Thrombus in transit through a patent foramen ovale: catch it if you can—a case report

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Background
Patent foramen ovale (PFO) is one of the most common congenital heart defects, but the finding of a thrombus in transit (TIT) through a PFO is extremely rare. It is a therapeutic challenge, and systemic anticoagulation, cardiac surgery, or fibrinolysis should be considered.

Case summary
A 43-year-old woman was admitted with intermediate-high-risk pulmonary embolism. Transthoracic echocardiogram revealed a large right atrial mobile mass that crossed the interatrial septum through a PFO, compatible with TIT, and the patient was started on unfractionated heparin. The diagnosis was confirmed by transoesophageal echocardiogram (TOE). However, during TOE probe removal, the patient developed dyspnoea, sudoresis, and peripheral desaturation, and new image acquisition revealed sudden mass disappearance. Due to the possibility of paradoxical embolization associated with Valsalva manoeuvre, fibrinolysis with alteplase was promptly started. The patient had no signs of embolic or haemorrhagic complications and remained clinically stable. She was discharged on warfarin and then underwent percutaneous transcatheter closure of PFO.

Discussion
The treatment strategy of a TIT through a PFO is controversial, but surgery might be the most appropriate treatment for haemodynamically stable patients, while thrombolysis should be used in cases of haemodynamic instability. Transoesophageal echocardiogram is generally a safe procedure but pressure changes associated with Valsalva manoeuvre may induce embolization of a TIT and attention should be given to patient sedation and tolerance. After complete embolization of a TIT, emergent thrombolysis may be the only treatment option, in order to prevent disastrous consequences related to paradoxical embolism.

Keywords
Thrombus in transit • Patent foramen ovale • Fibrinolysis • Pulmonary embolism • Case report

Learning points
- The finding of a thrombus in transit (TIT) through a patent foramen ovale (PFO) is extremely rare, and its treatment may include anticoagulation, fibrinolysis, or cardiac surgery.
- Transoesophageal echocardiogram is generally a safe procedure but pressure changes associated with Valsalva manoeuvre may induce embolization of a TIT.
- After spontaneous and complete embolization of a TIT, fibrinolysis may be the only treatment option, and PFO closure is recommended to prevent new episodes of systemic embolization.

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Introduction

Patent foramen ovale (PFO) is a congenital heart defect that affects 20–34% of the population. Most patients are asymptomatic but some may suffer from paradoxical embolization. Diagnosis of paradoxical embolization associated with PFO is generally presumptive, as the finding of a thrombus in transit (TIT) through a PFO is extremely rare. In this situation, the treatment is controversial and may include anticoagulation, fibrinolysis or cardiac surgery, or a combination of these.

We present a case of pulmonary embolism with a thrombus crossing a PFO with paradoxical embolization induced by Valsalva manoeuvre during transoesophageal echocardiogram (TOE), and discuss treatment options.

Timeline

| Time          | Event                                                                 |
|---------------|-----------------------------------------------------------------------|
| 2 days before admission | Symptom onset (chest pain and dyspnoea)                               |
| Admission (Day 0) | Diagnosis of pulmonary embolism                                       |
| Day 1         | Spontaneous embolization of thrombus in transit through the patent foramen ovale (PFO) during transoesophageal echocardiogram. Fibrinolysis. |
| Day 20        | Hospital discharge (on warfarin)                                      |
| 6 months      | PFO closure                                                           |
| 12 months     | Switch from warfarin to apixaban                                      |
| 24 months     | Follow-up without new embolic episodes                                 |

Case presentation

A 43-year-old Caucasian female was admitted to the emergency department with chest pain and dyspnoea that persisted for 2 days. She had history of erythema nodosum, thyroid nodules, and leg varicose veins treated with sclerotherapy in the previous month, and was medicated with a combined oral contraceptive (drospirenone/ethinyl estradiol 3 mg/0.03 mg). There was no history of smoking, trauma or immobilization, or relevant family history.

Physical examination revealed tachycardia (104 b.p.m.), normal blood pressure (135/89 mmHg), oxygen saturation of 98% on room air. The patient was eupeptic, cardiopulmonary auscultation was unremarkable and there were no signs of peripheral hypoperfusion or deep venous thrombosis. Arterial blood gas analysis showed respiratory alkalaeemia with normal lactate levels. Electrocardiogram revealed sinus tachycardia with T-wave inversion in right precordial leads and the chest X-ray was unremarkable. Laboratorial evaluation showed D-dimers of 11 014 ng/mL (normal <250) and troponin I of 0.24 ng/mL (normal <0.06). Chest computed tomography (CT) angiography identified extensive bilateral pulmonary embolism, and right atrial (RA), right ventricular (RV), and pulmonary trunk enlargement (Figure 1).

The patient was admitted to the cardiac intensive care unit due to unprovoked intermediate-high-risk pulmonary embolism. A bedside transthoracic echocardiogram (TTE) revealed signs of RV pressure overload, with right chambers dilation, flattened interventricular septum, RV-RA pressure gradient of 50 mmHg, tricuspid annular planar systolic excursion of 16 mm, and a RA mobile mass, suggestive of a thrombus, that apparently crossed the interatrial septum through a PFO (Figure 2 or Video 1). Anticoagulation, fibrinolysis, or cardiac surgery were considered but, due to the haemodynamic stability, unfractionated heparin was started.

After discussion with cardiothoracic surgery, a TOE was performed, under sedation with midazolam, revealing a big mobile form mass with ~60 mm, located in the RA and crossing the interatrial septum through a PFO, with extension to the left atrium and mitral valve, suggestive of a TIT (Figure 3 or Video 2). During probe removal, the patient developed dyspnoea, sudodesis, and peripheral desaturation. TOE probe was reintroduced and the mass had disappeared (Figure 4). Both pulmonary embolism and paradoxical embolization were suspected, as there was peripheral desaturation and the mass had a significant extension to the left cardiac chambers. Even though the patient was haemodynamically stable, without neurological deficits and stabilized with supplemental oxygen via Venturi mask at 28%, fibrinolysis with alteplase was promptly started, due to the possibility of paradoxical embolization. There were no clinically evident haemorrhagic or embolic complications. The patient developed drowsiness and vomiting but remained stable and the neurological examination and the cranioencephalic CT were normal.

Over the next days, the patient remained stable. Repeated TTE revealed normalization of right cardiac chambers dimensions and function. An exhaustive evaluation to exclude secondary causes of pulmonary embolism identified homozygosity for the 4G polymorphism of the plasminogen activator inhibitor 1 gene. Thoraco–abdomino–pelvic CT identified right common carotid artery thrombosis, involving external and internal branches.

The patient was discharged on warfarin to a target international normalized ratio (INR) of 2 to 3, and the oral contraceptive was stopped.

Six months after discharge, the patient was referred for percutaneous transcutaneous closure of PFO, and started a 1-month course of clopidogrel, while maintaining warfarin. Twelve months after discharge, a genetic thrombophilia screen was repeated and excluded thrombophilic disorders. After discussion with immunohematology and internal medicine, as this was the first episode of unprovoked pulmonary embolism, switch to lifelong oral anticoagulation with apixaban 2.5 mg bid was decided. After 24 months of follow-up, the patient is asymptomatic, without further evidence of pulmonary or systemic embolization.

Discussion

We present a rare case of a TIT through a PFO, treated with fibrinolysis after embolization induced by Valsalva manoeuvre during TOE.

PFO results from incomplete fusion of septum primum and septum secundum that generally occurs after birth. In the majority of time, PFO is functionally closed, but it can be opened by manoeuvres...
that change intrathoracic pressure, allowing interatrial passage of substances. Therefore, although most patients with PFO are asymptomatic, others may suffer from paradoxical embolization.

The incidence of paradoxical embolism associated with PFO is difficult to establish, because the diagnosis is usually presumptive and based on the concomitant presence of venous thromboembolic disease, arterial embolism, and a PFO. The finding of a TIT through a PFO is extremely rare. The first case diagnosed by TOE was reported in 1985 by Nellessen et al. and the most recent literature review included 194 patients, from 1991 to 2015.

Treatment of a TIT is controversial due to the lack of prospective randomized trials, but a cardiothoracic surgeon should be consulted after diagnosis.

Emergent thoracotomy with thrombectomy and surgical PFO closure may be the best option for haemodynamically stable patients, as studies have shown a lower incidence of post-treatment embolic events and mortality.
Anticoagulation alone is primarily used in patients with important comorbidities, high surgical risk, or when patients refuse invasive therapy.7,10

Fibrinolysis is generally reserved for poor surgical candidates, haemodynamically unstable patients with high-risk pulmonary embolism or for cases of acute ischaemic stroke, as it may cause thrombus fragmentation and/or embolization and is associated with higher mortality.7,11

To our knowledge, there is only one published case of a TIT through a PFO that embolized during TOE, after the patient coughed.7 Although TOE is associated with a low complication rate, oesophageal intubation can induce vagal and sympathetic reflexes, with blood pressure and heart rate fluctuations. Besides that, even after sedation and local anaesthesia of the pharynx, retching and coughing commonly occur, and the associated Valsalva manoeuvre induces changes in intrathoracic, central venous, and pulmonary pressures. These pressure variations may cause the mobilization of any intracardiac material, with subsequent pulmonary or systemic embolization. The extent of embolization will depend on the haemodynamic fluctuations associated with Valsalva manoeuvre as well as on mass characteristics, such as size, density, and mobility. In order to prevent embolization, sedation is very important to improve patient tolerance and under general anaesthesia retching and gag reflex are abolished.12

After embolization of a TIT through a PFO, emergent thrombolysis may be indicated due to the very high risk of paradoxical embolization with potential serious consequences.2

Regarding oral anticoagulation after surgery or fibrinolysis, most authors chose vitamin K antagonists with a target INR 2–3. We found one report of the use of apixaban 5 mg twice a day after surgical thrombectomy13 and another of dabigatran after thrombolysis.7 Nevertheless, the possible role of direct oral anticoagulants still remains undefined.13

Most paradoxical embolisms present as cerebrovascular events, given the anatomy of the aortic arch.1 Decision about PFO closure should be based on the probability that the foramen ovale has a relevant role in the observed clinical scenario and the likelihood of recurrence.14 In this case, the finding of a TIT and, after its embolization, of right common carotid artery thrombosis proves paradoxical embolization and is an indication for treatment.

In conclusion, this case reflects the therapeutic challenge of a TIT through a PFO. Although TOE is generally safe, pressure changes associated with Valsalva manoeuvre may induce embolization of a TIT, and careful consideration should be given to patient sedation and tolerance in order to prevent triggering this manoeuvre. After embolization of a TIT, fibrinolysis can be the only treatment option, in order to prevent disastrous consequences related to paradoxical embolism.
Lead author biography

Maria Inês Pires is a Cardiology resident in the Tondela-Viseu Hospital Centre, with interest in Heart Failure. She is graduated from the School of Health Sciences, University of Minho.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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