Emboli on the move

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Abstract - A pulmonary embolism with a free floating right atrial thrombus is a life threatening condition. In the case presented here, this condition was accompanied by an atrial septal defect causing paradoxical emboli. Thrombolytic therapy may seem counterintuitive at first. However, after reviewing the relevant literature, it seemed to be the best option open to us, as the case presented in this paper shows.

Keywords - paradoxical emboli, atrial septal defect, thrombolysis

Introduction
The atrial septal defect (ASD) and bicuspid aortic valve are the most common congenital heart lesions found in adults. Although the ASD is often asymptomatic until adulthood, potential complications of an ASD include right ventricular failure, atrial arrhythmias, paradoxical emboli, cerebral abscess, and pulmonary hypertension that can become irreversible and lead to right-to-left shunting (Eisenmenger syndrome).

Case report
A 44-year old male, cigarette smoker, was admitted to a cardiac emergency department because of dyspnoea and pain in his right leg. He had been complaining of progressive dyspnoea for 2 months and severe pain in his right leg for more than 2 weeks. On the initial physical examination a moderately dyspnoeic man was seen, with a blood pressure of 125/70 mmHg, heart rate 100 beats/min, a split first heart sound, a normal second heart sound, an oxygen saturation of 96%, normal breath sounds and no peripheral oedema. However, he had a bluish, cold right leg, which showed decreased sensibility.

The electrocardiogram (ECG) showed sinus tachycardia, with a right axis deviation and a pathological Q in leads I, II, AvL, V4-V6, without repolarisation disturbances. Haematology and biochemistry findings included: Hb 9.9 mmol/L, D-dimer >9999 μg/L (upper limit of normal (ULN) is 500 μg/L), troponin I 83 μg/L (ULN 0.16 μg/L). An arterial blood gas sample was not taken. A chest radiograph showed heterogeneous wedge shaped opacities in the peripheral zones of both lungs. Since the patient was complaining of dyspnoea and the D-dimer level was elevated, a contrast enhanced thoracic tomography angiography (CTA) was performed. The CTA showed large contrast filling defects in the right and left main pulmonary artery, consistent with pulmonary emboli. A large filling defect within the right atrium suggested an atrial thrombus. Since there was a difference in temperature and sensibility between the right and left leg, an arterial angiogram was performed. The angiogram revealed complete occlusion of the right-sided superficial femoral artery and multiple emboli within the deep femoral artery. Arteries were not visible at all below the knee. Furthermore, an ultrasound of the left leg revealed a deep vein thrombosis of the popliteal and femoral veins. An inferior vena cava filter was placed just distal from the origin of the renal veins to prevent further thrombo-embolic events. Further, an arterial sheath in the left common femoral artery was used for selective catheterization (over the aortic bifurcation) of the right-sided femoral arteries. An initial bolus of 50000U urokinase was administered and followed by continuous injection of 50000U urokinase per hour. Heparin (guided by APTT, target 60-80 seconds) was administered to treat the pulmonary embolism. Regarding these paradoxical emboli, we excluded a cardiac thrombus and a patent foramen ovale or ASD. Therefore, a transthoracic ultrasound was performed (figure 1). A large (± 6 cm), highly mobile, echo-dense structure was found in the right atrium, which protruded into the right ventricle across the tricuspid valve during diastole. The right ventricle and atrium were dilated; the left ventricle and atrium had normal dimensions and function.

Although the patient remained haemodynamically stable, we decided to administer systemic thrombolytic therapy. For this purpose, alteplase therapy (100 mg intravenously in 2 hours) was started, while heparin and urokinase therapy were continued. Three days after admittance, the persistent occlusions of the right-sided femoral and popliteal arteries were successfully recanalized with endovascular thrombosisuption (AngioJet Ultra Thrombectomy System, Possis Medical). Nine days after admittance, a transesophageal ultrasound (TEE) was performed (figure 2). The TEE showed a normal ventricles and the thrombotic mass was dissolved. Further, a large atrial septum defect (ASD type II) was found. After an uneventful stay in hospital, the patient was discharged home after 11 days with acenocoumarol. The patient was enlisted for surgical closure of the ASD and further analysis of coagulation disorders.

In short, this patient had a venous embolism in his left leg which led to a pulmonary embolism and ultimately a paradoxical embolism to his right leg through a large ASD.

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Discussion

The presence of a right heart floating (i.e. mobile) thrombus is a rare condition but has diagnostic and therapeutic implications in patients with pulmonary embolism [1]. It is a therapeutic emergency because any delay of treatment could be fatal [2-4]. Apart from thrombo-emboli, air, septic, catheter, fat and amniotic fluid emboli may occur with or without paradoxical emboli. Differentiation is helped by predisposing medical history or illness. Additional echocardiography and radiographic features may aid differentiation [5]. For example, fat embolism is a complication after long bone fractures, and appears as a combination of pulmonary cerebral and cutaneous symptoms up to three days after trauma. Chest radiographic abnormalities resemble those of ARDS or pulmonary oedema. Echocardiography may provide information on location and density aiding diagnosis.

The optimal management of right heart thrombo-emboli remains unclear since there are no prospective randomized trials comparing coagulation therapy, thrombolytic therapy and surgical removal. In a study by Chartier et al. [1] 21% of the patients with right heart thrombi and pulmonary embolism died within the first few days of admission. In cases with highly mobile thrombo-emboli in the right side of the heart, the mortality rate is even higher – up to 44% -- due to sudden pulmonary embolism [1].

In the case described in this paper, systemic thrombolytic therapy or surgery was not applied initially because of fears of mobilizing at least parts of the large right atrial thrombus, which could have led to recurrent and probably life threatening pulmonary embolism, as observed in a previous study [6]. We therefore administered systemic heparin (50000 units/24 hours) guided by APTT only, as well as local urokinase in the right leg to resolve the local thrombus. However, after reviewing the literature, we decided to switch to thrombolytic therapy. The reasons for this switch were a CT-derived vascular obstruction index of more >40%, which is associated with an 11.2 fold increased risk of dying of pulmonary embolism [7]. Furthermore, in a recent retrospective analysis of 177 record cases of patients with right heart thrombi and pulmonary emboli, the mortality rates in patients receiving anticoagulation therapy, surgical embolectomy and thrombolysis were 28.6%, 23.8% and 11.3%, respectively. Patients receiving no therapy had a 100% mortality rate [8]. In another study, excellent results were described following systemic thrombolysis in a series of 16 patients in which 100% of the atrial clots disappeared from the right atrium within 24 hours [9].

Another way of looking at the therapeutic options may be the finding by Ferrari et al. [9], that in patients presenting with lung emboli only, the incidence of a mobile clot in the right heart is 5.2%. Furthermore, 27% of the general population have a potential patent foramen ovale (1-19 mm, mean 5 mm) [10]. Clearly, the therapeutic consequence of mobile right heart thrombi should be thrombolytic therapy, as discussed above. Obviously, these patients were treated as common lung emboli with heparin, without physicians contemplating other therapeutic options, and probably without adverse effects. One wonders whether patients with a lung embolus should undergo cardiac echography in order to identify the 5.2% with right heart thrombi.

The presenting features of an ASD or patent foramen ovale (PFO) without a significant left-to-right shunt are non-existent. With significant left-to-right shunting a fixed splitting of the second heart sound is often audible, due to volume overload of the right atrium. Consequently, a mid systolic flow murmur can often be heard over the pulmonary area. The auscultatory findings in this patient are not typical for an ASD, however, a split S1 may be heard with a large left-to-right shunt.

Echocardiography is the principle means of diagnosis and

Figure 1. Transthoracic ultrasound view of free floating thrombus in right atrium (RA) through tricuspid valve into the right ventricle (RV) (arrow). LA is left atrium LV is left ventricle.

Figure 2. Transesophageal echocardiography showing a large ASD-II (arrow). LA is left atrium, RA is right atrium, LV is left ventricle and RV is right ventricle.
assessments and PFOs: The sensitivity of finding an ASD with trans thoracic ultrasound (TTE) is substantially less than with TEE [10, 11]. This may explain why the first ultrasound examination of the heart missed the ASD. Agitated saline contrast injection using the femoral vein during normal respiration and the Valsalva manoeuvre increases the sensitivity of detecting a PFO or ASD [10].

Patients with a PFO or ASD should avoid increasing their right-sided pressure through some activities – like trumpet playing or scuba diving, which can cause right-to-left shunting, and thus put the patient at risk of paradoxical emboli. A paradoxical embolus is often seen as the first presentation of an ASD or PFO. Also, patients presenting with platypnea-orthodeoxia, cryptogenic stroke, or paradoxical gas embolism in decompression sickness should be evaluated for a PFO or ASD.

The size of the PFO or ASD determines the ease, and thus the risk, of paradoxical emboli. In symptomatic patients the only therapeutic option is closure of the ASD. These patients should be given anticoagulation therapy whilst awaiting surgical closure, to reduce the risk of paradoxical emboli.

In conclusion, thrombolytic therapy can be administered quickly, and has been reported to reduce mortality in patients with pulmonary emboli and right heart thrombi. We reported on successful thrombolytic therapy in a patient with a pulmonary embolism, right heart mobile thrombi, and, furthermore, an ASD-II with paradoxical emboli.

References