

## CASE REPORT

# Arterial embolism as a first sign of pulmonary embolism: a case report

N. Kant<sup>1</sup>, J.J. Remmen<sup>2</sup>, J.J.J.P.M. van de Leur<sup>1</sup>

Departments of <sup>1</sup>Intensive Care Medicine, <sup>2</sup>Cardiology, Canisius Wilhelmina Hospital, Nijmegen, the Netherlands

## Correspondence

N. Kant – Niels.kant@hotmail.com

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## Abstract

This case report presents a female with a paradoxical embolism due to a patent foramen ovale (PFO). The patient initially presented with a fractured left foot. Despite thrombosis prophylaxis, she developed a pulmonary embolism. This caused the pressure in the right ventricle and atrium to rise, the PFO to open and a venous thrombus to pass on to the arterial circulation. Because the risk of recurrence of venous thromboembolism was considered high, lifelong rivaroxaban was prescribed. Although recent studies find the percutaneous closure of the PFO to be beneficial over antiplatelet therapy alone, the studies lack convincing evidence that suggests it is superior to the use of anticoagulants as well. Furthermore, percutaneous PFO closure is associated with new-onset atrial fibrillation and other problems related to the closure device. Therefore, when anticoagulants are prescribed, the additional risk reduction achieved by closing the PFO is limited and might not justify the risks associated with percutaneous closure.

## Introduction

Paradoxical embolism is the phenomenon in which a venous thrombus passes through a right-to-left shunt in the heart and causes an arterial blockade in the systemic arterial circulation. In most cases, the right-to-left shunt is caused by patent foramen ovale (PFO), with a prevalence of 25-30% in the healthy population.<sup>[1-3]</sup> Normally, the pressure on the right side of the heart is lower than on the left side. In case of pulmonary embolism, however, the pressure on the right side of the heart rises due to increased vascular resistance in the lungs. This may cause a PFO to open, thereby allowing blood flow from right to left and thrombi to find their way into the arterial circulation. This might lead to severe thromboembolic events including stroke and myocardial infarction.<sup>[4]</sup>

## Case report

A 57-year-old woman with no medical history was admitted to the emergency department in April 2019 with a fractured fifth metatarsal bone of the left foot due to a fall. The patient was

not using any medication and denied the use of tobacco, alcohol or illicit drugs. The patient was treated with a cast splint and received thrombosis prophylaxis with enoxaparin 2000 IU/day. Three weeks later, in May 2019, the patient was admitted to the emergency department with acute severe pain to the right calf since the night before presentation. Further complaints included dyspnoea for three days and mild chest pain during exercise which radiated to the jaw and left scapula. Physical examination showed the following: both lungs were clear to auscultation, tachypnoea of 20 breaths/min and blood oxygen saturation was 89%, which increased to 95% with five litres of oxygen. Cardiovascular examination showed a heart rate of 96 beats/min, blood pressure of 138/86 mmHg and normal heart sounds without murmurs. The left foot was covered in a cast splint, felt warm and showed normal capillary refill times. The right foot was pale, cold, had delayed capillary refill times and showed impaired movement and sensibility. No pulsations were detected in the right lower leg with Doppler ultrasonography. There were no other neurological symptoms present.

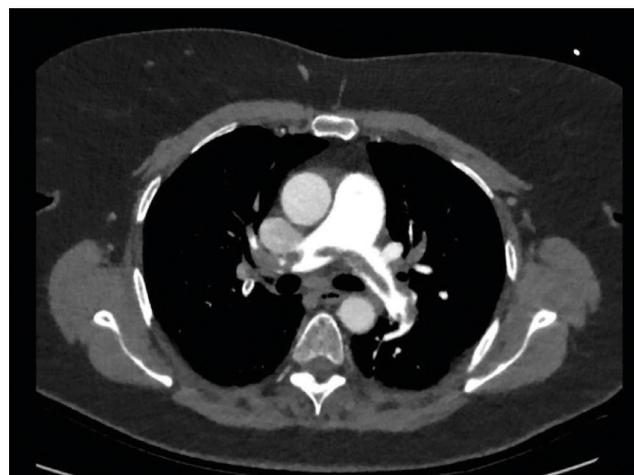


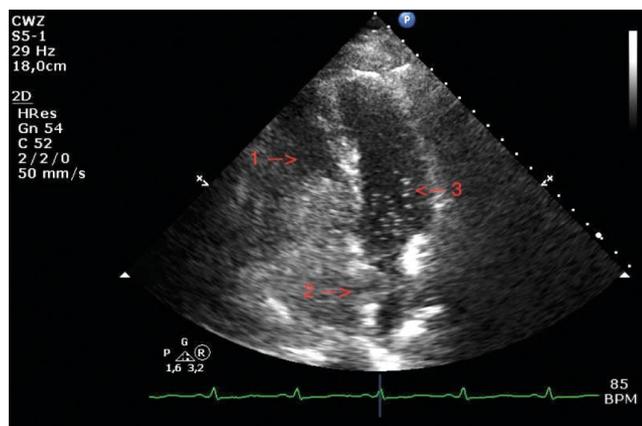
Figure 1. Chest CTA showing pulmonary embolisms with saddle component



**Figure 2.** Chest CTA showing a dilated right ventricle

Electrocardiography showed slow R progression over V1-V6, minimal ST depression in II and negative T waves in II, III, aVF, V3 and V5. The chest radiograph showed clear lungs and normal cardiac contours. Chest computed tomography angiography (CTA) showed severe pulmonary embolisms in both lungs with a clear saddle component (*figure 1*). Dilation of the right ventricle, with an estimated right ventricle / left ventricle ratio of 1.47, and an aneurysmatic atrial septum were described as well (*figure 2*).

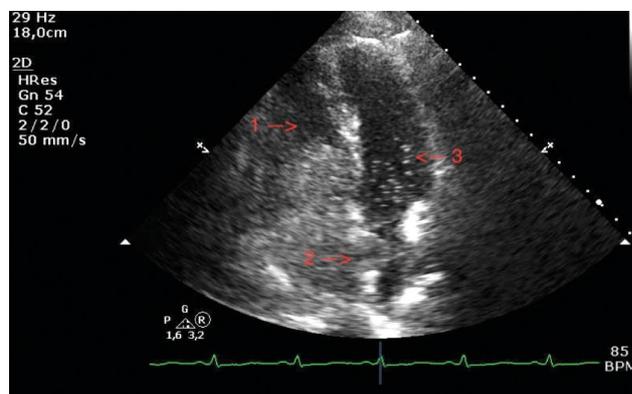
Echocardiography showed a severely dilated right ventricle and aneurysmatic atrial septum, which suggests increased pressure on the right side of the heart. The passage of air bubbles from the right to the left atrium was also visualised with and without Valsalva, suggesting the presence of a PFO (*figure 3*). Kent et al. developed the Risk of Paradoxical Embolism (RoPE) index to determine the probability of an arterial embolism being caused by a PFO.<sup>[5]</sup> In this case the RoPE index was 62%.



**Figure 3.** Echocardiography showing a dilated right ventricle (1), an aneurysmatic atrial septum (2) and air bubbles in the left atrium and ventricle (3)

The patient was admitted to the ICU and received 5000 IU of heparin, followed by a continuous heparin infusion of 1000 IU/hour. The circulation of the right leg recovered spontaneously

and the pain disappeared. Doppler ultrasonography showed the recovery of pulsations in the right leg. The patient showed clinical improvement, was haemodynamically stable and was discharged from the ICU two days later. The heparin was replaced by rivaroxaban. Taking into account the high risk of new venous thromboembolism, which occurred under prophylaxis, rivaroxaban was prescribed for life. To rule out a clotting disorder, the patient was referred to a vascular internist. Three months later, follow-up echocardiography (*figure 4*) showed no deviations. A normal aspect of the atria, atrial septum and the right ventricle were seen. The atrial septum was no longer pervious to bubbles without the Valsalva manoeuvre. In consultation with the patient, the PFO was not closed.



**Figure 4.** Echocardiography showing a normal aspect of the right ventricle and no aneurysmatic atrial septum

## Discussion

In the case of a right-to-left shunt, venous thrombi can pass from the venous to the arterial circulation. Although PFOs are common (25-30% in a healthy population), cryptogenic strokes among patients with PFO are rare.<sup>[1-3]</sup> This can be explained by the hypothesis that the PFO functions like a valve, only allowing flow when the pressure difference between the right and left atrium is positive.

In this case, the venous thromboembolism was most likely caused by immobilisation due to a fracture. It developed despite the use of thrombosis prophylaxis. Although thrombosis prophylaxis does not offer full protection from venous thromboembolism, the occurrence of a thromboembolic event during prophylaxis increases the risk of recurrence. The patient being overweight increased this risk even further, thus lifelong rivaroxaban was prescribed.

However, the question remains if the PFO should be closed in addition to anticoagulant therapy. A recent position paper published in 2019 summarises most of the reviews and meta analyses recently published on this topic. It states that a clinician must consider two things to determine the course of treatment: 1) the probability that the PFO has a relevant role in the observed clinical picture; 2) the likelihood that the observed clinical event will recur.<sup>[6]</sup>

Given the presence of deep vein thrombosis, the young age of the patient and the observed elevated right atrial pressures with a permeable PFO, the probability that the embolism was due to the PFO is considered high. This is supported by the RoPE index of 62%. The likelihood of recurrence is more difficult to estimate. Recurrence of a paradoxical embolism is certainly possible if the PFO is not closed. However, the venous thrombosis was most likely caused by immobilisation due to a fracture, which is transient. Therefore, recurrence risk is clearly reduced once the patient is mobile again. Moreover, the chance of new venous thromboembolic events is reduced by anticoagulant therapy. In addition, elevated right atrial pressure and aneurysmatic atrial septum were no longer present at follow-up, which reduces the chance of a right-to-left shunt occurring through the PFO.

In this case, the position paper does not make a clear statement about whether the PFO should be closed. It does say that medicinal therapy should be considered. Multiple studies find percutaneous PFO closure to be superior to medicinal therapy alone in preventing paradoxical embolisms and show a relative risk reduction ranging from 38.0% to 50.5%.<sup>[7-12]</sup> However, most studies compared percutaneous PFO closure to antiplatelet therapy alone instead of anticoagulants. The studies that did compare PFO closure with the use of anticoagulants did not find convincing evidence that PFO closure was beneficial.<sup>[12-14]</sup>

Moreover, the risks of percutaneous PFO closure need to be taken into account when deciding on the course of treatment. Multiple studies report an increased risk of new-onset atrial fibrillation, although mostly transient, with an incidence of 4.26% after percutaneous PFO closure versus 0.67% in patients being treated with medicinal therapy alone. In addition, patients developed complications related to the implantation of the device, such as device thrombosis (1-2%) and pericardial effusion (0.5-1%).<sup>[6,12]</sup> Finally, closing a PFO requires the use of double platelet aggregation inhibitors for three to six months, which is associated with an additional risk of bleeding. Despite these risks, the all-cause mortality rates between both groups are similar (RR 0.73,  $p=0.42$ ).<sup>[8,10,11,15]</sup>

In this case, because rivaroxaban was prescribed, the additional risk reduction achieved by closing the PFO is limited and might

not justify the risks associated with percutaneous closure.

In consultation with the patient and a multidisciplinary team, it was decided not to close the PFO.

### Conflict of interest

All authors declare no conflict of interest. No funding or financial support was received.

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