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Clinical Short Communication

Paradoxical embolism through a patent foramen ovale from central venous catheter thrombosis: A potential cause of stroke

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ABSTRACT

Paradoxical embolism refers to a potential condition in which an embolus arising from a venous source crosses into the systemic circulation through a right-to-left cardiac shunt causing an arterial embolism.

A 39-year-old woman carrier of a central venous catheter (CVC) without evident risk factors for stroke, developed an acute right homonymous hemianopia during hemodialysis. On neuroimaging, an infarct in the territory of the left posterior cerebral artery was demonstrated. Transesophageal echocardiography revealed a patent foramen ovale (PFO) and a large fluctuating thrombus in the right atrium on the tip of the CVC, thus allowing a diagnosis of ischemic stroke from paradoxical embolism. Oral anticoagulation therapy was started and the PFO was closed.

This case emphasizes the potential risk of paradoxical embolism in patients with CVCs and PFO. This condition should be prevented and identified in patients with specific risk factors, such as long-term catheterization and hemodialysis.

1. Introduction

Paradoxical embolism (PDE) is a potential condition in which an embolus arising from the venous source reaches the systemic circulation through cardiac defects and structures causing an ischemic stroke [1]. Patent foramen ovale (PFO), present in about 25% of the general population, is the most common cause of intracardiac shunting [1–3]. PDE occurs in the fourth-sixth decade without gender preferences [4], but it has been occasionally reported in young patients [5–8] and infants [9], especially in the presence of thrombosis of a central venous catheter (CVC) [1,10]. Furthermore, an observational study on 144563 patients in the perioperative period after surgery showed an increased risk of stroke in the presence of a PFO [11]. Hence, PDE may become a relevant threat in consideration of the more frequent placement of CVCs in major surgery and intensive care units.

In this paper, we discuss on the diagnosis and management of PDE associated with intracardiac thrombus and PFO in a young patient carrier of a CVC.

2. Case presentation

A 39-year-old woman abruptly developed visual disturbances shortly after starting hemodialysis. She was previously well, except for a history of chronic renal failure due to bilateral ureterohydronephrosis receiving hemodialysis since the year before and a breast cancer in remission since 2014. She was on prophylactic anticoagulation with low molecular weight heparin (LMWH) (enoxaparin 100 UI/Kg) on starting dialysis. A reverse-tunnelled catheter of 15 Fr/Ch (5.0 mm) x 33 cm (Palindrome™) had been implanted 6 months before because of malfunction the peritoneal dialysis catheter. The neurological examination showed right homonymous hemianopia in absence of sensory-motor deficits.

A non-enhanced Computed Tomography and a Computed Tomography Angiography (CTA) of the intracranial and extracranial vessels were unremarkable, but a magnetic Resonance imaging (MRI) demonstrated an infarct in the territory of the left posterior cerebral artery (PCA) (Fig. 1). At the beginning the neurologist decided not to treat the patient with intravenous thrombolysis because of the late diagnosis of ischemic stroke (outside time window) and the risk of

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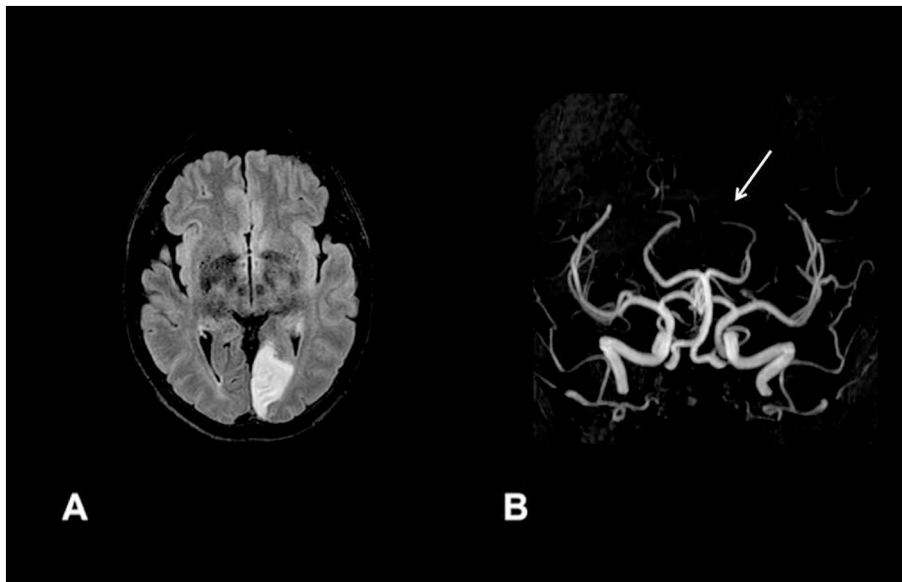


Fig. 1. MRI of the brain showing infarct in the territory of left PCA with a hyperintense signal on FLAIR sequences (A); MRA demonstrating absent flow (white arrow) in the P2 branch of left PCA (B). MRI, magnetic resonance imaging; FLAIR, fluid attenuated inversion recovery; MRA, magnetic resonance angiography; PCA, posterior cerebral artery.

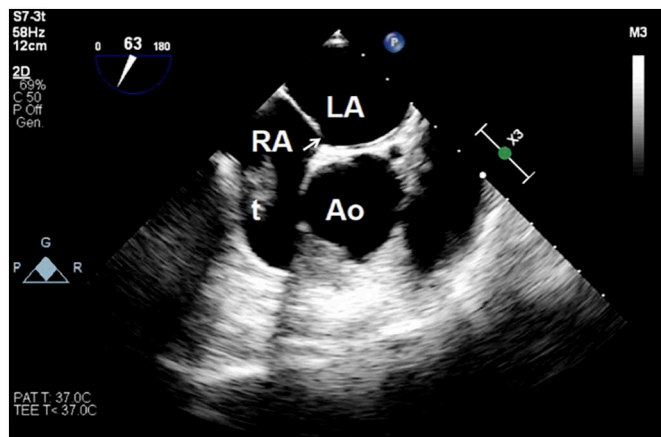


Fig. 2. Transesophageal echocardiogram showing a short-axis view which demonstrates a right-to-left shunt at atrial level through a PFO (white arrow). A large thrombus can be observed in the right atrium (t). RA, right atrium; LA, left atrium; PFO, patent foramen ovale; Ao, Aorta.

bleeding, as she was on prophylactic anticoagulation with LMWH and the activated partial thromboplastin time (aPTT) was 40 s.

Routine diagnostic workup for ischemic stroke came back negative. The CVC placement was correct, with the tip located in the centre of the right atrium, next to the emergence of the superior vena cava, as confirmed by echocardiography and dialysis monitoring system. As the initial transthoracic echocardiography study was unremarkable, transesophageal echocardiography (TEE) was performed as soon as available (after 5 days) to exclude endocarditis. Unexpectedly, TEE revealed a large fluctuating thrombus of 1.1×1.8 cm in size in the right atrium on the tip of the CVC and a medium-sized PFO (Fig. 2, Video 1, Video 2), characterized by a tunnel 1 cm long and 2 mm wide with an abundant passage of bubbles at rest and during the Valsalva manoeuvre. After the first echocardiogram, the patient started anticoagulation therapy bridging from LMWH to vitamin K antagonists (VKA) to obtain an international normalized ratio (INR) of 2–3. Then, anticoagulant therapy doses were increased to adjust the INR range between 2.5 and 3.5 due to the persistence of close thrombi and the need to continue dialysis with CVC (she was not able to receive an arteriovenous fistula). The patient underwent percutaneous closure of the PFO with an Amplatzer device after a significant reduction of the thrombus size. At last evaluation after six months of follow-up the

patient still presented mild residual visual deficits and echocardiography showed a significant reduction of the thrombus with residual smaller thrombotic materials. LMWH was interrupted and the patient is now on anticoagulation with VKA maintaining an INR of 2–3.

3. Discussion

We reported a case of ischemic stroke during hemodialysis due to the crossing of a large CVC thrombus through a PFO, thus responsible for paradoxical embolism. We found 6 cases of PDE associated with CVC thrombosis (Table 1) [5–9], whose only one occurred during hemodialysis [8]. In our patient, we hypothesized that at the beginning of hemodialysis an increase of venous pressure in the upper vena cava could have produced a right-to-left shunt through a PFO, leading to a right-to-left shunt and the passage of thrombotic material in systemic circulation. However, PDE was only an assumed albeit likely cause of the stroke as the passage of the embolus through the PFO was not witnessed.

The thrombogenicity of the material, the thickness of the catheter and the CVC-tip position can influence the risk of thrombosis, which is higher in patients with cancer, due to a hypercoagulable state [7,10,12]. Also, the chronic renal disease may have influenced the thrombogenic risk in our patient; in fact, the risk of stroke is 5–30 times higher in patients with chronic renal disease, especially on dialysis [13]. Of interest, an internal CVC-tip position peripheral to the atrio-caval junction more likely undergoes internal repositioning and venous thrombosis. Hence, the internal catheter tip should be positioned at the atrio-caval junction or within the right atrium [10,14]. However, current protocols do not include tip-confirmation in the right atrium or postprocedural scans looking for tip-related thrombosis; in addition, available data do not support the routine use of anticoagulants for thromboprophylaxis to prevent CVC-related thrombosis [14,15]. In recent years, VKA and aspirin are used as anticoagulant medications for the secondary prevention of PDE, while, there is no indication for direct-acting oral anticoagulants (DOAC) in this subset of patients [16–18].

Management of CVC-thrombosis is difficult: there have been cases of thromboembolic complications even after removal of the catheter [9,19] and thrombolysis might cause clot fragmentation [7]. Current guidelines recommend anticoagulation with or without CVC removal [15]; the choice of treatment should take into account the risk of bleeding. When started, anticoagulation should be given until the resolution of the thrombus. We suggest removing the catheter only after

Table 1
Previously reported cases of paradoxical embolism associated with CVC thrombosis. Age, gender, CVC characteristics, risk factors, diagnosis and management of previously reported cases of paradoxical embolism associated with CVC thrombosis.

Author	Year, sex	CVC	Risk factors	Intervention/ Prophylaxis	Diagnosis	Site of ischemia
Batsis J A et al., [5]	46 M	Triple-lumen (Swan-Ganz) CVC in the right jugular vein (fluid management)	Alcohol abuse, smoking, diabetic ketoacidosis, respiratory failure.	Subcutaneous heparin	Transesophageal echocardiography	Right occipital lobe
Osten M et al., [6]	72 F	Residual CVC in the right atrium	Breast cancer, incomplete removal of a Port-a-Cath	Retrieving embolized Port-a-Cath, PFO closure, ASA 81 mg + Plavix 75 mg	Intracardiac echocardiography	Not known (TIA with dysarthria and right facial drop)
Cardim N et al., [7]	57 F	CVC implanted in the superior vena cava	Colon adenocarcinoma, liver and lung metastasis, <i>Listeria monocytogenes</i> bacteraemia	Intravenous unfractionated heparin; surgery to remove the thrombus; PFO closure.	Trans thoracic and transesophageal echocardiogram	Left frontal lobe
Petrea RE et al., [8]	71 M	PICC in the superior vena cava prolapsing in the right atrium	Diabetes mellitus, hypertension, coronary artery and peripheral vascular disease	Removing PICC, antiplatelet therapy	Trans thoracic echocardiogram	Left cerebellar hemisphere
Petrea RE et al., [8]	64 F	CVC, while receiving hemodialysis	End-stage renal disease, diabetes mellitus, hypertension, congestive heart failure, obesity	Antiplatelet therapy	Trans thoracic echocardiogram	Right parietal lobe
Biermayr M et al., [9]	Preterm F	CVC (PICC) in the right atrium	Preterm	Removed CVC, unfractionated heparin	Trans thoracic echocardiogram	Left hemisphere
Present case	39 F	CVC, while receiving hemodialysis	Breast cancer, chronic renal disease	Anticoagulation with Vitamin K antagonists, PFO closure.	Transesophageal echocardiography	left posterior cerebral artery territory

proven dissolution of the thrombus on repeated echocardiograms secondary to adequate anticoagulation therapy.

Further discussion emerges about the choice of PFO closure in patients with CS [17,20,21]. PFO closure has been proposed for the secondary prevention of stroke in patients with CS and PFO; recently, several randomized controlled trials have investigated this problem with conflicting results, but meta-analyses and more recent trials provided evidence that PFO closure is superior to stroke prevention with antiplatelet therapy in patients with CS and an age range of 18–60 years [17,20]. In our case, a PFO was detected in a patient with CVC thrombosis and intracardiac thrombus, thus complicating the management. However, the abundant passage of bubbles on TCD and TEE features of the PFO pushed us to decide to close it. As a first step, anticoagulation was increased with the goal of an INR range of 2.5–3.5; finally, the PFO was closed after a significant reduction in the size of the thrombus because of the high risk of stroke recurrence and the need to maintain catheterization to continue dialysis.

This case underlines the importance of searching for PFO in CVC-carriers looking for possible sources of embolism especially in patients with thrombophilia and chronic renal disease. Finally, a particular attention should be taken in patients undergoing hemodialysis due to the possible increase of venous pressure producing a right-to-left shunt.

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Author contribution

LD, MVD and MD provided clinical care to the patient. VD drafted the first version of the manuscript, and all authors contributed to and have approved the final version of the manuscript.

Ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informant consent

Obtained.

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Declaration of Competing Interest

On behalf of all authors, the authors declare that there is no conflict of interest.

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