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Stressed out with Sepsis.

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Stressed out

The Clinical Challenge

A 46-year-old woman presented to the emergency department with a few days of progressive malaise, confusion, abdominal pain, and fevers. The patient had recently been hospitalized for a urinary tract infection and had completed an appropriate course of antibiotics. The patient's medical history was significant for seizures and surgical history was notable for a remote tracheostomy as a child resulting in chronic tracheal stenosis. There was no history of cardio-pulmonary disease.

At the time of her admission, physical examination revealed a temperature of 102.6° F, blood pressure 74/48 mmHg, heart rate 112 beats per minute, respiratory rate 28 breaths per minute, and hemoglobin oxygen saturation of 98% while breathing ambient air. The patient was in moderate respiratory distress, exhibiting tachypnea, restlessness, and pallor with dry mucous membranes. She had normal breath and heart sounds without murmurs or gallops, the abdomen was mildly tender to palpation without guarding or rigidity, and her extremities were warm without edema. A portable chest x-ray at admission was normal. Urinalysis revealed cloudy urine with leukocytosis, and urine and blood cultures quickly grew *Escherichia coli*. Abdominal imaging did not show pyelonephritis or hydronephrosis.

After twelve hours of antibiotics and four liters of normal saline, the patient had worsening respiratory distress and required invasive ventilatory support. Intubation was challenging and prolonged due to her tracheal stenosis, but oxygenation and ventilation were provided throughout the procedure. With concerns of a difficult airway, the patient received minimal sedation, was awake during the intubation, and was visibly distressed during the placement of the endotracheal tube. Following intubation, the patient developed hypotension with cool extremities that did not improve with additional volume resuscitation and initiation of vasopressors. A repeat chest x-ray (Figure 1) at that time was consistent with new pulmonary edema, and an ECG showed ST-depressions and T-wave inversions (Figure 2).

Question

- *When assessing the patient in septic shock, what cardiac complications should be considered?*
- *How can we quickly differentiate which of the potential cardiac complications are playing a role in this case?*

Clinical Reasoning

The evaluation of shock requires rapid assessment of multiple potential etiologies. For our patient there was high suspicion that septic shock was the primary driver of her hypotension and poor systemic perfusion. However, because of her refractory hypotension, it was necessary to consider additional contributing factors. In this case, the presence of new pulmonary edema

and an abnormal ECG demanded further cardiac evaluation before attributing her pulmonary edema to sepsis-related acute respiratory distress syndrome.

Septic shock can trigger cardiogenic shock by multiple mechanisms. Arrhythmias, for example, commonly complicate systemic inflammation and can lead to under-filled cardiac chambers and uncoordinated heart rhythms. In addition, pre-existing coronary disease may be exacerbated by deficits in oxygen extraction or increases in the oxygen demand of cardiac muscle, which can lead to myocardial ischemia or even infarction. Similarly, stress cardiomyopathy without intrinsic coronary disease can precipitate abnormal cardiac contractility. In the setting of sepsis, the activated sympathetic nervous system results in a surge of catecholamine release both into the circulation and sympathetic nerve endings.

The differentiation of these mechanisms relies on and is facilitated by point-of-care ultrasound. A bedside ultrasound, performed by an intensivist, can quickly assess left ventricular preload, identify isolated wall motion abnormalities or global hypokinesis, and at the same time rule out previously undiagnosed right ventricular failure or hemodynamically-significant pericardial effusions.

The Clinical Solution

Point-of-care ultrasound revealed a hypokinetic left ventricular apex concerning for takotsubo cardiomyopathy (Video 1). Based on this finding, intravenous fluids were stopped, and an inotropic agent, dobutamine, was used to improve cardiac output. During the next 48 hours, diuresis ensued and the inotropes and vasopressors were discontinued. A week later, an echocardiogram showed normal left ventricular function and wall motion (Video 2), and the patient was eventually discharged home. Return of normal cardiac function following resolution of the acute stressor confirmed the diagnosis of takotsubo, also known as “stress” cardiomyopathy.

The Science behind the Solution

“Stress Cardiomyopathy”

Among its earliest descriptions, takotsubo cardiomyopathy (TCM) was also known as “apical ballooning syndrome,” because of the typical characteristics seen on dynamic imaging. The name “takotsubo” comes from the Japanese word for an octopus trap, which the anatomic features of the cardiomyopathy so closely resemble (Figure 3). As evidence of this entity steadily increased, the diagnosis expanded to a more generalized cardiomyopathy distinct from coronary vaso-occlusive disease and incorporated not only emotional stressors but physiologic stressors as well. The most recent Mayo Clinic definition of takotsubo cardiomyopathy requires: 1) regional wall motion abnormalities that are not in a single coronary distribution; 2) ECG changes, cardiac enzyme elevation, or both, with no evidence of obstructive coronary disease or plaque rupture; and 3) evidence that the insult was transient and the patient was able to recover.

Now commonly referred to as “stress cardiomyopathy,” TCM is increasingly recognized in the ICU setting. Although TCM is a rare cause of acute heart failure in the general population, reversible myocardial dysfunction is well documented in the critically ill, and it is estimated that it occurs in up to 28%-44% of septic patients. In fact, septic patients may have as much as nine times the risk of developing a cardiomyopathy compared to non-septic ICU patients. The combination of myocardial dysfunction and sepsis significantly increases the risk of death, and mortality rates as high as 70% have been reported. Takotsubo cardiomyopathy is being diagnosed more frequently because of increased recognition of this disease. Case reports have gone from single digits in 1998 to over 200 per year. Furthermore, other sepsis-related cardiac conditions like dynamic left ventricular outflow tract obstruction, demand ischemia, conduction delays, and tachyarrhythmias, have been tied to stress cardiomyopathy in the setting of overwhelming sepsis.

Pathophysiology

There are several means by which the dysfunctional contraction in TCM spirals into worsening shock. In a normally-contracting heart, the His-Purkinje system activates the apex of the left ventricle (LV) first followed by progressive contraction toward the base. This pushes blood in one coordinated motion, from apex to base. This is analogous to squeezing a new tube of toothpaste from the bottom to the top to effectively empty its contents. With TCM, apical ballooning is present and the apex is hypokinetic. This regional weakness of squeeze alone would be enough to drop effective cardiac output, but the mechanics get even worse. While at one end the apex is failing to play its role, the rest of the left ventricle does contract, sometimes even more forcefully, at the base. This is like squeezing a tube of toothpaste near the middle rather than at the bottom (Figure 4), choking off forward flow from the apex. As a result, stroke volume falls not only due to the loss of contractility at one end, but also because the relative hyper-contractility at the base produces intraventricular pressures that cannot be overcome by the hypokinetic apex.

This phenomenon can eventually produce a functional LV outflow tract obstruction, where gradients as high as 60 mmHg have been reported (Figure 5). With mechanical limitations to effective contraction, as well as more generalized loss of vigorous contractility, the decrease in LV systolic function seen in TCM can be equivalent in severity to that caused by an acute occlusion of the left anterior descending coronary artery – commonly referred to as a “widow-maker.”

The underlying cause of TCM remains under investigation. Although theories have proposed a role for surges in catecholamine release, abnormal glucose and fatty acid metabolism, coronary microvascular disease, and even diffuse coronary artery spasm, it is likely that TCM is an endpoint for multiple forms of physiological stress. Whether it is directly caused by the sepsis-induced inflammatory cascade or an independent entity is up for debate. What is incontrovertible is the importance of considering, diagnosing, and treating TCM in a timely manner in a patient with refractory septic shock. Availability of bedside cardiac ultrasound in the ICU provides the ability to answer diagnostic questions quickly and improves patient care.

Answer:

When assessing the patient in septic shock, what cardiac complications should be considered?

Possible cardiac complications in the patient with septic shock include stress cardiomyopathy, dynamic LV outflow tract obstruction, demand ischemia or infarction, cardiac conduction delays, and destabilizing tachyarrhythmias.

How can we quickly differentiate which of the potential cardiac complications are playing a role in this case?

In addition to history, physical, electrocardiogram, and standard lab testing, a bedside cardiac ultrasound provides useful and efficient information about cardiac complications which may be contributing to sepsis and septic shock.

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