

A Woman in Her 30s With Acute Refractory Hypoxemia and a History of Intravenous Drug Use



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CHEST 2016; 150(5):e129-e131

Case

A woman in her 30s with a past medical history of hepatitis C and intravenous drug abuse presented to the hospital with a 2-day history of fever and malaise. Initial assessment in the ED revealed hypotension and severe hypoxemia. Initial investigations were notable for a markedly elevated white blood cell count ($30.8 \times 10^9/L$), mild lactic acidosis (2.6 mM), and a chest radiograph showing a left basal airspace opacity. Initial treatment included empiric antibiotics, intravenous fluid, vasopressor initiation, and high-flow supplemental oxygen. She received a diagnosis of severe sepsis and was admitted to the ICU, where she was subsequently intubated for hypoxemia and decreased level of consciousness. Initial transthoracic echocardiography (TTE), performed by a cardiologist, revealed a large vegetation on the septal leaflet of the tricuspid valve, and a dilated hypokinetic right ventricle (Video 1 Sets 1 and 2). The interatrial septum was not well visualized by TTE, and an atrial septal defect (ASD) could not be excluded because of poor apical and subcostal windows. Blood cultures returned positive results for methicillin-sensitive *Staphylococcus aureus*,

confirming infective endocarditis. Chest CT imaging also revealed multiple septic emboli to her lungs, but her burden of parenchymal disease was not believed to be the primary contributor to her hypoxemia. Despite all attempts at optimizing antibiotic therapy, mechanical ventilation, and hemodynamics, the patient continued to deteriorate.

Because of the growing suspicion for shunt pathology, point-of-care transesophageal echocardiography (TEE) was performed by the attending ICU physician. The TEE was performed without difficulty to reveal a midesophageal four-chamber (ME4C) view (Video 1 Set 3). Color Doppler was also applied to the tricuspid valve (Video 1 Set 4), interatrial septum (Video 1 Set 5), and the magnified bicaval view (Video 1 Set 6). A bubble study was subsequently performed, with 9 mL of agitated saline injected into the antecubital fossa (Video 1 Set 7). Transgastric short-axis views are shown in Video 1 Set 8.

Question: What is the cause of this patient's refractory hypoxemia, based on this point-of-care (POC) transesophageal echocardiography?

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DOI: <http://dx.doi.org/10.1016/j.chest.2016.04.039>

Answer: ASD with right-to-left intracardiac shunting. Ventricular signs of right ventricular (RV) pressure and volume overload.

Video 2 Set 3 demonstrates impaired biventricular function and a grossly dilated right atrium. The left ventricular function appears globally depressed (< 50%) with septal hypokinesis. There is also a large mobile vegetation on the atrial side of the septal leaflet, as previously documented by TTE, but no visible lesions on the mitral valve. **Video 2 Set 4** reveals significant tricuspid regurgitation, which is likely associated with the tricuspid lesion. The application of color flow across the atrial septum in the ME4C view (**Video 2 Set 5**) suggests right-to-left intracardiac shunting (RLICS).

In the magnified bicaval view (**Video 2 Set 6**), application of color flow across the interatrial septum again shows flow acceleration directed across the septum toward the left atrium. A bubble study was also conducted to semiquantify the degree of RLICS (**Video 2 Set 7**: ME4C), which revealed gross opacification of the left side of the heart. A “bubble” or agitated saline study is considered positive for RLICS if bubbles are visible in the left atrium within three cardiac cycles of injection, which we can see in this video. Finally, the transgastric short-axis view (**Video 2 Set 8**) demonstrated interventricular septal flattening in systole and diastole, suggestive of pressure and volume overload. Overall, these findings are suggestive of an ASD with flow reversal and associated RV pressure/volume overload.

It is suspected that the patient had an undiagnosed ASD, with subsequent flow reversal in the setting of worsening pulmonary hypertension and RV volume overload. Given the patient’s refractory hypoxemia, RLICS, and dysfunction of the right side of the heart, the patient was administered inhaled nitric oxide and milrinone, with transient improvements in oxygenation. An urgent cardiovascular surgery consult regarding closure of the ASD was obtained. Because of high pulmonary arterial pressures and hemodynamic instability, she was deemed not to be a surgical candidate at that time. In addition, it was discovered that the patient had experienced further deterioration of her neurological status with presumed paradoxical septic emboli to the posterior cerebral circulation, resulting in a brainstem stroke. Given the severity of her comorbid illnesses, the patient was changed to comfort care after discussion with the family. The patient died shortly thereafter of severe hypotension and hypoxemia.

Discussion

POC ultrasound examination by either TTE or TEE can play a vital role in the assessment of shunt pathology in the critically ill patient with refractory hypoxemia.

Differentiation of physiological shunt (ie, blood flow in consolidated lung) and anatomical shunt (ie, ASD, intrapulmonary shunts, etc) has practical implications for the treatment of unrelenting hypoxemia.¹

Investigation for shunt can be performed by clinicians who are competent in obtaining traditional TTE acoustic windows and performing color Doppler interrogation. The apical four-chamber (A4C) view is the first acoustic window used to facilitate interrogation of the interatrial/ventricular septa. Visual and Doppler examination of the septum may reveal visual abnormalities such as discontinuities and transeptal flow, respectively. Size and maximal velocity of the shunt often dictate how easily such an abnormality can be recognized. It must be acknowledged that the A4C view provides a parallel orientation of both septa to the ultrasound beam and Doppler analysis, which may lead to low signal output and risk of potential false negative results.

The subcostal four-chamber (S4C) view is more ideally oriented for interrogation of shunt pathology because of its perpendicular orientation of the ultrasound beam to the septal tissue.² In this patient, TTE S4C was unable to adequately evaluate the interatrial septum. TEE is an accepted additional approach for the trained clinician that offers unparalleled visualization of cardiac structures and higher sensitivity for interatrial defects.³ Like the A4C, the TEE ME4C is often the first view obtained and investigated (**Video 2 Set 3**). Again, similar to the S4C, the bicaval view (**Video 2 Set 6**) allows visualization for the presence of interatrial flow, perpendicular to the ultrasound beam for Doppler analysis.

If the index of suspicion remains high despite a negative interrogation result, an agitated saline or “bubble” study can be performed. Bubble studies are used primarily for detection of occult shunt, with a reported sensitivity of 62% and specificity of 100%,⁴ but can also be used for semiquantification of septal defects. The preferred acoustic window for this type of study is the TTE A4C or the TEE ME4C as seen in **Video 2 Set 7**. An intravenous injection of agitated saline, preferably in the antecubital fossa, results in air microbubble contrast opacification of the right side of the heart. Importantly, the air microbubbles are transient, dissolve in the pulmonary circulation, and can be seen only in the left side of the

heart if they are able to bypass the pulmonary circulation via RLICS or extracardiac shunts. Although complications of bubble studies are rare, there are published case reports of stroke and transient ischemic attacks shortly after several studies with right-to-left shunting.⁵ In general, bubbles are seen within the first three to five cardiac cycles from opacification of the right side of the heart for the presence of RLICS. Later appearance can be suggestive of pulmonary arteriovenous shunting. The degree of opacification closely approximates the degree of shunting, with minimal amounts displaying reduced specificity.⁶ In this case presentation, the ME4C view revealed early dense opacification of the left side of the heart and color flow revealed gross right-to-left shunt, suggesting a large-volume interatrial shunt.

This case demonstrates the ability of POC echocardiography to provide crucial time-sensitive information in a critically ill patient with refractory hypoxemia. In the event of unrelenting hypoxemia despite conventional strategies (increased positive end-expiratory pressure, increased fraction of inspired oxygen, etc), concern should be raised for occult shunt pathology. POC ultrasound TTE should be the first step for evaluation of shunt pathology, but TEE is an additional POC modality for the trained clinician that offers improved specificity. If the index of suspicion remains high despite a negative study result, an agitated saline study can be performed with near 100% sensitivity.

Reverberations

1. *Point-of-care ultrasonography can be crucial in the evaluation of the patient with refractory hypoxemia to identify shunt pathology.*
2. *The initial interrogation of the atrial/ventricular septum includes transthoracic two-dimensional-mode*

examination and application of color Doppler in the A4C and S4C views.

3. *In the case of poor TTE acoustic windows, TEE can be employed by the trained clinician to further facilitate evaluation of possible shunt pathology with improved specificity.*
4. *Careful analysis of a bubble study can help differentiate physiological and anatomical shunts and help with semiquantitation.*

Acknowledgments

Financial/nonfinancial disclosures: None declared.

Author contributions: B. B., R. L., and R. A. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects.

Other contributions: CHEST worked with the authors to ensure that the Journal policies on patient consent to report information were met.

Additional information: To analyze this case with the Videos, see the online version of this article.

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