ILLUSTRATIVE CASE

Cardiac Tamponade in a Child With Fever of Unknown Origin

Susan S. Li, MD,[a,b] Zachary Rossfeld, MD,[a,b] Sanmit K. Basu, MD, MS[a,c]

CASE

An 8-year-old girl with neurofibromatosis type 1 and mild intermittent asthma presented with an 8-day history of a daily fever between 101°F and 105°F, a nonproductive cough, congestion, a sore throat, and myalgias, despite treatment with amoxicillin for bronchitis and cefazolin for a *Staphylococcus epidermidis* urinary tract infection. She presented on day 8 of her illness with a macular hand rash, flank pain, and strawberry tongue and was admitted for evaluation of a fever of unknown origin. She did not have any weight loss or joint pain. Admission laboratory values were notable for a white blood cell count of 26 800 cells/mm^3 with 15% bands and 74% segmented neutrophils, an erythrocyte sedimentation rate of 52 mm per hour, C-reactive protein levels of 21.5 mg/dL, ferritin levels of 1129 ng/mL, normal results from liver function tests, a respiratory virus film array with results positive for sapovirus, and sterile blood and urine cultures. She was started on empirical ceftriaxone coverage with no improvement in symptoms. Computed tomography of the head, chest, abdomen, and pelvis revealed cervical, axillary, mediastinal, mesenteric, and inguinal lymphadenopathy. A transthoracic echocardiogram showed no evidence of intracardiac vegetations but revealed a small pericardial effusion. She remained hospitalized with almost daily fevers despite antibiotics but was otherwise hemodynamically stable.

On hospital day 9, the patient developed tachycardia (130–140 beats per minute), respiratory distress (tachypnea to 62 breaths per minute with accessory respiratory muscle use), hypoxemia (pulse oxygen saturation of 89%), and hypotension (77/42 mm Hg). On examination, she had nasal flaring and subcostal retractions; her lungs were clear to auscultation. She had no visible jugular venous distention (JVD), hepatomegaly, or lower extremity edema, and her heart sounds were not muffled.

A chest radiograph (CXR) revealed a newly enlarged cardiac silhouette and clear pulmonary fields (Fig 1). An electrocardiogram (ECG) showed sinus tachycardia with normal axis, low voltages, and T-wave inversions in the lateral precordial leads. A repeat echocardiogram revealed a 2.2 cm circumferential pericardial effusion with right atrial collapse in diastole, increased atrioventricular valve inflow respiratory variation, and inferior vena cava plethora consistent with tamponade physiology (Fig 2).

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Address correspondence to Susan S. Li, MD, Department of Internal Medicine and Pediatrics, Nationwide Children's Hospital, 700 Children's Drive, Columbus, OH 43205. E-mail: susan.li@nationwidechildrens.org

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[a]Department of Pediatrics and [c]The Heart Center, Nationwide Children's Hospital, Columbus, Ohio; and [b]Department of Internal Medicine, Wexner Medical Center, The Ohio State University, Columbus, Ohio

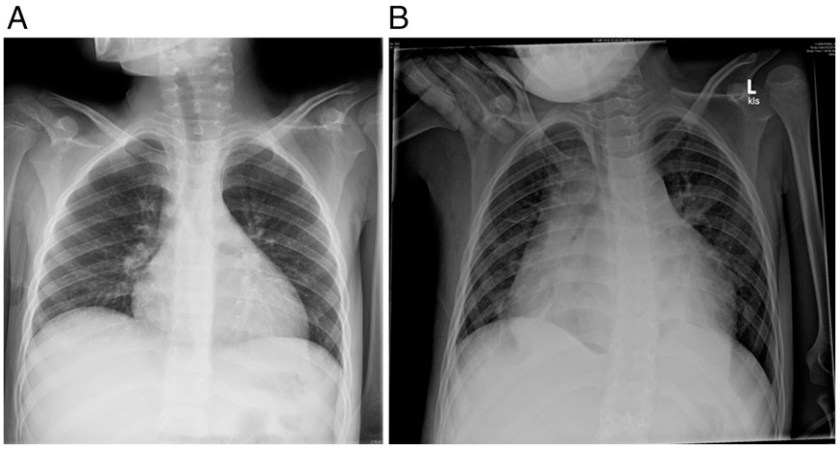

FIGURE 1 CXRs demonstrating no cardiopulmonary disease on admission (A) and a significantly enlarged cardiac silhouette consistent with large pericardial effusion and clear lung fields (B).

Question: What are the evidence-based clinical findings for cardiac tamponade?

Discussion

The pericardium is a multilayer membranous sac surrounding the heart. It normally contains <50 mL of fluid to reduce friction during cardiac contraction and prevent acute distention of the cardiac chambers.[1] The outer fibrous pericardial layer has limited compliance, and fluid collection within the pericardial space can significantly increase intrapericardial pressures, causing tamponade physiology with reduced venous return and diminished cardiac output. On the basis of the rate of fluid accumulation, pericardial tamponade manifests on a continuum from elevated venous pressure without hemodynamic changes or symptoms to cardiogenic shock and death. Fatal cardiac tamponade has been described with acute effusions of as little as 2 mL in neonates[2] and 200 mL in adults,[3] although relative hemodynamic stability can be maintained with slowly-accumulated effusions of 10 times that volume in chronic disease.[3,4]

The etiology of cardiac tamponade can be organized into traumatic (blunt or penetrating) and nontraumatic causes. Nontraumatic etiologies present more insidiously and, in decreasing order of prevalence, include malignant, postoperative and/or procedural, idiopathic, connective tissue disease, infectious, postradiation, ischemic, and uremic effusions.[1,5,6]

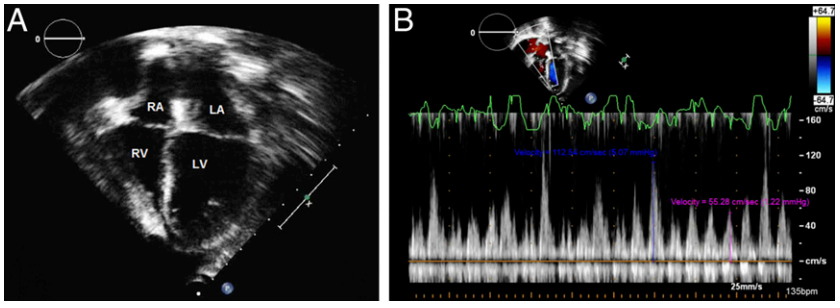

FIGURE 2 Four-chamber transthoracic echocardiogram view demonstrating tamponade physiology with right atrial collapse (A) and increased tricuspid valve inflow respiratory variation by Doppler (B). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Tamponade is a clinical diagnosis, with the classic triad of hypotension, JVD, and muffled heart sounds described by Beck in trauma patients with intrapericardial hemorrhage.[4] Beck's triad, however, is rarely complete for any 1 patient. In fact, the authors of a recent retrospective study found that 0 of 153 adults with pericardial effusion on echocardiogram presented with all 3 findings.[7,8] Consequently, other evidence of tamponade must be considered, particularly in children for whom there is a paucity of literature on its clinical presentation and management. Table 1 provides a summary of the diagnostic utility of various clinical findings for cardiac tamponade. Most of the values come from primarily adult studies and are intended to assist in clinical decision-making. Age-appropriate norms should be applied when assessing vital signs such as tachycardia and hypotension.

Tachycardia is one of the earliest clinical signs of tamponade, representing a physiologic response to decreasing stroke volume. It has a sensitivity of 77% for tamponade,[9] except in those with uremia and hypothyroidism.[3] Tachypnea has a sensitivity of 87% to 89% and has frequently been described in the pediatric literature.[10,11] It should particularly raise concern in the setting of clear pulmonary fields on auscultation and imaging. JVD is almost always present in euvolemic adult patients[3] but is much less commonly seen in children[10,11] and has an overall sensitivity of 76%.[9] Regardless of age, JVD is unreliable if a patient is hypovolemic.[3] Quiet or muffled heart sounds have a sensitivity of only 28%[9] and are difficult to appreciate in the pediatric population because they can vary on the basis of body habitus and body position and may be overlooked during resuscitative efforts.[10] Hypotension and narrow pulse pressure develop because of decreased cardiac output,[3,10,11] although 64% of patients are able to maintain systolic pressure ≥100 mm Hg.[12] Frank hypotension has only 26% sensitivity.[9] Pulsus paradoxus, a systolic blood pressure decrease >10 mm Hg on inspiration, is secondary to reduced left-sided filling,[1,3] and when it is seen with a pericardial effusion, it increases the likelihood of tamponade by 3.3 times.[9]

TABLE 1 Diagnostic Utility of Various Clinical Findings for Cardiac Tamponade

	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Subject Age Range, y
Clinical findings				
Tachycardia	69[8]	77[9]	—	≥18 only
Tachypnea	87–89[9]	—	—	≥18 only
JVD	13[8]	76[9]	—	≥18 only
Cardiomegaly on CXR	89[9]	—	—	≥18 only
Pulsus paradoxus >10 mm Hg[a]	98[9]	70[9]	—	≥18 only
Hypotension	38[8]	26[9]	—	≥18 only
Diminished heart sounds	38[8]	28[9]	—	≥18 only
ECG findings				
Low voltage	76[15]	60[15]	81[15]	15–95, mean 53
Electrical alternans	23[15]	98[15]	95[15]	15–95, mean 53
Sinus tachycardia	76[15]	60[15]	79[15]	15–95, mean 53
Low voltage + alternans + sinus tachycardia	8[15]	100[15]	100[15]	15–95, mean 53
Echocardiography findings				
Any chamber collapse	90[16]	65[16]	—	15–88, mean 53
Right atrial collapse for greater than one-third of cardiac cycle	94[17]	100[17]	—	10–82, mean 52

[a] When seen with a pericardial effusion, likelihood ratio (LR) of tamponade increased by 3.3 times.[9]

Its use, however, is limited in the agitated child and has not been widely cited within the pediatric literature as a clinical indicator of cardiac tamponade.[10,11]

CXR has 89% sensitivity for pericardial effusion if cardiomegaly is seen with clear lung fields.[9] However, the cardiac silhouette may not be appreciably enlarged on CXR until at least 200 mL of fluid accumulates in the pericardium, representing a late finding in tamponade. Furthermore, a normal cardiac silhouette cannot rule out a pericardial effusion.[3]

ECG signs may be specific in certain cases, but they lack the sensitivity to serve as an effective screening tool to exclude significant pericardial effusions or cardiac tamponade. Low Q, R, and S wave voltages in patients with a known pericardial effusion are more specific for a large pericardial effusion or tamponade.[13,14] Electrical alternans (beat-to-beat voltage and polarity alteration of ECG complexes) portends a 98% specificity[15] and increases to almost 100% in the presence of both P-wave and Q-, R-, and S-wave alternans.[3] The combination of low-voltage complexes, electrical alternans, and sinus tachycardia has 100% specificity and positive predictive value for tamponade.[15]

Echocardiography is the primary tool for confirming the presence of a significant pericardial effusion and associated tamponade physiology. Representative findings include cardiac chamber collapse, increased atrioventricular valve inflow respiratory variation, and inferior vena cava plethora. Any chamber collapse offers 90% sensitivity and 65% specificity for tamponade,[16] but right atrial collapse for greater than one-third of the cardiac cycle increases sensitivity to 94% and specificity to 100% and has a positive predictive value of 100%.[17]

CASE CONTINUATION

The patient received a rapid 60 mL/kg normal saline bolus with blood pressure improvement to 92/58 mm Hg and underwent emergent pericardiocentesis and pericardial drain placement in the cardiac catheterization laboratory with removal of 345 mL of serous fluid. A follow-up echocardiogram showed resolved effusion. A bone marrow biopsy revealed macrophages with hemophagocytosis. On the basis of the constellation of multisystem illness with serositis, adenopathy, laboratory data (ferritin levels of 1129 ng/mL, aspartate aminotransferase levels of 102 U/L, triglyceride levels of 217 mg/dL, and fibrinogen levels of 217 mg/dL), and hemophagocytosis, the diagnosis of macrophage activation syndrome (MAS) was made.[18] This diagnosis was further supported by elevated soluble interleukin-2 receptor levels (2848 U/mL, reference range: 45–1105 U/mL). She was started on corticosteroid therapy and anakinra (an interleukin-1 antagonist) with significant symptom improvement. Serial laboratories revealed a normalization of inflammatory markers, ferritin levels, and liver function tests. Further rheumatologic workup was unrevealing. The lack of joint pain did not support a diagnosis of systemic juvenile idiopathic arthritis, a condition known to be associated with MAS in up to 30% to 40% of cases.[18] The patient's MAS trigger remains unknown at the time of this case report.

Question: How is cardiac tamponade treated?

Discussion

Tamponade is a medical emergency. Stabilization in this preload-dependent state requires volume expansion with crystalloids for the hypovolemic patient. However, aggressive fluid resuscitation in the normovolemic or hypervolemic patient will increase intracardiac pressures, further increasing pericardial pressures and precipitating tamponade.[19,20] Care must be taken with any fluid administration with close monitoring of clinical response. Definitive treatment entails pericardial fluid reduction, which may necessitate invasive techniques by a pediatric cardiologist. Studies should be performed on the drained fluid to investigate the etiology of the effusion.

Determining and treating the underlying cause may prevent recurrence. For the patient in this case, the primary treatments after fluid drainage were immunosuppression with corticosteroids and immunomodulation with anakinra caused by MAS. The standard of care for treatment of acute pericarditis is a 2-week

course of colchicine (level A evidence from the American Heart Association and American College of Cardiology, studies from multiple large clinical trials), corticosteroids if intolerant of nonsteroidal antiinflammatory drugs (level B evidence, single randomized clinical trial), and immunomodulatory therapy (such as intravenous human immunoglobulins, azathioprine, and anakinra) for multiple recurrences (level C evidence, based on expert opinion and case studies).[21]

Question: What is the role of bedside ultrasonography in the diagnosis of cardiac tamponade?

Discussion

Because pediatric cardiologists and echocardiographers are not always readily available, a noncardiologist should be able to confirm the diagnosis of cardiac tamponade on the basis of the presence of a pericardial effusion in the context of appropriate clinical findings. A potentially more accessible diagnostic tool is the focused assessment with sonography in trauma (FAST) examination used by emergency departments. The standard FAST examination includes a subxiphoid window to evaluate the heart and pericardial space. For this view, the ultrasound transducer is placed just inferior to the xiphoid process and directed into the chest toward the left shoulder in a cephalad-anterior direction. It can be used to visualize pericardial effusions but may not specifically allow users to distinguish between pleural and pericardial effusions. If an effusion is seen, pericardial location is confirmed by using the parasternal long axis view, with the transducer placed on the fourth intercostal space along the left midclavicular line.[22] Studies have shown that noncardiologists and novice learners are able to perform these ultrasound techniques and diagnose pericardial effusions with accuracy similar to that of experienced echocardiographers.[23–28] Although FAST examinations cannot routinely reveal the ultrasound findings of tamponade such as cardiac chamber collapse, they may provide the capability of confirming a significant pericardial effusion diagnosis based on clinical suspicion. This will help expedite the mobilization of expert teams in removing the fluid.

CONCLUSIONS

This case involves a child with no underlying cardiac disease who developed cardiac tamponade as a complication of MAS. Cardiac tamponade is a medical emergency manifesting with reduced ventricular filling and cardiac output caused by a significant pericardial effusion. It presents on a continuum ranging from subtle clinical findings to hemodynamic collapse. Notably, Beck's triad of hypotension, JVD, and muffled heart sounds has poor sensitivity for cardiac tamponade. Furthermore, physical examination signs found in adults, such as JVD, muffled heart sounds, and pulsus paradoxus, can be difficult to appreciate in an irritable child. Instead, a high index of suspicion should be raised in the presence of evidence-based, highly sensitive clinical markers (tachycardia, tachypnea, low voltages on ECG). The presence of highly specific clinical signs (sinus tachycardia, low voltages on ECG, and electrical alternans) should further increase clinical suspicion. The diagnosis can be confirmed by a generalist via the FAST examination through the subxiphoid and parasternal long views. Arranging for prompt fluid removal by appropriately trained personnel is imperative in preventing further hemodynamic decompensation.[9,12,29,30]

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