Multiorgan paradoxical embolism in an elderly female with a patent foramen ovale: a case report

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Abstract
Paradoxical embolism is an uncommon cause of arterial occlusion with a high mortality burden. Current evidence suggests that patent foramen ovale is the most important etiological factor of paradoxical embolism, by acting as a pathway for a thromboembolic material originating from the peripheral veins, passing through the lungs and entering the systemic circulation. Here we present a case of paradoxical embolism in the mesenteric and renal arteries associated with pulmonary embolism and deep vein thrombosis in an elderly woman with no predisposing risk factor. A diagnosis of paradoxical embolism was considered and the presence of a patent foramen ovale was consequently confirmed with a transesophageal echocardiography. Urgent thrombolysis saved the life of the patient. Paradoxical embolism represents an emergency and therefore prompt diagnosis and initiation of therapy may prevent adverse outcomes.

Keywords: patent foramen ovale, paradoxical embolism, pulmonary embolism, deep vein thrombosis, diagnosis

Introduction
Paradoxical embolism (PDE) is a potentially fatal phenomenon, characterized by the passage of a thrombus from the venous to the arterial circulation through an intracardiac defect [1]. The diagnosis is most often presumed following a cerebrovascular event which represents the most usual clinical manifestation of PDE [1]. It is often discovered incidentally and in some cases is associated with severe thromboembolic events with fatal outcome. Here we present an unusual clinical case of PDE, pulmonary embolism, deep vein thrombosis in an elderly woman with a patent foramen ovale (PFO).

Case presentation
A 77 year old woman was referred to the Emergency Department of the Saint George General Hospital of Chania, Crete, complaining of blunt epigastric abdominal pain, fatigue and malaise for the previous 48 hours. Her past medical history was unremarkable. On physical examination the patient presented hypotension (blood pressure: 75/30 mmHg), tachypnea (respiratory rate 22 breathes per minute) and sinus tachycardia (heart rate: 105 beats per second). Physical examination yielded abdominal tenderness on deep palpation of the epigastrium and of left lower quadrant with normal bowel sounds. Femoral pulse was equal bilaterally. Digital rectal examination was positive for blood.

Laboratory work up including hematological, liver and renal function tests were all normal except of elevated D-dimmers values >20 mg/L (normal <0.5 mg/L). Troponin test was negative. Arterial blood gas analysis disclosed pH 7.34, pO2:108 mm Hg, PCO2: 30.6 mmHg on ambient air.

An initial resuscitation with intravenous administration of fluids and inotropes was performed. After the patient was clinically stabilized she was transferred to the radiology department for a Computed Tomography (CT) abdominal and thoracic scan. The abdominal CT showed thrombosis of the superior mesenteric artery, inferior mesenteric artery, and the renal arteries (Figure 1, 2). Thoracic CT showed bilateral pulmonary embolism (Figure 3).
Figure 1. CT abdominal scan demonstrates occlusion of the superior mesenteric artery (red arrow).

Figure 2. CT scan disclosing embolism of renal artery (blue arrow).

Figure 3. CT thoracic scan showing pulmonary embolism (black arrow).
The patient was admitted to the Intensive Care Unit and underwent thrombolysis with alteplase 6.8mg (0.1 mg/kg) by trans-catheter intra-arterial infusion for 3 hours followed by oral anticoagulation therapy with warfarin. She was gradually ameliorated and remained at nil per os until the 5th day of hospitalization. Her clinical and laboratory status returned to normal with no tenderness in the abdomen. Trans-esophageal echocardiography was performed after injection of agitated saline contrast medium in the antecubital vein during the first phase of the Valsalva manoeuvre. At the second phase of the Valsalva manoeuvre, right to left shunt was detected by the visualization of approximately 10 contrast bubbles across the interatrial septum to the left atrium.

Ultrasound of the lower limbs disclosed thrombosis of the right and distal common femoral vein. Tumor markers were within normal limits. Thrombophilia testing was also performed and was negative for factor V Leiden, prothrombin gene G20210A mutation as well as for antiphospholipid antibody.

A follow up CT thoracic and abdominal scan showed improvement of PE with fewer and smaller deficits in the lumen of splanchnic arteries, mainly in peripheral branches. The splenic parenchyma was visualized with multiple infarcts.

The patient was discharged home with no recurrence of thrombosis. A lifelong antithrombotic therapy with warfarin was strongly recommended.

Discussion

In our patient emboli from the venous system caused the PE. PFO was the main predisposing factor for the PDE. Coexistence of a DVT with arterial occlusion raised the suspicion for PDE. PFO represents an anatomical abnormality characterized by interatrial communication leading to right to left shunt [1]. It is considered the most common intracardiac shunt encountered in 3 out of 10 healthy people from the general population [1]. Its presence was first described in 1564 by Leonardo Botallo, an Italian surgeon [2]. Data derived from observational studies suggest that the prevalence of detected PFOs does not differ in males and females, it declines with age, and is lower in the elderly patients [3]. The vast majority of the patients with PFO remain asymptomatic, and the diagnosis is often made during autopsy [4].

PDE was first described by Julius Friedrich Cohnheim (1839–1884) in 1877 [5,6]. He introduced the term PDE when during autopsy in a 35 years old female observed the concurrent occurrence of venous thrombosis in the lower extremity, a clot in the middle meningeal artery, and a patent foramen ovale (PFO) [5,6].

Hypercoagulable states (prothrombin G20210A mutation and Factor V Leiden) in the context of PFO are considered important risk factors for a cryptogenic stroke [7]. Other traditional risk factors for DVT in the setting of the PFO, such as prolonged immobility, malignancy and oral contraceptives may increase the risk of PDE [4].

Criteria for the diagnosis of paradoxical embolism include: 1) embolism in the arterial system 2) visualization of abnormal communication between arterial and venous system through imaging investigations 3) detection of a clot in the venous circulation or PE and 4) a communication between right to left heart [8,9]. Regarding the clinical presentation of PDE, it is nonspecific and depends on the size of embolic particles as well as the site of embolization [1].

It is often presented with neurological symptoms of ischemic stroke [10]. However, as in our case, PDE may involve the arterial system of various anatomic sites. Therefore it may present with thoracic pain and electrocardiographic abnormalities suggestive for ischemic heart disease [1], acute abdominal pain due to mesenteric ischemia [1], back pain due to renal artery infarction [1], cold lower limbs and absence of pulse due to peripheral arterial thrombosis [1].

Transoesophageal echocardiography (TEE) is considered the gold standard for the diagnosis of PFO with a high sensitivity and specificity rate (100%) [10, 11]. Through TEE clinicians may evaluate cardiac and valvular function, as well as the existence of intracardiac myxoma or clots [1]. TEE represents the optimal investigation for the assessment of the size of PFO as well as details on shunt quantity and direction. Furthermore, TEE is the appropriate test in order to rule out large and mobile plaques in the ascending aorta and aortic arch, which have been associated with an increased risk of stroke [1].

Therapeutic assessment for the secondary prevention of PDE includes percutaneous or surgical closure of the PFO as well medical therapy in order to diminish the risk of venous thrombosis [1]. Uncertainty exists regarding the optimal medical therapy for the prevention of recurrent events in patients with PDE. Acetylsalicylic acid, warfarin, or a combination of both medicines can be administered [1]. However, it has been reported that balancing the low risk of stroke recurrence and the increased bleeding risk of warfarin over aspirin, anti-platelet therapy is more relevant in patients with PFO and cryptogenic stroke [4]. Summarizing, data retrieved from randomized control trials do not suggest superiority of the PFO closure over medical treatment [1]. Certain high risk patients with a hypercoagulable state, DVT, PE and multiple paradoxical infarctions may benefit from the percutaneous closure with good short term prognosis [1]. In patients with cryptogenic stroke PFO closure is the optimal therapeutic approach [12,13].

The diagnosis of proven PDE is challenging and in most cases remains presumptive [1,14]. For this reason early recognition of paradoxical embolism is of paramount importance in order to prevent a fatal event through urgent anti-coagulation, thrombolysis or embolectomy. Physicians involved should always suspect the diagnosis of PDE in case of concomitant arterial and venous thromboembolism.
Informed consent
Written informed consent was given for the publication of this case report.

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