[1,3]

Abstract

Background We report a rare case of new onset autoimmune adrenal insufficiency in childhood, presenting with severe shock requiring mechanical circulatory support. In the current era of readily available imaging, laboratory and other diagnostic investigations, medical history and careful physical exam can often provide valuable diagnostic information for timely therapy.

Case presentation A 7-year-old boy with a history of mild intermittent asthma, presented with severe cardiogenic shock requiring extracorporeal membrane oxygenation (ECMO). Bronzing of his entire body was noted on physical exam. Stress dose hydrocortisone was given for suspected adrenal insufficiency. After weaning from ECMO and extensive rehabilitation, the patient recovered and was discharged home.

Conclusion Primary adrenal insufficiency (PAI) should be considered in the context of physical exam and laboratory findings, even in the presence of circulatory shock.

Keywords Circulatory shock, Autoimmune adrenal insufficiency, Extracorporeal membrane oxygenation (ECMO)

Case presentation

A 7-year-old boy with mild intermittent asthma presented to an outside hospital with 3 days history of lethargy and vomiting. Initial investigation revealed left lower lobe pneumonia. Because of severity of illness, he was transferred to a quaternary pediatric emergency department with clinical signs of hypotensive shock manifesting as lethargy, lactic acidosis and hypotension despite standard resuscitative measures including fluids and inotropic medications. On arrival to the emergency department at our institution he remained in profound shock but was initially mentating well and breathing unassisted with nasal canula oxygen supplementation. His initial vital signs were as follows: temperature 35 °C, heart rate 160 bpm, blood pressure 74/32 mmHg, and respiratory rate 35. He had a Glasgow Coma Scale score of 10. The patient's weight was 23 kg (around the 25th percentile), and his height was 124 cm (50th percentile). Physical exam was notable for skin hyperpigmentation of the entire body. Apart from the diffuse skin hyperpigmentation, there was no rash present on the body. The

*Correspondence:
Yahia Hejazi
yahia.hejazi@cchmc.org
[1]Cardiac Critical Care, The Heart Institute, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, MLC 2003, Cincinnati, OH 45229, USA
[2]Division of Critical Care Medicine, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, MLC 2003, Cincinnati, OH 45229, USA
[3]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

parents denied any sore throat, headache, diarrhea or sick contacts. His laboratory findings were notable for hyponatremia, refractory hypoglycemia, hepatic insufficiency, and acute kidney injury. The viral PCR (polymerase chain reaction) from nasopharyngeal swab tested positive for rhinovirus/enterovirus and he received stress dose hydrocortisone for suspected primary adrenal insufficiency (PAI). On attempted transport to the Pediatric Intensive Care Unit (PICU), he had severe symptomatic bradycardia with poor perfusion that responded to a brief run of cardiopulmonary resuscitation (CPR) as were indicated by Pediatric Advanced Life Support management algorithm. At that point he was intubated in the emergency department (ED) then admitted to the PICU. Over the next few hours, despite escalation of inotropic medications in the PICU, he continued to deteriorate with both hypotension and bradycardia. His echocardiogram initially showed normal biventricular systolic function that progressed to severe dysfunction and cardiogenic shock. He had a series of brief cardiac arrests for which he achieved return of spontaneous circulation (ROSC) with compressions and code dose epinephrine. Given his clinical state, he was cannulated via a cervical approach to veno-arterial (VA) extracorporeal membrane oxygenation (ECMO). Given the concomitant concern for acute fulminant myocarditis given the constellation of cardiac findings (troponin leak, ventricular dysfunction, rhythm disturbance along with non-specific ST changes on electrocardiogram (Fig. 1) and refractory shock), he was also treated with intravenous immunoglobulin and methylprednisolone. In the hours following ECMO cannulation, lung compliance worsened, pink frothy sputum was present in the endotracheal tube, and chest-x-ray demonstrated white out lungs, concerning for left atrial (LA) hypertension. He was taken to the cardiac catheterization laboratory for balloon atrial septostomy. During this procedure, air bubbles were noted in the left atrium, left ventricle, and ascending aorta (Fig. 2A and B) with extensive thrombus in the right ventricle (Fig. 3). He was subsequently converted to central VA ECMO. Following cannulation, he developed complete cardiac standstill. In addition, his neurologic exam lacked purposeful movements and head computed tomography demonstrated ischemic strokes in frontal and cerebellar areas, suggestive of diffuse anoxic injury of high severity. However, in the subsequent 48 h, he clinically improved with return of a pulsatile arterial waveform and normalization of ventricular systolic dysfunction, and he was decannulated from ECMO. Antibodies for 21-hydroxylase returned positive confirming the diagnosis of autoimmune adrenal

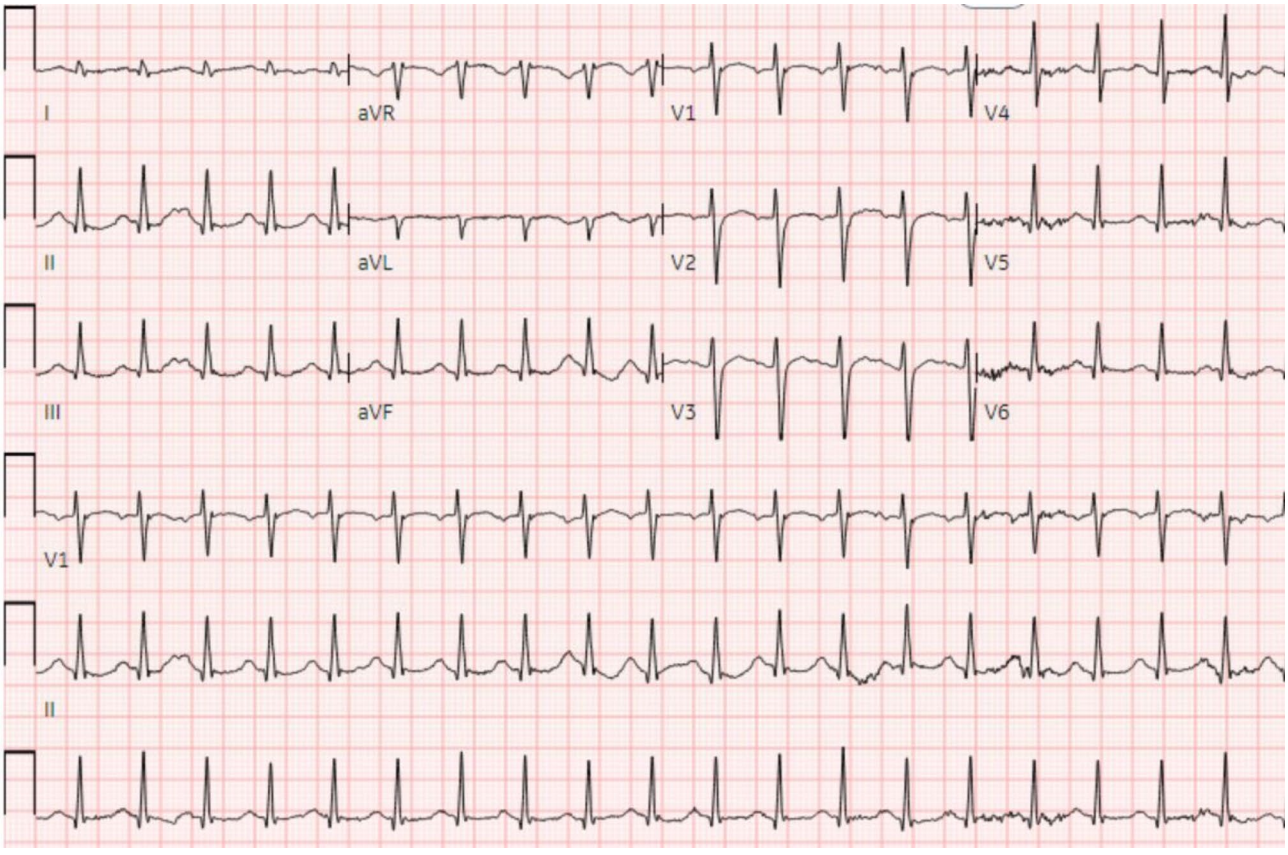

Fig. 1 Electrocardiogram at initial presentation showing sinus tachycardia with non-specific ST changes

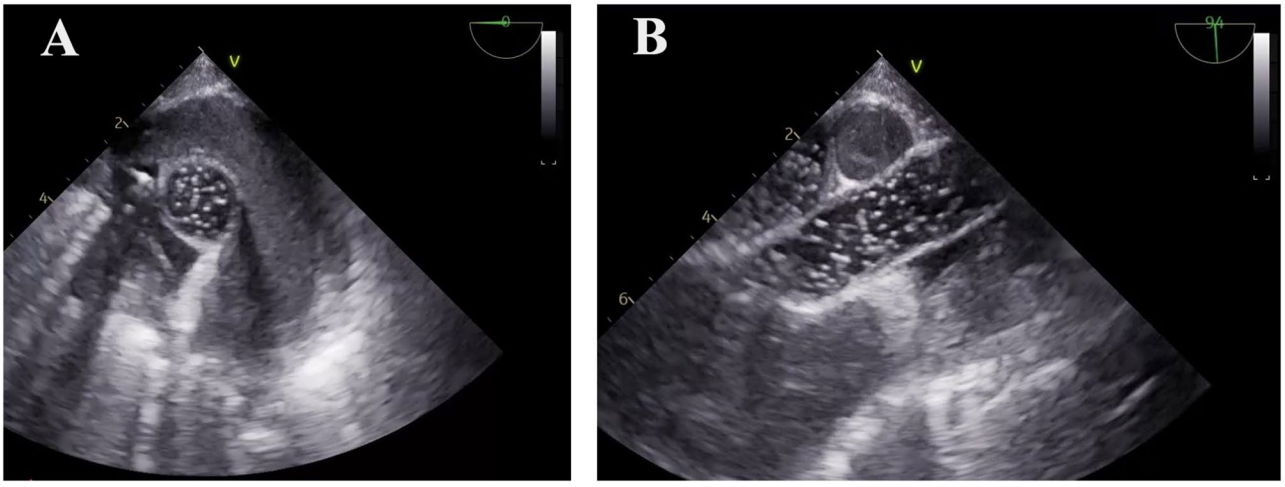

Fig. 2 Transesophageal echocardiogram still images at upper esophageal level angle 0 (**A**) and angle 94 (**B**): significant air bubbles burden are noticed in the aorta

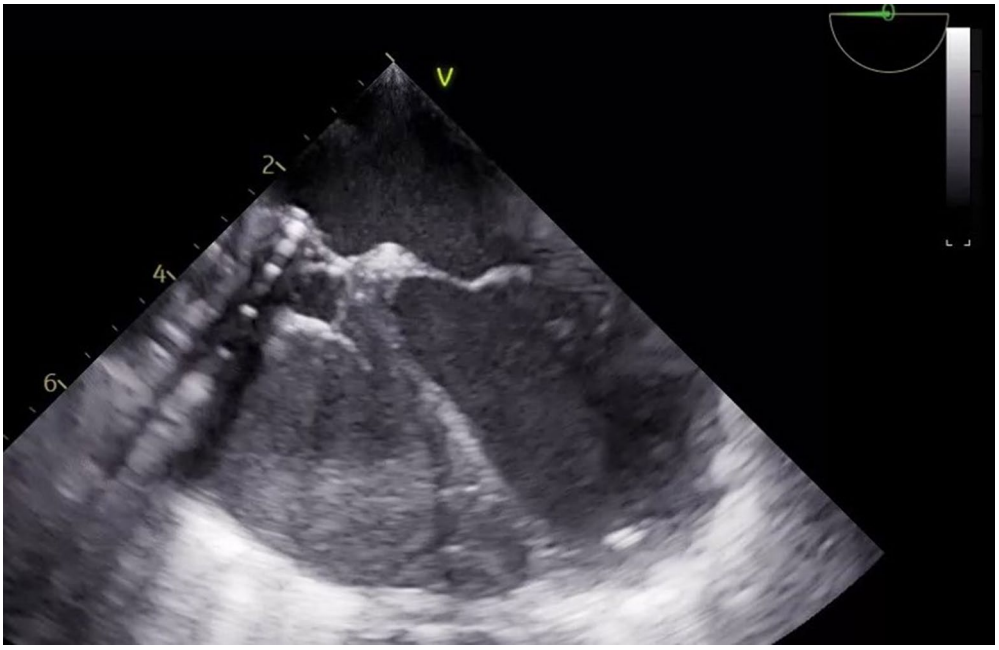

Fig. 3 Transesophageal echocardiogram still image at mid esophageal level at angle 0: a large thrombus is seen in the right ventricle cavity

insufficiency (Addison's Disease). Antibodies for hypothyroidism and type 1 diabetes were also evaluated, and he was found to have a mild positivity for glutamic acid decarboxylase (GAD) antibodies for which he will be clinically monitored. The patient was transferred from the PICU to the inpatient unit and then rehabilitation unit. He was discharged home with impaired functional mobility, balance and gait disturbance. However, with an extensive rehabilitation program, he regained much of his functional capacity. He is now able to attend school, play soccer, and perform daily activities independently.

Discussion

We present a case of circulatory collapse found to be due to autoimmune adrenal insufficiency. Cardiac arrest and circulatory collapse occur uncommonly in children, with respiratory causes (e.g., pneumonia and bronchiolitis) being the most common [1]. Other common etiologies include congenital heart diseases, sepsis, arrhythmias, fulminant myocarditis, blunt trauma and sudden infant death syndrome (SIDS). In considering the differential diagnosis, especially in the absence of known congenital heart disease, and the constellation of clinical and laboratory findings, other etiologies should be considered, especially reversible ones. The H's and T's mnemonic in

Table 1 Clinical features of adrenal insufficiency

Nonspecific symptoms	Symptoms of hypoglycemia	Symptoms of mineralocorticoid deficiency	Features of elevated ACTH* concentrations	Laboratory findings
Fatigue, vomiting, nausea, abdominal pain, weakness, morning headaches, and failure to thrive	Pallor, sweatiness, disorientation and mood swings	Dehydration, collapse, hypotension, tachycardia, weight loss, dizziness and salt craving	Hyperpigmentation of nail beds, mucous membranes, palmar creases and scars	Hyponatremia (90%), hyperkaliemia (50%), hypochloremia, metabolic acidosis, fasting hypoglycemia with low cortisol, high ACTH and high renin

ACTH Adrenocorticotropic hormone

Pediatric Advanced Life Support algorithm [1] provides a useful quick screening method when triaging patients presenting with shock/cardiac arrest.

PAI results from decreased production of glucocorticoids or both gluco- and mineralocorticoid and is a life-threatening condition. This disease can be congenital or acquired. Congenital adrenal hyperplasia due to 21- Hydroxylase deficiency is the most common cause of congenital PAI [2]. Addison's disease characterized by autoimmune destruction of adrenal cortex is the most common cause of acquired PAI [3]. This autoimmune process is defined by exaggerated humoral and cellular immune response in genetically predisposed patients. Usually, there is a trigger for the autoimmune process, including viral infections, drugs, or stress [4]. Another rare cause of primary PAI, especially in newborn infants, includes birth injury to the subcapsular vascular plexus, which can result in subcapsular bleeding in the adrenal glands, leading to subsequent ischemic injury [5].

The clinical presentation of PAI is nonspecific, often delaying diagnosis (Table 1), including a more chronic indolent course. As is illustrated in this case, the disease can also present as a life-threatening endocrine emergency, or so-called adrenal crisis. The manifestations include altered mental status, severe weakness, hypotension, hypoglycemia, and electrolyte disturbances (mostly hyponatremia and hyperkalemia) [4]. Hypoglycemia is more common in children compared to adults [3]. This patient presented in decompensated shock which rapidly progressed to cardiopulmonary arrest requiring ECMO. This is an extremely rare presentation and has been rarely reported [6]. Clinicians should be vigilant to clues that help reach prompt diagnosis. The most helpful exam and laboratory findings include skin hyperpigmentation, hyponatremia, and hypoglycemia respectively. Patients with Addison's disease have high levels of proopiomelanocortin. The cleavage of proopiomelanocortin produces Adrenocorticotropic hormone (ACTH) and melanocyte-stimulating hormone, resulting in bronzing/hyperpigmentation of the skin [2]. The presence of 21-hydroxylase autoantibodies is diagnostic of autoimmune PAI but are only positive in approximately 50% of cases [4].

When PAI is suspected, stress dose intravenous (IV) hydrocortisone is the treatment of choice and is lifesaving. IV hydrocortisone should be continued until clinical improvement and/or diagnosis of PAI is ruled out. When clinical and laboratory presentation do not fit the picture of adrenal insufficiency, the use of stress dose steroids is controversial, though considered not unreasonable as it is often used in refractory shock in patients undergoing cardiac surgery [7]. Steroids are also commonly used in catecholamine-resistant septic shock. Despite the frequent use of hydrocortisone, a systematic review and meta-analysis on the effects of steroids for relative adrenal insufficiency in pediatric shock showed no benefit [8].

It is known that patients with adrenal shock have poor response to vasoactive medications [9]. The unique feature of this case is the associated myocardial stunning and severe biventricular dysfunction. One might speculate that the air bubbles seen on transesophageal echocardiogram during cardiac catheterization were significant enough to cause myocardial ischemia and worsened dysfunction. This may have contributed to prolonged myocardial recovery time. Furthermore, adrenal crisis usually presents with hypovolemic shock [10], rather than a cardiogenic shock. In the rare cases of decompensated shock that have been reported on patients with newly diagnosed Addison's disease, it was speculated that congestive heart failure and resulting cardiogenic shock could be secondary to severe cachexia and malnutrition [11]. However, this patient had normal growth parameters.

Conclusion

In summary, as in this case, adrenal insufficiency should be considered in the context of physical exam and laboratory findings, even in the presence of circulatory shock. Steroid replacement is critical and lifesaving and should be administered expeditiously.

Abbreviations

ECMO	Extracorporeal membrane oxygenation
PICU	Pediatric intensive care unit
ED	Emergency department
VA	Veno-arterial
LA	Left atrial
GAD	Glutamic acid decarboxylase
SIDS	Sudden infant death syndrome

PAI	Primary adrenal insufficiency
ACTH	Adrenocorticotropic hormone
IV	Intravenous

Author contributions
YH collected data and wrote the manuscript. KT and MC revised the manuscript. KG had made a substantial contribution to the concept and design of the manuscript. All the authors have read and approved the final manuscript.

Funding
None.

Data availability
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate
Not Applicable.

Consent for publication
Informed consent from the patient and his legal guardians for publication of identifying information/images in an online open-access publication was obtained.

Competing interests
The authors declare no competing interests.

Received: 24 January 2024 / Accepted: 4 October 2024
Published online: 14 October 2024

References

1. Zeleke BG, Biswas ES, Biswas M. Teaching cardiopulmonary resuscitation to Young Children (< 12 years old). Am J Cardiol. 2019;123(10):1626–7. https://doi.org/10.1016/j.amjcard.2019.02.011. Epub 2019 Feb 21. PMID: 30879607.
2. Park J, Didi M, Blair J. The diagnosis and treatment of adrenal insufficiency during childhood and adolescence. Arch Dis Child. 2016;101(9):860–5. https://doi.org/10.1136/archdischild-2015-308799. Epub 2016 Apr 15. PMID: 27083756.
3. Bornstein SR, Allolio B, Arlt W, Barthel A, Don-Wauchope A, Hammer GD, Husebye ES, Merke DP, Murad MH, Stratakis CA, Torpy DJ. Diagnosis and treatment of primary adrenal insufficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2016;101(2):364–89. https://doi.org/10.1210/jc.2015-1710. Epub 2016 Jan 13. PMID: 26760044; PMCID: PMC4880116.
4. Zorko DJ, Samaan MC, Gupta R. Vomiting and cardiac arrest in a 10-year-old girl. Pediatr Emerg Care. 2021;37(12):e1747-e1749. https://doi.org/10.1097/PEC.0000000000001957. PMID: 32011558.
5. Khuri FJ, Alton DJ, Hardy BE, Cook GT, Churchill BM. Adrenal hemorrhage in neonates: report of 5 cases and review of the literature. J Urol. 1980;124(5):684–7. https://doi.org/10.1016/s0022-5347(17)55609-8. PMID: 7005460; PMCID: PMC7131664.
6. Wells Collins S, Piebenga EC, Shaw E, Toth H, Fish R, Dueker D, Sadiq R, Wolff Y. Index of suspicion. Pediatr Rev. 2009;30(2):65–70. https://doi.org/10.1542/pir.30-2-65. PMID: 19188302.
7. Ando M, Park IS, Wada N, Takahashi Y. Steroid supplementation: a legitimate pharmacotherapy after neonatal open heart surgery. Ann Thorac Surg. 2005;80(5):1672-8; discussion 1678. https://doi.org/10.1016/j.athoracsur.2005.04.035. PMID: 16242437.
8. Menon K, McNally D, Choong K, Sampson M. A systematic review and meta-analysis on the effect of steroids in pediatric shock. Pediatr Crit Care Med. 2013;14(5):474 – 80. https://doi.org/10.1097/PCC.0b013e31828a8125. PMID: 23867428.
9. Annane D, Pastores SM, Rochwerg B, Arlt W, Balk RA, Beishuizen A, Briegel J, Carcillo J, Christ-Crain M, Cooper MS, Marik PE, Umberto Meduri G, Olsen KM, Rodgers SC, Russell JA, Van den Berghe G. Guidelines for the diagnosis and management of critical illness-related corticosteroid insufficiency (CIRCI) in critically ill patients (Part I): society of critical care medicine (SCCM) and European society of intensive care medicine (ESICM) 2017. Crit Care Med. 2017;45(12):2078–2088. https://doi.org/10.1097/CCM.0000000000002737. PMID: 28938253.
10. Orth DN, Kovacs WJ, DeBold CR. The adrenal cortex. In: Wilson JD, Foster DW, editors. Williams textbook of endocrinology_. Philadelphia: Saunders; 1992. pp. 489–619.
11. Derish M, Eckert K, Chin C. Reversible cardiomyopathy in a child with Addison's disease. Intensive Care Med. 1996;22(5):460-3. https://doi.org/10.1007/BF01712167. PMID: 8796402.

Publisher's note