A Case of Complex PFO Leading to Ischemic Stroke: A Practical Clinical Pearl for Neurohospitalists

The Neurohospitalist
2016, Vol. 6(3) 114-117
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DOI: 10.1177/1941874415588750
nhos.sagepub.com

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Abstract

Patent foramen ovale (PFO) has been proposed as a mechanism for cardioembolic stroke, especially in younger patient populations. Complex PFOs, with tunnel lengths exceeding 8 mm, lead to a higher risk of neurological sequelae than simple PFOs and may also be harder to detect with transthoracic echocardiography (TTE). In this article, we present a 29-year-old woman who, after polypharmacy overdose, developed deep venous thrombosis and multiple pulmonary emboli (PE) and subsequent cardioembolic stroke. Initial TTE showed intact interatrial septum with late appearance of agitated saline in the left atrium after the seventh cardiac cycle. Subsequent transesophageal echocardiography, after treatment of PE with an intravenous thrombolytic (alteplase) and anticoagulation with heparin, showed a complex PFO with a 19-mm overlap of the septum primum and secundum without active flow. It is suggested that this PFO allowed for flow only in the situation of elevated right heart strain with PE, causing cardioembolic stroke and detection of agitated saline in the left atrium on TTE. However, under normal physiological situations, which resumed after treatment of PE with alteplase and heparin, the PFO did not allow for flow. This case demonstrates the potential importance of recognition of complex PFOs in diagnosis and management of cardioembolic stroke.

Keywords

patent foramen ovale, stroke, pulmonary embolism

Introduction

Studies have estimated that ~25% of the population has a patent foramen ovale (PFO). This congenital anatomic variant has been proposed as a mechanism for stroke, especially in younger patients.¹⁻³ Detection of PFOs can be performed with transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE), although TEEs are considered to have a higher sensitivity and specificity for diagnosis.⁴ Complex long-tunnel PFOs, defined as having an overlap between the septum primum and the secundum of more than 8 mm, may be more difficult to detect.^{5,6} However, long-tunnel PFOs can themselves be a source of stagnated blood and subsequent thrombus development and may place patients at a higher risk of neurological sequelae than simple PFOs.^{7,8} We describe a case of a young patient with deep venous thrombosis (DVT), pulmonary emboli (PE), and cardioembolic stroke in the setting of a complex right to left PFO.

Case

A 29-year-old woman with a past medical history of depression, chronic pain, oral contraceptive use, and tobacco abuse presented with altered level of consciousness 2 hours after last

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Figure 1. Duplex ultrasound showing segmental deep vein thrombosis (DVT) in the left proximal popliteal vein (arrows) with long axis (A) and transverse (B) views. (C) Computerized tomography (CT) scan of the chest showing enlargement of the right atrium (arrow) and ventricle in comparison to the left atria and ventricle, indicative of elevated right heart pressures secondary to multiple pulmonary emboli (PE).

being seen as normal. On inspection, approximately 3 days of the patient's acetaminophen/hydrocodone, clonazepam, and quetiapine were missing from her pillbox. Urine drug screen was positive for cocaine and opiates. Polysubstance overdose was thought to be the etiology of her encephalopathy. Initial electrocardiography was unremarkable, and arterial blood gases showed adequate pulmonary ventilation.

After approximately 20 hours of observation, the patient opened her eyes and asked "where am I?" She then became unresponsive and was noted to have Mobitz type I heart block, ST-segment elevation, and subsequent pulseless electrical activity (PEA) with cardiopulmonary arrest. Advanced cardiac life support (ACLS) was initiated, and the patient had a return of spontaneous circulation 2 minutes after the cardiac arrest. However, there was difficulty obtaining any measurable oxygen saturation level for 100 minutes, despite mechanical ventilation via endotracheal intubation and multiple modalities of assessing the oxygen saturation level.

Transthoracic echocardiography showed preserved biventricular systolic function. The visualized interatrial septum appeared intact, but there was a late appearance of agitated saline contrast in the left atrium, greater than 7 cardiac cycles later. Doppler venous ultrasound showed DVT located in the

Figure 2. A, magnetic resonance imaging (MRI) brain, diffusion-weighted imaging sequence showing multiple areas of restricted diffusion in the cerebellum. B, MRI brain, apparent diffusion coefficient (ADC) sequences showing corresponding areas of hypointensity. Quality is reduced secondary to patient motion artifact.

left popliteal vein, and spiral chest computerized tomography scan (CT) showed multiple acute pulmonary emboli in the right lung with a dilated right cardiac atrium and ventricle (Figure 1). There was no evidence of pulmonary arteriovenous malformation on spiral chest CT. Initial head CT showed mild diffuse cerebral edema but no acute hemorrhage. Due to the level of PE clot burden and subsequent cardiopulmonary decompensation, intravenous thrombolytics were given, resulting in the return of adequate pulmonary oxygenation.

Magnetic resonance imaging (MRI) of the brain, performed 17 hours after PEA arrest, revealed multiple small areas of restricted diffusion in the cerebellum and bilateral occipital lobes (Figure 2). Imaging study findings confirmed multiple embolic ischemic strokes and did not have the typical appearance of anoxic brain injury. Given the bilaterality of the foci, paradoxical embolism associated with the DVT was suspected.

Transesophageal echocardiography showed a 19 mm septal overlap between the septum secundum and the septum primum with the presence of a thick septum secundum (Figure 3). Redundancy was noted in the septum primum with approximately 5 mm of excursion into the left atrium. No spontaneous shunting across the interatrial septum was seen at rest or with provoked Valsalva maneuver, performed by pressing on the abdomen, during agitated saline contrast test. These findings suggest that at the time of the TEE, in the absence of right heart strain, there was no active right to left cardiac shunt. The overall clinical picture suggested the presence of a complex PFO that allowed for flow only in situations of elevated right

Figure 3. A, Transesophageal echocardiogram (TEE) showing complex patent foramen ovale (PFO) with a 19-mm overlap of the septum primum and septum secundum. B, TEE showing 5-mm excursion of the septum primum into the left atrium. SVC indicates superior vena cava.

atrial pressure. Serological evaluation for hypercoagulable state showed an elevated lupus anticoagulant.

The unifying stroke mechanism was hypothesized to be a polysubstance overdose leading to an immobilized state in the setting of hypercoagulable disorder due to the presence of lupus anticoagulant and oral contraceptive pill administration, subsequent development of left popliteal DVT and propagation of clot causing acute PE with respiratory failure and right heart strain. This resulted in patency of a right to left shunt in an otherwise clinically inactive complex PFO, resulting in a “paradoxical” cardioembolic ischemic stroke.

Discussion

Although this patient has several risk factors for hypercoagulable state, including elevated lupus anticoagulant and tobacco and oral contraceptive use, the sudden onset and bilateral nature of the ischemic stroke increase the likelihood that the stroke was secondary to a cardioembolic source.^{9,10} The patient underwent a TTE and TEE with agitated saline, the first of which showed the appearance of bubbles in the left atrium after the seventh cardiac cycle. The appearance of bubbles in the left atrium before the third to fifth cardiac cycle is generally attributed to cardiac shunts, with later detection attributed to pulmonary shunting. However, consensus groups have determined that there is no value in considering a strict cutoff limit for PFOs.¹¹ There was no evidence of pulmonary arteriovenous malformation on spiral CT chest in this patient. Conventional angiography was thought not to be a necessity in this case, as spiral CT chest has high sensitivity and specificity in detection of pulmonary arteriovenous malformation. Although a very small pulmonary shunt cannot be excluded completely without conventional angiography, in this patient the detection of a complex PFO during TEE suggests that the PFO was present during initial TTE and was responsible for the delayed appearance of agitated saline in the left atrium.

The delayed appearance of saline may be due to the elongated and angular nature of the long-tunnel complex PFO,

which we hypothesize may cause slower flow through the defect. Additionally, complex PFOs may be closed under normal physiological situations, allowing for flow only in the setting of elevated right heart pressure.^{12,13} In this patient, multiple pulmonary emboli led to elevated right heart strain, allowing for flow through the physiologic shunt between the right and the left atrium and subsequent development of cardioembolic stroke. However, after treatment of the pulmonary emboli with heparin, it would be expected that the right heart strain would resolve, and the shunt to effectively seal off, as was visualized with the later TEE. Although induced Valsalva was attempted to increase right heart strain during TEE, varying efficacy of this maneuver, especially in patients with neurological disorders, has been found, and right heart pressure may not have been elevated enough to induce flow through the PFO.¹⁴ Clinicians should be aware of the possibility of a diagnosis of complex PFO, especially when dealing with cryptogenic stroke in young patients.

Acknowledgments

Mercy Health Saint Mary's Institutional Review Board's permission and written informed consent was obtained from the patient's next of kin (Mom) for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor in chief of this journal.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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