Thrombus in the right atrial appendage during pulmonary and paradoxical embolism: a case report

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We report the case of a 56-year-old woman who was admitted because of left pulmonary embolism. An episode of ischemic stroke occurred during hospitalization. Transesophageal echocardiography revealed a right atrial appendage thrombus and a patent foramen ovale with right to left shunting. This suggested paradoxical embolism across a patent foramen ovale as the most reasonable explanation of the ischemic stroke in this patient, in the presence of right cardiac overload secondary to the hemodynamically significant pulmonary embolism. The patient's clinical conditions dramatically improved after anticoagulant therapy.

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Introduction

Right atrial appendage thrombus is clinically rare, it is very difficult to detect, and often missed at routine transthoracic echocardiography (TTE). On the other hand, transesophageal echocardiography (TEE) allows the assessment of the right atrial appendage morphology. It is also the technique of choice for the diagnosis and consequently for the correct management of patients when right atrial appendage thrombi are suspected. We describe the clinical course of a 56-year-old woman who suffered from left pulmonary artery embolism and experienced a sudden and unexpected ischemic stroke during hospitalization. TEE revealed the presence of a thrombus in the right atrial appendage and a patent foramen ovale (PFO) with right to left shunting. The pathogenesis of paradoxical embolism was thus disclosed and the clinical diagnosis clarified.

Case report

A 56-year-old woman with a history of lymphoma (Hodgkin's disease) and complaining of chest pain was transferred to our Emergency Department.

Twenty-two years previously (1979), the patient had developed Hodgkin's disease and had been submitted to radiotherapy and splenectomy. Four months before the present hospital admission, the patient was hospitalized in the Pneumology Department because of right pleural effusion. Thoracocentesis yielded 100 ml of fluid; laboratory analyses were negative for cell abnormalities, indicating exudative pleurisy. Her clinical conditions stabilized after standard treatment. Two months later the follow-up chest X-ray showed incomplete expansion of the right lung, torsion and fibrosis of the homolateral hilus of the lung but no evolution of the effusion.

Three days before the last admission, the patient experienced an episode of retrosternal chest pain at rest. The pain was described as a squeezing pain radiating to the left shoulder and accompanied by diaphoresis. The attack lasted approximately 45 min, and resolved spontaneously. A similar attack recurred 2 days later; this time the pain lasted about 20 min, and again resolved spontaneously. In the meantime, another puncturing chest pain without radiation persisted during these 3 days. Its severity was modified by the respiratory and trunk movements and was accentuated by the supine decubitus. On arrival to our Emergency Department, the puncturing chest pain was still present. The patient's blood pressure was 100/60 mmHg and her heart rate was 70 b/min and rhythmic but with occasional premature beats; a grade 2/6 systolic ejection murmur was detected in the mesocardiac area. Percussion of the right inferior lung field revealed dullness. Respira-

tion sounds were still present, but faded and remote. No rales or other pathologic sounds were audible. The electrocardiogram showed normal sinus rhythm and conduction, with a few supraventricular ectopic beats (Fig. 1). ST segment elevation (0.1-0.3 mV) was detected in the anterior leads (V_1-V_3), and T wave inversion in the inferior leads (III, avF). The serum levels of the cardiac enzymes were increased, with maximal values of creatine kinase-MB and troponin I of 17.5 and 16.8 ng/ml respectively (at our institution the normal values for creatine kinase-MB and troponin I are < 5.0 and < 0.13 ng/ml respectively). On the basis of a clinical suspicion of an acute coronary syndrome, the patient was then admitted to the coronary care unit.

TTE showed a moderately enlarged and hypokinetic right ventricle and flattening of the interventricular septum, suggesting right ventricular pressure overload (Fig. 2, upper panel). The left ventricular dimensions and regional wall motion were normal and the left ventricular ejection fraction was 65%. At this point, it was decided to submit the patient to lung perfusion scintigraphy which confirmed the suspicion of pulmonary embolism. The result was positive for a focal perfusion defect of the left lung highly suggestive of left pulmonary embolism. Unfortunately, during the following hours the patient suddenly presented with right-side hemiplegia and aphasia suddenly occurred. Cerebral computed tomography was initially negative and did not reveal any evidence of focal hemorrhage. TEE confirmed the dilation of the right chambers and pulmonary artery. Furthermore, an evident, partly oscillating and protruding thrombus was localized inside the right atrial appendage (Fig. 3). Color Doppler and contrast echocardiography revealed spontaneous minimal right to left intra-atrial shunting across a PFO (Fig. 4). Vascular echo-Doppler examination showed that the iliac veins were bilaterally patent and no lower limb thrombus was detectable; diffuse intimal thickening was found bilaterally in the carotid arteries, with a minimal fibrous plaque at the bifurcation and origin of the internal carotid artery.

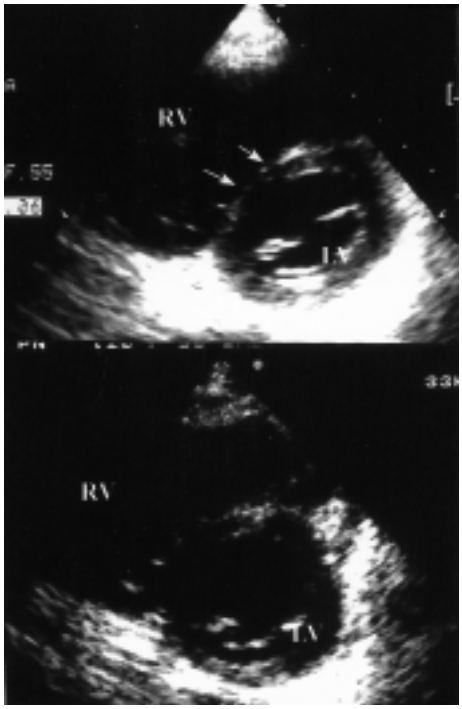

Figure 2. Upper panel: *transthoracic echocardiography on the day of admission. The left ventricular short-axis parasternal view shows an enlarged and hypokinetic right ventricle (RV) with flattening of the interventricular septum* (arrows)*, suggesting right ventricular pressure overload.* Lower panel: *transthoracic echocardiography on day 35 of follow-up. The left ventricular short-axis parasternal view shows a completely normal RV. LV = left ventricle.*

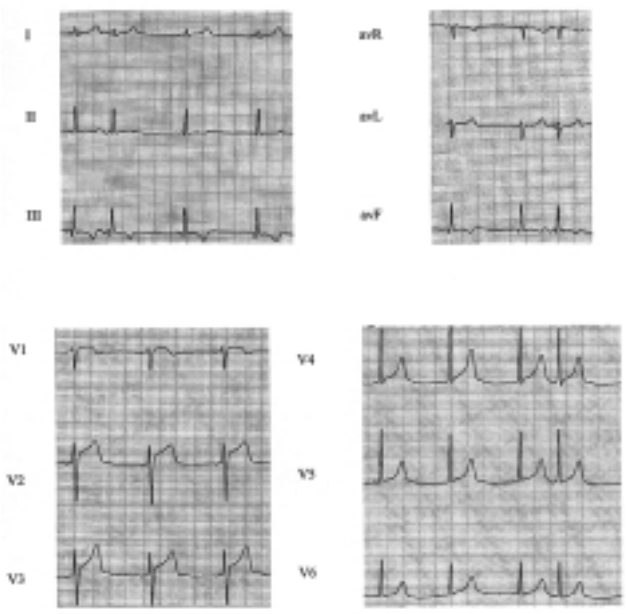

Figure 1. *The 12-lead electrocardiogram at the time of admission shows normal sinus rhythm and conduction, with a few supraventricular ectopic beats. ST segment elevation (0.1-0.3 mV) was detected in the anterior leads (V_1-V_3), and T wave inversion in the inferior leads (III, avF).*

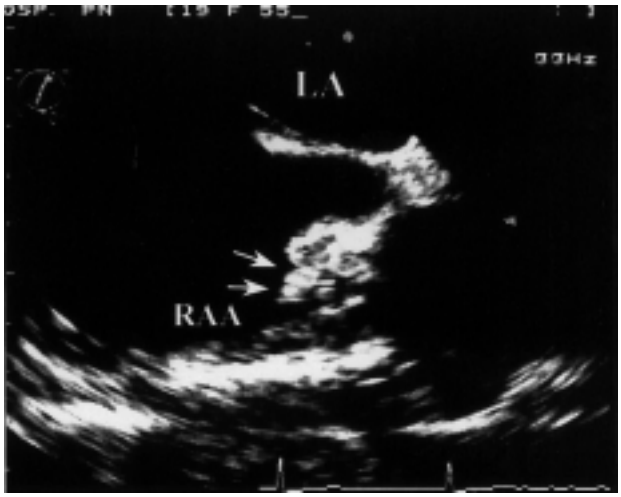

Figure 3. *Transesophageal echocardiography on the third day of admission shows a thrombus* (arrows) *within the right atrial appendage (RAA, long-axis view), partly oscillating and protruding in real time. LA = left atrium.*

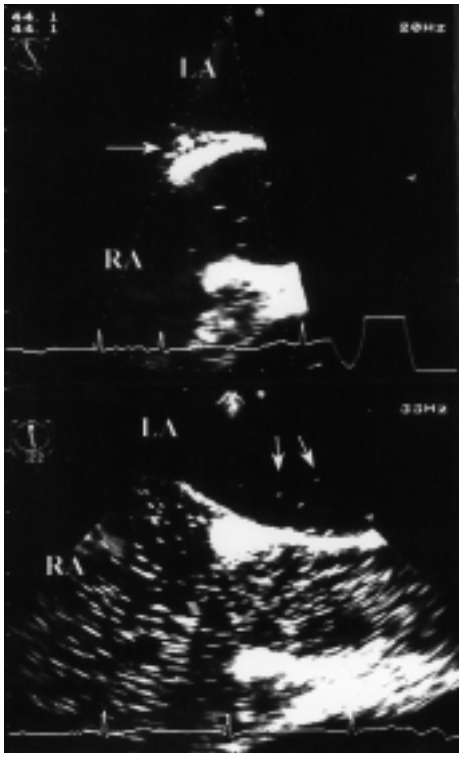

Figure 4. Upper panel: *color Doppler imaging on the transesophageal echocardiography revealed minimal right to left intra-atrial shunting* (arrow) *across a patent foramen ovale.* Lower panel: *contrast echocardiography from a peripheral vein during transesophageal echocardiography shows the shunting of some bubbles originating within the right atrium (RA) into the left atrium (LA,* arrows*) through a patent foramen ovale.*

The patient was started on anticoagulant therapy with warfarin and her clinical conditions remained stable. Neurological symptoms and signs gradually improved during the rehabilitation period. At 35 days of follow-up, the patient was asymptomatic and the neurological signs had resolved completely. TTE showed a completely normal right ventricle (Fig. 2, lower panel).

Discussion

A correctly diagnosed right atrial appendage thrombus is a rare event in clinical practice. This is partly because of its anatomic morphology and partly due to diagnostic technical limitations. The right atrial appendage has a triangular shape, with a wide base and blunt border, while the left atrial appendage is digitiform in appearance with a narrow base. Hence, the detection of a thrombus inside the right atrial appendage is very rare as compared with a correctly diagnosed thrombosis of the left atrial appendage. Besides, the right atrial appendage may not be adequately visible during routine TTE; therefore thrombi in this location are liable to be missed often. Occasionally, right atrial appendage thrombi are diagnosed at autopsy[1,2]. During the last decade, with the development and utilization of TEE, few cases have been reported[3,4]. Most of these patients had atrial fibrillation or flutter; some underwent the Fontan procedure for congenital heart disease or developed an acute right ventricular myocardial infarction. Although often coexisting with left atrial thrombi, isolated right atrial appendage thrombosis may occur, and may be a source of pulmonary embolism[4]. It seems that right atrial and right atrial appendage dysfunction due to various causes can play an important role in the generation of intracavitary thrombi. TEE allows one to assess the morphology and function of the right atrial appendage and to identify thrombi within this location; it is the technique of choice and is helpful for the diagnosis and management of patients when right atrial thrombi are suspected. The diagnosis of a right atrial appendage thrombus remains however technically difficult, and it requires carefulness and experience. In the present patient, an isolated right atrial appendage thrombus was detected in the presence of sinus rhythm with no other evident clinical predisposing factor. Hence, it may be considered as a possible cause of pulmonary and paradoxical embolism across a PFO. It represents a clinically rare event, and the etiology of right atrial appendage thrombus formation is unclear. A possible explanation of the phenomenon could be the occurrence of a transient episode of right cardiac ischemia which compromises the right atrial and right atrial appendage function, rendering the blood flow within the right atrial appendage very slow and consequently leading to thrombus formation within this structure. This hypothesis, however, is still to be proved.

PFO is a common finding in the normal healthy population. A large necropsy study of 965 normal human hearts showed an overall prevalence of 27%, with no differences between sexes and a mean PFO diameter of 5 mm[5]. Although most PFO are innocent and considered to be a normal anatomical variant, an association between PFO and adverse events, especially cerebrovascular accidents, has been reported by several investigators[6-10]. One retrospective study demonstrated a higher prevalence of PFO in patients who had developed stroke as compared with age-matched controls (40 vs 10%). The incidence was higher still (54%) in cryptogenic stroke (unexplained stroke despite extensive investigation)[11]. However, in patients who had developed stroke with a known etiology, the prevalence of PFO was 25.5% which is similar to that of the general population[12]. On the other hand, the recurrence rate of cryptogenic stroke is higher if a PFO is present[13-15]. A large PFO has been identified as a risk factor for ischemic stroke. A stroke odds ratio of 3.0 (95% confidence interval 1.1-8.1) has been reported for a patient with isolated PFO, and of 33.3 (95% confidence interval 4.1-270) for a patient with both PFO and atrial septal aneurysm[8].

A phenomenon contributing to the association between PFO and cryptogenic stroke is paradoxical embolism. In patients with PFO, when the right atrial pressure is increased, right to left interatrial shunting can occur and consequently deoxygenated blood and emboli may enter the systemic circulation. Right to left interatrial shunting across a PFO may transiently take place, for example, during sneezing or during Valsalva maneuvers.

In other cases it may persist, and provide a potential persistent source of paradoxical embolism. PFO is, in fact, a strong risk factor for paradoxical embolism[16-19], especially in patients with right ventricular myocardial infarction[20], structural tricuspid diseases[21] and, more frequently, following acute pulmonary embolism[22-26].

The assessment of paradoxical embolism through a PFO ideally requires documentation of the "triad" consisting of PFO, an increased right atrial pressure and a venous origin of the thrombus. Our patient fulfilled all these criteria. The patient experienced a cerebrovascular accident with specific neurological symptoms; cerebral computed tomography excluded focal hemorrhage. The characteristics of the stroke (sudden onset, subsequent gradual improvement of symptoms) are consistent with an embolic event. Besides, the patient was relatively young with no history of hypertension, primary neurological etiology, atrial fibrillation, and without any other known disease which could adequately explain the ischemic etiology of the stroke. Furthermore, a PFO with right to left shunting was detected at TEE. We believe that paradoxical embolism across the PFO was the most reasonable explanation for the ischemic stroke in this patient. This, especially in conditions of right cardiac overload secondary to the hemodynamically significant pulmonary embolism. TEE revealed the simultaneous presence of a right atrial appendage thrombus, lending direct and strong support for this potential mechanism.

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