



Recurrent paradoxical cerebral embolism caused by a thrombus entrapped in a patent foramen ovale: a case report

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Introduction: A thrombus straddling the patent foramen ovale (PFO) is a very rare clinical entity. Optimal management remains unclear due to the availability of various therapeutic options; thus, an individualized approach is recommended.

Case presentation: The authors describe a case presenting with recurrent cerebral embolism and a large and mobile thrombus straddled in the PFO. Historically, cardiac surgery, thrombolysis or anticoagulation were possible management options for this patient. However, there are no guidelines on what the optimal treatment is. Our patient was a poor surgical candidate because of advanced age and multiple comorbidities. Furthermore, she had a recent ischaemic stroke which was a relative contraindication to thrombolysis. After consulting the Heart Team, medical treatment alone with systemic anticoagulation was administered. Subsequent transthoracic echocardiography (TTE) after 1 week showed complete thrombus resolution. After 4 months, the PFO was successfully occluded with an Amplatzer device. The patient received rehabilitation therapy and had good functional recovery.

Clinical discussion: Anticoagulant therapy alone was chosen because of high risk for surgery. Complete thrombus resolution was achieved after 1 week although the initial thrombus size was quite large. Nevertheless, this approach may not be applicable to every patient. In addition to TTE, multimodality imaging using transesophageal echocardiography and cardiac magnetic resonance is helpful to identify the mechanism of stroke, which in our case is a thrombus-straddled PFO, and to make early treatment decisions. Serial TTEs help assess the response to anticoagulation. An individualized approach should be made with a multidisciplinary Heart Team.

Conclusion: Echocardiography plays an important role in the diagnosis and treatment evaluation for patients with a thrombus straddling a PFO. An individualized approach to manage the patient should be made with a multidisciplinary Heart Team.

Keywords: recurrent cerebral embolism, paradoxical embolism, patent foramen ovale, straddling thrombus

Introduction and importance

A paradoxical embolism is characterized by the occurrence of systemic embolism due to a venous thrombosis passing through an intracardiac or pulmonary shunt^[1]. The primary cause of intracardiac shunting is often a patent foramen

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HIGHLIGHTS

- Echocardiography plays an important role in the diagnosis and treatment evaluation for patients with a thrombus straddled in a patent foramen ovale.
- Management options include surgical thrombectomy with patent foramen ovale closure, thrombolysis and systemic anticoagulation.
- Optimal treatment should be made through team-work discussion including all specialists potentially involved.

ovale (PFO), prevalent in approximately a quarter of the adult population, which typically remains asymptomatic. Nevertheless, it can be associated with cryptogenic strokes resulting from systemic embolism. While instances of thrombus straddled within the PFO are exceedingly rare, they pose a significant clinical urgency due to the impending systemic embolism^[2]. The presence of a PFO in a patient with right heart thrombus is associated with a 27–45% increase in mortality^[3]. Available therapeutic approaches encompass surgical removal, systemic anticoagulation, and thrombolysis. However, a consensus on the most effective treatment strategy has not been reached^[4–6]. The case report was presented in line with the SCARE criteria^[7].



Figure 1. Echocardiography upon hospitalization. (A) Transthoracic echocardiography image (TTE) revealed the mobile mass in both the left and right atriums. (B) Follow-up after 1 week using TTE demonstrated a reduction in the thrombus size, with it now confined to the left atrium. (C) TEE showcased the presence of the mobile mass.

Case presentation

We present the case of a 67-year-old woman who was admitted to the hospital due to right-sided weakness, confusion, aphasia, and dysphagia. She had experienced recurrent strokes in the 3 months preceding this hospitalization. Her history was notable with a poorly controlled hypertension. She did not have any remarkable family history, diabetes, dyslipidemia, or thrombophilia. On admission, the patient was hemodynamically stable, and had no murmur on cardiac auscultation. She displayed complete right-sided hemiplegia with mild cognitive impairment (Glasgow Coma Scale score of 13). Careful examination of the lower extremities did not reveal signs of venous thrombosis. At the time of admission, she was taking Amlodipine 5 mg and Aspirin 81 mg as part of her daily medication.

Laboratory testing indicated mildly elevated levels of high sensitivity troponin and D-dimer, while other findings were within the normal range with no apparent cause for hypercoagulable states. An ECG displayed sinus rhythm with left axis deviation and no S1Q3T3 pattern. Doppler ultrasound results revealed the absence of deep vein thrombosis. Chest X-ray imaging yielded normal results. Brain magnetic resonance imaging unveiled acute pontine infarctions along with some older, smaller

infarctions (Fig. 2A). Transthoracic echocardiography (TTE) revealed the presence of a mobile mass within both the left and right atriums (Fig. 1A), along with a systolic pulmonary arterial pressure of 40 mmHg. The left ventricular ejection fraction was within the normal range at 67%. Subsequently, a transesophageal echocardiography (TEE) was performed, revealing a thrombus measuring 13×29 mm in cross-sectional area straddling a PFO, occasionally protruding through the tricuspid valve (Fig. 1C). A subsequent cardiac MRI depicted a sizable mobile thrombus spanning the PFO, with no thrombus detected in the pulmonary artery (Fig. 2B).

The patient was diagnosed with recurrent paradoxical cerebral embolism attributed to a thrombus straddling a PFO. Following diagnosis, anticoagulation with intravenous heparin was initiated. Due to concerns regarding elevated embolic risk during antithrombotic treatment, surgery was initially considered. However, on careful evaluation, our patient was a poor surgical candidate because of her advanced age and multiple comorbidities. Furthermore, her stroke-related neurologic deficits may complicate the postoperative course. On the other hand, her recent ischaemic stroke was a relative contraindication to thrombolysis. After consulting a multidisciplinary Heart Team, it was decided that a conservative

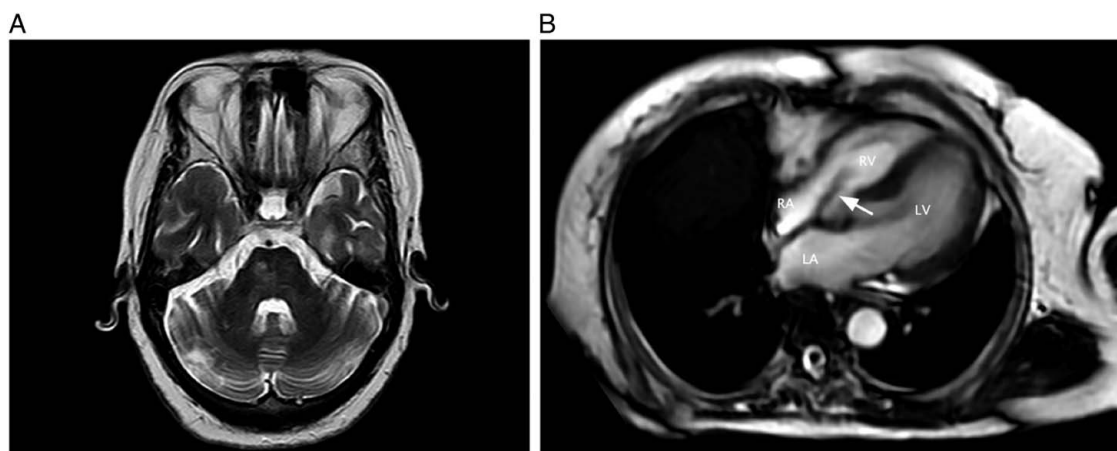


Figure 2. Magnetic resonance imaging. (A) Brain MRI exhibited acute pontine infarctions along with some smaller, pre-existing infarctions. (B) Cardiac MRI depicted a significant mobile thrombus spanning within the patent foramen ovale, with no thrombus observed within the pulmonary artery.

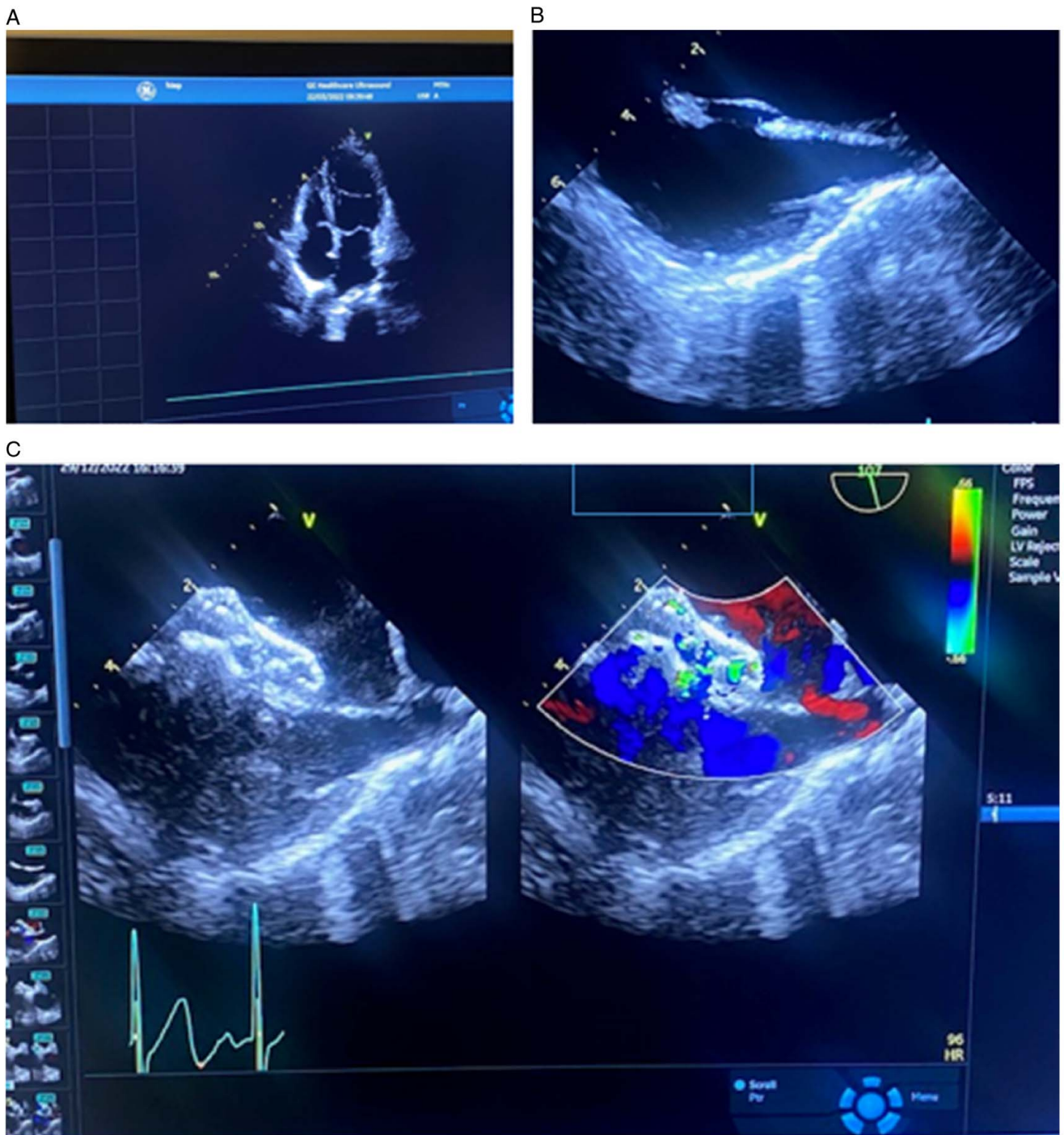


Figure 3. Echocardiography images after anticoagulation treatment and follow-up until patent foramen ovale (PFO) occlusion: (A) Transthoracic echocardiography (TTE) image demonstrates the full dissolution of the thrombus. (B) TEE reveals the complete resolution of the thrombus. (C) TEE demonstrating the PFO occluded by an Amplatzer septal occluder.

approach be implemented. Systemic anticoagulation using unfractionated heparin (with target activated partial thromboplastin time between 2.0 and 3.0) was administered. Her subsequent TTE after one week demonstrated partial resolution of the thrombus that was entirely localized in the left atrium (Fig. 1B). The patient was transitioned to warfarin therapy. A follow-up TTE after 3 weeks showed complete

dissolution of the thrombus (Fig. 3). She was discharge on long-term oral anticoagulation with warfarin to maintain an International Normalized Ratio of 2.0–3.0 and is scheduled for percutaneous PFO closure. The patient underwent a successful PFO occlusion procedure and participated in a comprehensive rehabilitation program, yielding remarkable improvements in her clinical status.

Clinical discussion

Although a PFO is found in about 27% of the general population, this condition often remains asymptomatic. The occurrence of an intracardiac thrombus-in-transit straddled within a PFO is linked to significant mortality, marked by an 18.4% mortality rate within 30 days, with a striking 62.5% of these fatalities happening within the initial 24 h of presentation. Furthermore, this condition is associated with notable morbidity, encompassing isolated pulmonary embolism (53%), isolated systemic embolism (7%), or a combined embolic event (40%)^[4].

A large systematic review was carried out spanning the years 1991 through 2015, identifying a total of 194 patients (from 185 articles) presenting with a trapped thrombus in the patent foramen ovale (PFO) condition. Among these patients, 166 underwent TEE, revealing suspected trapped thrombus in PFO for 145 individuals (resulting in a diagnostic accuracy rate of 87.3%). The remaining 176 patients underwent TTE, which confirmed trapped thrombus in PFO for all of them (yielding a diagnostic accuracy rate of 100%). TEE outperformed TTE in directly visualizing the thrombus and the patent foramen ovale^[6]. Therefore, TEE should be considered for patients suspected of having a paradoxical embolic event.

Among the cohort of patients, 57.7% underwent surgical intervention, 14.5% received thrombolysis, and 27.8% were treated solely with anticoagulation. Recent systematic reviews focused on thrombus-in-transit treatment underscore the efficacy of surgical thrombectomy and PFO closure in reducing 30-day and 60-day mortality rates, as well as the occurrence of systemic embolism. The overall 60-day mortality was 13.9%. Favourable outcomes were more common in the surgical group (6.3%) compared to thrombolysis (35.7%) and anticoagulation alone (18.5%). Another systematic review by Myers and colleagues, involving 154 studies, revealed no significant survival difference among thrombolysis, anticoagulant therapy, or thrombectomy. However, surgery emerged as an effective deterrent against systemic embolism^[4]. Due to the rarity of this clinical entity and a wide array of patient comorbidities, drawing generalized conclusions is challenging. Hence, determining the optimal treatment for each individual patient necessitates comprehensive discussions with all involved specialists^[8]. Although surgical embolotomy displayed a trend toward better survival, its postoperative mortality rate remains elevated. In certain cases, like the one reported by Lu *et al.*^[9], thrombolytic and anticoagulant therapies can serve as alternatives when surgical risk is exceedingly high. In our case, our elderly patient with multiple comorbidities posed an unfavourable surgical candidate and faced elevated bleeding risks with thrombolysis. Consequently, we elected to pursue anticoagulation treatment exclusively. This approach resulted in an uneventful recovery, with subsequent echocardiography confirming the complete resolution of the thrombus. Multiple randomized controlled trials have underscored the efficacy of percutaneous PFO closure for secondary prevention of cryptogenic stroke when compared to medical therapy^[10–14]. In our patient's case, successful PFO closure was achieved using the Amplatzer device, leading to remarkable clinical improvement.

AngioVac is a percutaneous device that has gained approval within the past 10 years for the extraction of vascular and right heart thrombi. A noteworthy milestone in its application was recorded in March 2021, when Deanne Gill *et al.* reported the

first documented instance of successful utilization of AngioVac to extract a thrombus trapped within the PFO, as published in the *Journal of the American College of Cardiology*^[15]. This case prompted us to consider the feasibility of employing this method during the acute phase for our patient and ponder its potential broader application in future similar cases.

Conclusion

Echocardiography, being easily accessible, plays a pivotal role in diagnosing and evaluating treatment for patients with a thrombus straddling the PFO. Determining the best treatment approach for each patient necessitates collaborative discussions among all relevant specialists, fostering a team-based decision-making process involving the Heart Team.

Ethical approval

This study received ethical approval (Ethical Committee N° 3983/QD-BYT) from the Ethical Committee of Bach Mai Hospital, Hanoi, Vietnam, in October 2022.

Consent

The patient provided written informed consent for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.P.D. conceptualized the manuscript. A.P.D., H.M.N., H.T.T.N., C.M.T., H.M.P. belonged to the patient's management team. A.P.D., H.M.P., S.T.T.B. revised the manuscript. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

As this is a case report and not a human study, it is exempt from registering.

Guarantor

Hung Manh Pham.

Provenance and peer review

This manuscript was not commissioned and underwent external peer-review.

Data availability statement

Any datasets generated during and/or analyzed during the current study are publicly available.

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