

Case Report

Acute venous thromboembolic disease and paradoxical embolism

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Background: We report two cases of paradoxical cerebral embolism associated with acute venous thromboembolic disease.

Case report: The first case corresponds to a 49-year-old woman with sudden onset of dyspnea and syncope, followed by right upper extremity paresis, aphasia and dysarthria.

The admission brain computed tomography (CT) was unremarkable, but lung CT showed multilobar and multisegmentary pulmonary embolism.

Echocardiography showed dilated right ventricle with impaired systolic function, moderate tricuspid regurgitation, moderate pulmonary hypertension and positive bubble test, suggestive of a patent foramen ovale (PFO) which was successfully closed by endovascular Amplatzer device placement. The patient was discharged with anticoagulation therapy and permanent antiplatelet aggregation therapy.

The second case is a 60-year-old woman found unconscious. Neurological examination revealed expressive aphasia, right hemianopsia, right central facial paralysis and right-sided paresis with a National Institute of Health Stroke Scale of 19. Brain CT showed signs of acute left middle cerebral artery infarction. Later, she developed greater impairment of consciousness.

A new brain CT showed significant edema with mass effect requiring a decompressive craniotomy.

Echocardiography showed PFO and lower extremities' Doppler ultrasound showed a left infrapopliteal posterior tibial right deep venous thrombosis. An inferior vena cava filter was placed and two days after surgery, anticoagulation was started.

Keywords: Acute pulmonary embolism, Patent foramen ovale, Ischemic stroke

Introduction

Normally the foramen ovale closes after the establishment of the adult circulation, but it may remain in approximately 25% of individuals. This anatomical communication between the venous and arterial circulation can be associated with the passage of venous thromboembolic material into the systemic circulation.¹

The combination of venous thromboembolic disease and ischemic stroke suggests the diagnosis of paradoxical embolism. Also, the presence of ischemic stroke without a clear source such as arrhythmias, carotid disease or aortic thrombus, may be associated with undiagnosed paradoxical embolism.²

Recent data suggest that the clinician should bear in mind the possibility of silent pulmonary embolism in patients with cryptogenic stroke and patent foramen ovale.³

Also in patients with high-risk of pulmonary embolism, echocardiographic detection of patent foramen ovale means a particularly high risk of death and arterial thromboembolic complications.³

Here we report two cases of patients with brain paradoxical embolization, even multiple embolic infarcts through a patent foramen ovale after an episode of deep vein thrombosis and a pulmonary thromboembolism. In addition, we reviewed the medical literature relevant to the subject matter.

Case 1

A 49-year-old woman was admitted to the emergency department brought by her family with a history of sudden onset of dyspnea and syncope, followed by right upper extremity paresis, aphasia and dysarthria. Her past medical history included the use of oral contraceptives for metrorrhagia and cholecystectomy for cholelithiasis.

At admission, the patient did not present febrile, with a heart rate up to 120 beats per minute, blood pressure 130/70 mmHg, respiratory rate of 23 per minute, her oxygen saturation was 86% while breathing

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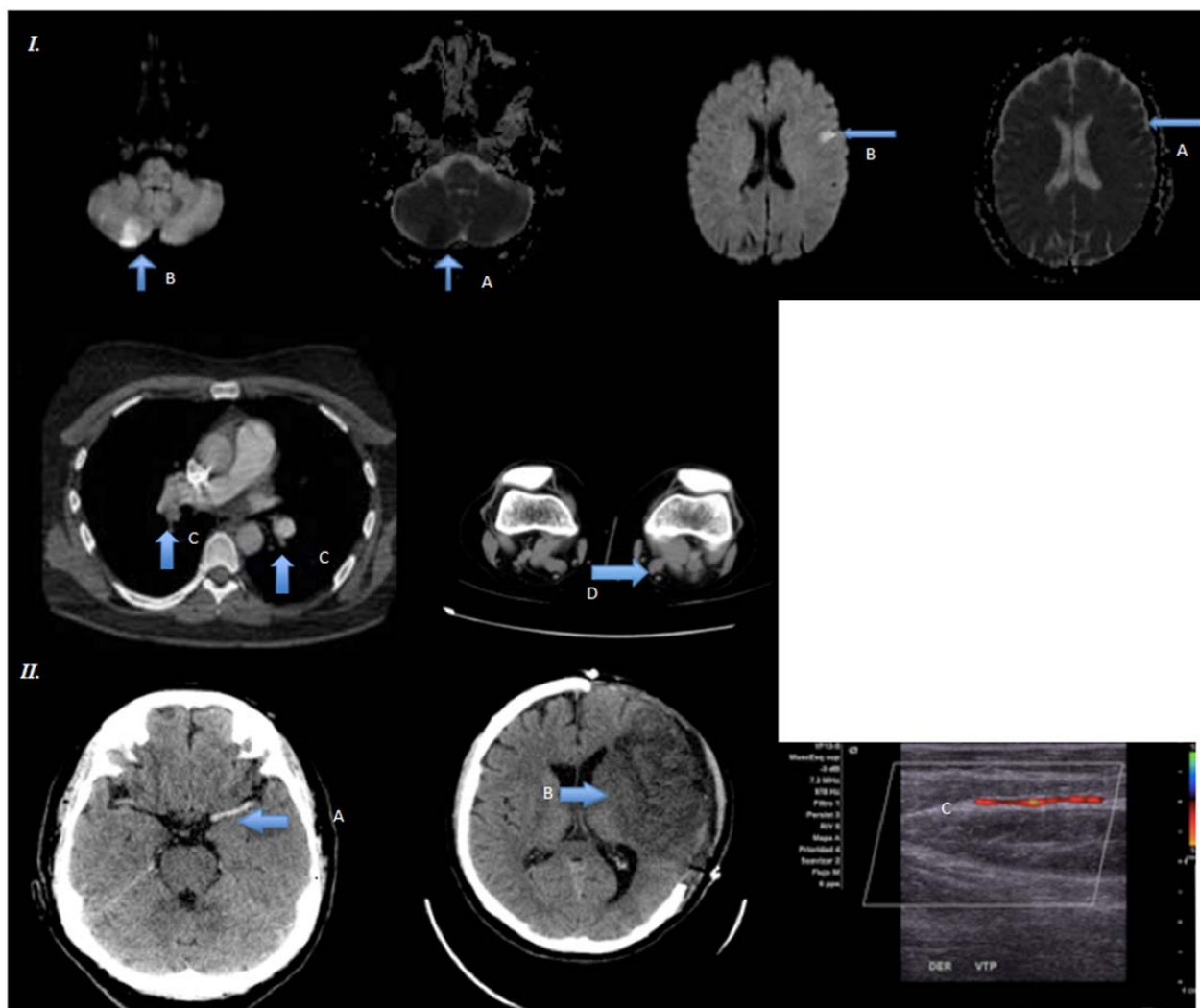


Figure 1 (I) Brain MRI in case 1. Supra and infratentorial infarctions seen as areas of restricted diffusion on diffusion weighted imaging (DWI) (A, arrow) with apparent diffusion coefficient (ADC) correlate (B, arrow). Pulmonary embolism of the left segmental and right pulmonary arteries (C arrow). Deep venous thrombosis of the left popliteal vein (D arrow). (II) Acute sign ('cord sign') of middle cerebral artery intraluminal thrombosis (A, arrow). Infarction of the middle cerebral artery (MCA) territory (9 days after), with fronto-temporo-parietal decompressive craniectomy (B, arrow). Deep venous thrombosis of the right posterior tibial vein (C).

ambient air, without hemodynamic compromise. Neurological examination showed right brachial paresis with modified Rankin scale of 1.

Arterial blood gases showed acute respiratory failure and some degree of hyperventilation (pH 7.43, PaCO₂ 22.1, PaO₂ 53.9, HCO₃ 14.3, SatO₂ 87%). Her brain computed tomography (CT) on admission was unremarkable.

During the first hours a chest CT angiography was performed and showed multilobar and multisegmentary pulmonary embolism, with CT suggestive of right-sided overload. Computed tomography venography showed popliteal and infrapopliteal left deep venous thrombosis (Fig. 1(I)).

She was transferred to the ICU and placed on noninvasive mechanical ventilation.

She did not require vasoactive drug support. Portable echocardiogram showed dilated right ventricle with impaired systolic function, moderate

tricuspid regurgitation, arterial pulmonary pressure of 45 mmHg and positive bubble test, which suggest a patent foramen ovale. Brain MRI showed right cerebellar infarcts, periatrial, left superior and middle frontal embolic strokes (Fig. 1(I)).

The patient was managed with unfractionated heparin and a transient inferior vena cava filter was placed. Subsequently, the foramen ovale was closed by an endovascular Amplatzer device placement, without any incident and with satisfactory results, echocardiogram showed resolution of the defect. The patient was discharged with anticoagulation therapy with acenocoumarol and permanent antiplatelet aggregation therapy was indicated.

Case 2

A 60-year-old woman, previously asymptomatic, was admitted to the emergency department, brought by her relatives. She was found unconscious lying down

in her bathroom after about an hour, without sphincter relaxation.

Her past medical history included longstanding hypertension, dyslipidemia, bilateral carpal tunnel syndrome and use of hormone replacement therapy. She had a family history of a brother with paradoxical embolism.

At admission, she was hemodynamically stable, without supplemental oxygen requirements. The neurological examination revealed expression aphasia, right hemianopsia, right central facial paralysis, right-side paresis and right Babinski with a National Institute of Health Stroke Scale of 19.

Her brain CT showed signs of recent left middle cerebral artery infarction, and images consistent with an intraluminal thrombus in the left supraclinoid carotid segments M1 and M2 (Fig. 1(II)).

She was managed with intravenous thrombolysis with Alteplase, but without clinical improvement. Afterwards, a brain MRI showed recent infarction in the territory of the middle cerebral artery without significant diffusion/perfusion mismatch images. An electroencephalography showed no epileptic activity or crisis pattern.

In the following hours, the patient developed greater consciousness impairment and a new brain CT showed significant edema with mass effect and midline 5 mm deviation. A decompressive craniectomy was performed (Fig. 1(II)).

Within the etiological study, echocardiography showed patent foramen ovale, with spontaneous passage of bubbles from right to left. Lower extremities Doppler ultrasound showed a left infra-popliteal posterior tibial right deep venous thrombosis (Fig. 1(II)).

Considering recent decompressive craniectomy, an inferior vena cava filter was placed.

Afterwards, unfractionated heparin was initiated and then overlapping with oral anticoagulation.

Discussion

We report two cases of acute embolic stroke associated with patent foramen ovale (PFO), and venous thromboembolic disease.

Ischemic cerebrovascular diseases are the third leading cause of death and the main cause of disability in developed countries. In approximately 40% of cases no classical causal etiology can be found despite an exhaustive study, and are defined as 'cryptogenic'. In about 50% of these cases the presence of patent foramen ovale is found.¹

There are only few clinical manifestations that can make a physician suspect about the presence of a patent foramen ovale.⁴

There is conflicting data with low grade of evidence about the relationship between the presence of PFO

and migraine, based in studies that showed an improvement in the frequency and severity of migraine headaches in patients with PFO closed for other reasons.⁴

Also there is an association between the presence of PFO and an increased risk of Decompression Illness in scuba divers.⁴

Another clinical manifestation could be the platypnea-orthodeoxia syndrome that is also observed in severe lung disease.

It is characterized by subjective dyspnea and objective hypoxemia on assuming an upright posture.⁴

When PFO is present, there is a venous to arterial shunting at an atrial level that increases when the patient assumes the upright posture via the redirection of inferior vena cava inflow towards the interatrial septum.

Device closure of the PFO is an effective treatment.⁴

In a meta-analysis of nine case-control studies involving 566 patients and 458 non-stroke controls, younger than 55 years with a stroke had an odds ratio of 3.1 for having a PFO.²

The association of venous thrombosis with an acute hemodynamically significant pulmonary embolism explains the physiopathology of the disease. Thereby an acute pulmonary embolism leads to an increase in right-sided pressures, which in turns open the PFO and facilitates the passage of the thromboembolic material from the right-side to the systemic circulation. This enables a paradoxical embolism in the presence of a PFO, reaching the left circulation rather than the lung. Chronic pulmonary hypertension also may cause right-to-left shunting across a PFO and predispose development of a paradoxical embolism.

Paradoxical embolism to the cerebral circulation is often difficult to diagnose clinically, but in absence of evidence for classical causes new diagnostic evaluation could be performed, including contrast-transesophageal echocardiography showing transit of agitated saline 'bubbles' from right atrium to left heart, that is accepted as the gold standard to detect right-to-left shunt across a PFO.²

Patients with PFO and previous strokes are at higher risk for developing recurrent cerebrovascular events compared to patients without PFO.

There is no established treatment for patients with stroke and PFO. Some therapeutic options include anticoagulants, surgical closure, or percutaneous closure devices.⁵

There is evidence for a decrease in recurrent strokes with foramen closure, and current practice consensus in the United States is PFO closure in these cases. With growing data on safety of the closure devices, a single event might justify placing one in such patient.⁵

Observational studies have shown that the risk of recurrent stroke, with aspirin or anticoagulation treatment varies from 3.4 to 13%.⁵

The Austrian Paradoxical Cerebral Embolism Trial compares outcomes of patients with cardiac right-to-left shunt and demonstrated a trend for fewer recurrences with interventional management (closure: 4 transient ischemic attacks vs medical: 3 strokes and 7 transient ischemic attacks in 9 patients; $P=0.066$). The complication rate of the procedure was 13.4, and 5.7% had residual shunting.⁶

Our cases emphasized the need to consider the role of paradoxical embolism by a PFO as an important cause of ischemic stroke in order to make an early diagnosis and a proper treatment, particularly in cases of transient increases in right-side pressures such as in pulmonary embolism.

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