CASE REPORT

Systemic and venous thromboembolism: think about paradoxical embolism

Monique Cachia, Michael Pace Bardon, Peter Fsadni, Stephen Montefort

Department of Medicine, Mater Dei Hospital, Msida, Malta

Correspondence to

Dr Monique Cachia,
mono488@gmail.com

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SUMMARY

Patent foramen ovale (PFO) is one of the most important causes of paradoxical embolism; it is found in about 25–30% of the population. In most patients, it is asymptomatic and diagnosis is usually made during routine echocardiography. In a small proportion of patients, PFO is diagnosed after paradoxical embolism is suspected. We present a case of a middle-aged smoker who was admitted with lower limb deep vein thrombosis and pulmonary embolism, who developed acute upper limb ischaemia during his inpatient stay. Since doctors might dismiss such cases as routine, this report highlights the importance of detailed history taking and examination in patients with venous thromboembolism. Paradoxical embolism should always be considered as a possible diagnosis when managing patients with concomitant venous and arterial embolism.

BACKGROUND

Paradoxical embolism is a rare cause of arterial embolism, involving the passage of thrombi from the venous circulation into the systemic arterial circulation through a right to left cardiac shunt.^{1 2}

Patent foramen ovale (PFO) is the most important cause of paradoxical embolism in up to 30% of the general population. Other less common intracardiac defects that can result in paradoxical embolism include pulmonary arteriovenous malformations (PAVMs), atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA) and tetralogy of fallot (TOF).³ Patients with paradoxical embolism may initially present with symptoms and signs of venous thromboembolism, arterial embolism or both, and thus one should have a low threshold for investigation as, if untreated, it could lead to recurrent thrombosis, organ damage and death.

CASE PRESENTATION

A middle-aged smoker with a history of chronic obstructive pulmonary disease (COPD) and systemic hypertension presented to the accident and emergency department at Mater Dei Hospital with a 2-day history of pain and swelling in the right calf, together with dyspnoea on exertion and a cough productive of white sputum. The patient was at the time being treated with clarithromycin and cefuroxime, which were started by his general practitioner, for a community-acquired pneumonia. On examination, blood pressure was 110/64 mm Hg, coarse crackles were heard over the right base of the chest and the right calf was tender and swollen.

Arterial blood gases showed a type 1 respiratory failure (pH 7.48, pO₂ 59.1 mm Hg, pCO₂ 34.4 mm Hg and SaO₂ of 59.1%).

An ECG showed sinus rhythm at 90 bpm and a chest X-ray showed right lower lobe opacification. A qualitative D-dimer test was positive and an ultrasound Doppler of the calves was carried out, which confirmed the presence of a right peroneal vein thrombosis.

The patient was admitted with a diagnosis of right deep vein thrombosis (DVT) and community-acquired pneumonia. Initial management included oxygen via a Venturi mask at 28% and Enoxaparin 1.5 mg/kg daily while clarithromycin and cefuroxime were continued. The patient was then started on a loading dose of warfarin. In view of the hypoxia, respiratory alkalosis and DVT, a presumptive diagnosis of pulmonary embolism was high on the list, so a CT pulmonary angiogram was performed on day 1 postadmission. This revealed multiple thrombi in the main lobar and segmental bronchial vessels.

On the third day postadmission, the patient started reporting pain, paraesthesia and weakness of the left arm. On examination, a cold, pale upper limb with an absent radial pulse was evident. An urgent CT limb angiogram was carried out, which confirmed a left brachial artery embolus.

INVESTIGATIONS

In view of the presence of concomitant venous and arterial embolism, paradoxical embolism was suspected. A transoesophageal echocardiogram was performed and this confirmed the presence of a small PFO (figure 1).

Figure 1 Transoesophageal echocardiography showing a long axis view with passage of saline microbubbles from the right to the left atrium.

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DIFFERENTIAL DIAGNOSIS

The differential diagnosis of PFO includes other causes of paradoxical embolism, comprising of VSD, ASD, PAVMs, PDA and TOF.

TREATMENT

The patient underwent successful emergency left brachial embol-ectomy and was initially treated with unfractionated heparin, which was then substituted with oral vitamin K antagonist.

OUTCOME AND FOLLOW-UP

The patient was worked up for a hypercoagulable state and this resulted in a positive anticardiolipin antibody.

He had a hypercoagulable state requiring lifelong warfarin. Owing to the conflicting data available, the patient was informed about the benefits and risks of PFO closure versus medical therapy alone. A multidisciplinary team assessment concluded that this patient would benefit from PFO catheter closure in addition to lifelong anticoagulation.

DISCUSSION

The commonest cause of paradoxical embolism is PFO, which occurs in about a quarter of the general population and accounts for 95% of cases of paradoxical embolism.⁴

Shunt reversal of the PFO may occur secondary to raised pulmonary pressures from possible pulmonary thromboembolism or may be a consequence of Valsalva manoeuvres.

The sequelae of paradoxical embolism may vary depending on the site of embolisation and these may include stroke in 55% of cases, acute peripheral arterial limb occlusion in 40% of cases, coronary artery occlusion leading to myocardial infarction, and mesenteric, renal and retinal artery occlusion.^{2,3}

This case highlights the importance of detailed history taking and clinical examination. In a patient with DVT and/or pulmonary thromboembolism, one should have a low threshold for investigation if the patient concurrently reports other systemic symptoms such as chest pain, abdominal pain, back pain, haematuria, visual disturbance or limb weakness.

If there is clinical suspicion of intracardiac shunts, the primary investigation of choice would be that of echocardiography, with contrast-enhanced transoesophageal echocardiography being superior to transthoracic echocardiography for diagnosis.⁵ Clinicians should request specifically for right ventricular evaluation in such clinical scenarios.

Large intracardiac shunts such as ASD or VSD may be detected by echocardiography with colour flow Doppler. However, a PFO may not be evident during a resting two-dimensional (2D) echo since a PFO is a functional deficiency rather than an anatomical one.

Consequently, bubble studies can be performed. A PFO will become apparent on 2D echocardiography when saline contrast, which is injected at rest, transfers from the right to the left atrium.⁶ The severity of the PFO can be assessed by the number of microbubbles evident and the size of the PFO. The latter appears to be directly related to the risk of paradoxical embolism.⁷ Eustachian valves, Chiari network and atrial septal aneurysm may all be associated with the presence of a PFO.⁷⁻⁹ PFO's may be persistent or intermittent. The latter may occur secondary to acute changes in pulmonary vascular resistance in patients having chronic lung disease. Our patient suffered from an acute pulmonary embolus and COPD exacerbation, thus increasing

the risk of reopening of the PFO due to increased pulmonary vascular resistance.

Various manifestations of paradoxical embolism have been recorded in the literature. Some patients initially present with systemic embolism and, later, venous embolism, others present initially with venous thromboembolism while other patients present with concomitant venous and arterial embolism.

Controversy surrounding optimal strategies (medical vs surgical) for treatment of PFO still exists. To date, three randomised controlled studies comparing medical versus surgical management of PFO failed to show a significant benefit of percutaneous closure versus medical management.³ The Amplatzer closure device was shown to be superior to medical therapy in the prevention of stroke in patients with cryptogenic embolism.¹⁰

Although our patient was treated with an Enoxaparin 1.5 mg/kg daily regime as per local anticoagulation guidelines, clinicians should be aware that the 1 mg/kg twice daily regime is another suitable therapeutic option.

Learning points

- ▶ It is important to consider paradoxical embolism as a possible diagnosis when managing patients with concomitant venous and arterial embolism.
- ▶ Good management involves input from a multidisciplinary team and includes diagnosis of the cardiac shunt with echocardiography.
- ▶ Prevention of further paradoxical embolism through closure of the intracardiac defect with percutaneous or open surgery should be considered in carefully selected patients.³
- ▶ Treatment of acute ischaemia in the acute phase includes thrombectomy/thrombolysis and anticoagulation.¹¹
- ▶ Lifelong anticoagulation for patients with hypercoagulable states is of utmost importance to prevent future occlusive disease.¹²

Contributors All the authors were responsible for the care of the patient during his hospital stay. MPB, PF and SM contributed in part to the write up of this article.

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REFERENCES

- 1 Abad-Arranz M, Jara-Palomares L, Martos-Maine JL, *et al.* Pulmonary embolism and concomitant paradoxical embolism. A case report. *Arch Bronconeumol* 2014;50:120–2.
- 2 Pirkil M, Myjavec A, Daněk T, *et al.* A case of pulmonary thromboembolism with synchronous and metachronous paradoxical embolism through the patent foramen ovale—A case report. *Cor et Vasa* 2012;54:e314–e22.
- 3 Windecker S, Stortecky S, Meier B. Paradoxical embolism. *J Am Coll Cardiol* 2014;64:403–15.
- 4 Rigatelli G, Giordan M, Braggion G, *et al.* Incidence of extracerebral paradoxical embolisms in patients with intracardiac shunts. *Cardiovasc Revasc Med* 2007;8:248–50.
- 5 Seiler C. How should we assess patent foramen ovale. *Heart* 2004;90:1245–7.
- 6 Davison P, Clift PF, Steeds RP. The role of echocardiography in diagnosis, monitoring closure and post-procedural assessment of patent foramen ovale. *Eur J Echocardiogr* 2010;11:27–34.

- 7 Homma S, Sacco RL. Patent foramen ovale and stroke. *Circulation* 2005;112:1063–72.
- 8 Schuchlenz HW, Saurer G, Weihs W, *et al.* Persisting eustachian valve in adults: relation to patent foramen ovale and cerebrovascular events. *J Am Soc Echocardiogr* 2004;17:231–3.
- 9 Laguna G, Arce N, Blanco M. Giant chiari network, foramen ovale, and paradoxical embolism. *Rev Esp Cardiol* 2015;68:250.
- 10 Stortecky S, Da Costa BR, Mattle HP, *et al.* Percutaneous closure of patent foramen ovale in patients with cryptogenic embolism: a network meta-analysis. *Eur Heart J* 2015;36:120–8.
- 11 Mintz R, Brody K. Impending paradoxical embolism: a case report. *J Emerg Med* 2013;45:19–21.
- 12 Kumar S, Khan I, Milton R, *et al.* Pulmonary and paradoxical embolism in protein C and S deficient patient. *Ann Thorac Surg* 2005;80:324–6.

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