Fibromuscular Dysplasia in Children and Adolescents

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Introduction

FM D is a non-atherosclerotic, non-inflammatory disease that predominately affects the renal and carotid arteries, although it has been described in all vascular beds. Approximately 60–75% of all FM D cases involve the renal rather than the carotid vessels; the renal predilection, however, may be greater in children. FM D more commonly affects women and younger individuals, though the sex distinction has not been proven in children. While its pathogenesis is not completely understood, hormonal, mechanical, and genetic factors, as well as mural ischemia, are thought to play a role. The natural history may be relatively benign, with progression occurring in only a minority of the patients. Depending on the arterial layer that is affected, the disease may be characterized by multifocal, tubular, or focal stenosis, which is a narrowing of the arterial vessel caused by a deposition of collagen that extends into the lumen. In addition to stenosis, vessels with FM D may develop weak points in the vessel wall that then can become aneurysmal. The most prevalent form of FM D identified in children and young adults is intimal fibroplasia, typified by long, irregular or smooth, focal stenosis. Persons with FM D may be asymptomatic and only diagnosed at routine medical visits or even at work up for organ donation.

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Carotid Stenting: An update

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Case Report

Cerebral Vascular Accident Following a Pulmonary Embolism: Search for the Hidden Patent Foramen Ovale

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Cerebral Vascular Accident Following a Pulmonary Embolism: Search for the Hidden Patent Foramen Ovale

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Introduction
We present a case of an 83-year-old male who developed a pulmonary embolism (PE) and then suffered a cerebral vascular accident (CVA) three days later as a result of an unsuspected patent foramen ovale (PFO). This example emphasizes the importance of considering and identifying a PFO as an unsuspected cause of CVA, especially in the setting of proven venous thromboembolic disease.

Case Report
An 83-year-old male with multiple medical problems was admitted to the hospital for intravenous antibiotic treatment of a severe lower extremity cellulitis. He suffered from longstanding diabetes mellitus and resultant chronic kidney disease with nephrotic range proteinuria and hypoalbuminemia. In addition, he was a former smoker and has mild chronic obstructive pulmonary disease (COPD) as well as heart failure with preserved left ventricular ejection fraction. On the third day of his hospitalization, he became progressively short of breath and hypoxic. Physical examination and routine testing did not readily identify a cause for his sudden dyspnea and hypoxia. Empiric treatment with diuretics and nebulized bronchodilators failed to improve his symptoms.

The patient had normal pulmonary arterial systolic pressure (PASP) was estimated at 44 mmHg, elevated from his prior baseline of 28 mmHg a few months prior. Left ventricular function was globally normal with an ejection fraction of 60-65%. His right heart function was also normal and without evidence of right ventricular hypertrophy or dilatation.

Cardiology consultation was requested to assist in the evaluation and management of the right-to-left shunting across the PFO. At this time, physical exam revealed an elderly, ill-appearing male who was afibrile. Blood pressure was 150/80, pulse was 96 and regular, respiratory rate was 22 and his oxygen saturation was 93% on 4 liters of oxygen via nasal cannula. Neck exam revealed mild jugular venous distention estimated at 9 cm of water and no carotid bruits. Cardiac examination demonstrated a regular rate and rhythm with no appreciable murmurs, rubs, or gallops. Pulmonary exam revealed tachypnea, faint scattered wheezing diffusely, but otherwise clear to auscultation and percussion bilaterally. His abdomen was obese, but soft and with normal bowel sounds and no appreciable hepatosplenomegaly. He had cellulitis of his lower extremities with bilateral upper and lower extremity 3+ pitting edema. Laboratory data revealed a hemoglobin of 9.8 mg/dL, a creatinine of 3 mg/dL, blood urea nitrogen (BUN) of 38 mg/dL, an albumin of 1.7 mg/dL, and a type natriuretic peptide (BNP) of 133 pg/mL. His electrocardiogram was shown in Figure 1. His oxygen saturations were noted at rest with diuretics and nebulized bronchodilators failed to improve his symptoms.

Pulmonary angiogram was deferred given the high risk for developing contrast-induced nephropathy. A ventilation perfusion (V/Q) scan demonstrated a large right lower lobe perfusion defect suggestive of a PE. Anticoagulation treatment with intravenous heparin was started. The intra-atrial communication was determined to be a PFO. Prior echocardiograms were reviewed and did not have any findings of an intra-atrial communication or shunting by color Doppler when the patient had normal PASP. The PE was thought to increase pulmonary vascular resistance and thereby increase right atrial pressures, which opened a previously closed PFO and allowed for right-to-left shunting.

Unfortunately, 3 days after the initiation of anticoagulation, the patient was observed to have right upper extremity weakness. A magnetic resonance imaging (MRI) of the brain showed an acute right parietal lobe infarct with surrounding edema measuring approximately 3.3 x 3.8 cm. After several days, the patient’s right upper extremity strength and respiratory status returned to his baseline. A repeat echocardiogram with agitated saline bubble study was obtained 10 days after the initiation of treatment with anticoagulation to reassess the degree of right-to-left shunting.
shunting and demonstrated no shunting at rest (Figure 3). Only a few bubbles could be visualized crossing into the left atrium with Valsalva maneuver. The patient is doing well six months later.

Discussion
This case demonstrates a hidden cause of CVA and how a PFO allows right-to-left shunting with elevated right-sided cardiac pressures, posing a significant risk for paradoxical embolism. The septum primum and septum secundum fuse by age two in about 70 to 75 percent of children, with the remaining 25 to 30 percent having a PFO. This anatomy can lead to right-to-left shunting when the right atrial (RA) pressure is greater than the left atrial (LA) pressure (Figure 4). This can be demonstrated with maneuvers that increase RA pressures, such as the Valsalva maneuver, or in pathologic conditions that increase right-sided cardiac pressures. An important distinction is Eisenmenger’s syndrome.

A PFO is a congenital cardiac lesion that can persist into adulthood and is extremely common, with a prevalence estimated at 25–30% of the general adult population. The septum primum and septum secundum fuse by age two in about 70 to 75 percent of children, with the remaining 25 to 30 percent having a PFO. This anatomy can lead to right-to-left shunting when the right atrial (RA) pressure is greater than the left atrial (LA) pressure (Figure 4). This can be demonstrated with maneuvers that increase RA pressures, such as the Valsalva maneuver, or in pathologic conditions that increase right-sided cardiac pressures. An important distinction is Eisenmenger’s syndrome.

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Discussion
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The mechanism of stroke in this patient is postulated as follows: the acutely elevated right-sided cardiac pressures caused by the PE resulted in the patient’s PFO to open and allow for right-to-left shunting of blood. This shunting created a situation where a paradoxical embolus could occur where a venous thromboembolism could cross the intra-atrial communication and cause an arterial embolic phenomenon, i.e., an ischemic stroke.

Acute PE causes increased pulmonary vascular resistance (PVR) that impedes right ventricular outflow. PVR is increased by the physical obstruction of the vascular bed with thrombus as well as vasoconstriction caused by inflammatory mediators and hypoxia. The correlation of pulmonary artery pressure (PAP) to thrombus size and/or burden is limited by the variable contribution of vasoconstriction among subjects. However, when obstruction of the vascular bed approaches 75%, the right ventricle must generate a systolic pressure in excess of 50 mmHg and a mean PAP...
Individuals with Eisenmenger’s syndrome initially have substantial left-to-right shunting — generally through an ASD or ventricular septal defect (VSD) — and, as a result, morphologic alterations occur in the small pulmonary arteries and arterioles leading to pulmonary hypertension and the resultant reversal of the intracardiac shunt, i.e., right-to-left. These individuals demonstrate central cyanosis and digital clubbing on exam, ECG shows right atrial and ventricular enlargement with right axis deviation, and echocardiography shows signs of chronic right ventricular volume and pressure overload with ventricular hypertrophy and enlargement. Our patient had none of these findings.

**Literature Review of PFO and DVT in Cryptogenic Stroke**

On review of the literature, there are six large studies that report a prevalence of PFO in cryptogenic stroke ranging from 38 to 50% as compared to controls (4 to 18%) (Table I). Furthermore, a few studies have assessed the prevalence of DVT in patients with a PFO and cryptogenic stroke and found 10 to 57% of patients to have demonstrable DVT (Table II).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Type</th>
<th>Number of Subjects (N)</th>
<th>PFO Prevalence</th>
<th>Comparison Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lechat</td>
<td>1988</td>
<td>Case-control</td>
<td>60</td>
<td>40% vs. 10%</td>
<td>721 controls</td>
</tr>
<tr>
<td>Webster</td>
<td>1988</td>
<td>Case-control</td>
<td>40</td>
<td>50% vs. 15% (&lt; 0.001)</td>
<td>100 “normals”</td>
</tr>
<tr>
<td>Di Tullio</td>
<td>1992</td>
<td>Cross-sectional with nested case-control</td>
<td>146</td>
<td>48% vs. 4% (&lt; 0.001) vs. 15% (&lt; 0.001)</td>
<td>Cryptogenic stroke vs. Identifiable origin of stroke</td>
</tr>
<tr>
<td>Overell</td>
<td>2000</td>
<td>Meta-analysis of case-control studies</td>
<td>892</td>
<td>40% vs. 18% (&lt; 0.001) vs. 15% (&lt; 0.001)</td>
<td>Venography</td>
</tr>
<tr>
<td>Mas</td>
<td>2001</td>
<td>Prospective observational</td>
<td>581</td>
<td>46%</td>
<td>None</td>
</tr>
<tr>
<td>Homma</td>
<td>2002</td>
<td>Prospective multicenter randomized controlled treatment trial</td>
<td>250</td>
<td>39%</td>
<td>None</td>
</tr>
</tbody>
</table>

**Summary**

In summary, the evaluation of patients with cryptogenic stroke should include a search for the hidden PFO. And in the setting of a PFO, an increase in right-sided cardiac pressures — like that which occurs with an acute PE — can result in right-to-left shunting and pose a risk for a paradoxical embolism.

**Table I.** Prevalence of a PFO in patients with cryptogenic stroke

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Type</th>
<th>Number of Subjects (N)</th>
<th>DVT Prevalence</th>
<th>Comparison Group</th>
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<tr>
<td>Stollberger</td>
<td>1993</td>
<td>Cross-sectional observational</td>
<td>42</td>
<td>57%</td>
<td>Venography</td>
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<tr>
<td>Lethen</td>
<td>1997</td>
<td>Cross-sectional observational</td>
<td>53</td>
<td>10%</td>
<td>Venography</td>
</tr>
<tr>
<td>Cramer</td>
<td>2004</td>
<td>Cross-sectional observational</td>
<td>46</td>
<td>20%</td>
<td>MRI Venogram (MRV)</td>
</tr>
</tbody>
</table>

In the setting of a PFO, an increase in right-sided cardiac pressures — like that which occurs with an acute PE — can result in right-to-left shunting and pose a risk for a paradoxical embolism.