Abstract. – OBJECTIVE: Paradoxical embolism represents a rare condition occurring when a thrombus originating from venous system produces pulmonary embolism and systemic embolization through an intracardiac or pulmonary shunt. The evidence of a thrombus entrapped in a patent foramen ovale (PFO) is an even more rare condition. There is uncertainty about the optimal treatment strategy.

PATIENTS AND METHODS: A 58-year-old male patient was admitted to our Internal Medicine Unit with the diagnosis of bilateral bronchopneumonia. During hospitalization, the co-occurrence of chest pain and amaurosis led us to hypothesize a paradoxical embolism.

RESULTS: Transthoracic echocardiography showed the presence of a thrombus stuck over the interatrial septum. A contrast-enhanced chest CT scan showed multiple pulmonary embolisms and brain CT scan documented a hypodense area, of ischemic significance, in the left occipital lobe near tentorium. In order to prevent further embolization, emergency cardiac surgery (right atriotomy, removal of thrombus and closure of the PFO, pulmonary thrombectomy) was performed without complications.

CONCLUSIONS: Although rare, the evidence of a thrombus stuck in a patent foramen ovale represents a clinical emergency. The optimal therapeutic approach is still debated. The surgical correction seems to be a safe and effective option for these patients.

Key Words: Embolism, Thrombosis, Pulmonary embolism, Stroke, Patent foramen ovale.

Introduction

Paradoxical embolism is defined as a venous thrombosis producing systemic embolism through an intracardiac or pulmonary shunt. The most common cause of intracardiac shunt is represented by patent foramen ovale (PFO). This last can be found in about a quarter of the adult population and it is generally asymptomatic. However, it could predispose to cryptogenic stroke due to systemic embolism. On the contrary, the exact incidence of paradoxical embolism is not known.

The evidence of a thrombus entrapped in a PFO is even more rare and it constitutes a clinical emergency due to the risk of massive systemic embolization. Given the rarity of this condition, there are no standardized guidelines for the treatment of these patients. The aim of the present review is to focus on this condition and to discuss the available treatment strategies.

Case Report

A 58-year-old male patient presented to the Emergency Department (ED) because of the persistence, for about two weeks, of fever (maximum 38°C), dry cough and arthralgia. The appearance of chest pain – elicited by breathing – represented the reason for ED referral. At home he had taken aspirin, paracetamol and antibiotics without
effect. Patient’s medical history was significant for arterial hypertension and chronic obstructive pulmonary disease. He was an active smoker (20 pack/year). His home therapy consisted of ramipril and carvedilol.

### Blood and Instrumental Tests

At the ED, blood pressure was normal (125/80 mmHg), pulse rate was 120 bpm, oxygen saturation in room air was 94%, temperature was 38.5°C. Lab tests showed mild leukocytosis (WBC 11280/μl, Neu 80.9%). An electrocardiogram (ECG) showed sinus tachycardia. Chest X-ray showed thin and circumscribed basal opacities bilaterally (Figure 1a-b). Thus, the patient was admitted to our Internal Medicine Unit with the diagnosis of bilateral bronchopneumonia. In our ward, after cultural exams (blood, sputum and urine), treatment with levofloxacin was started. The day after the admission, the patient complained of right hemianopsia lasting about 2 hours. Laboratory results showed significantly elevated D-dimer (19351 ng/ml, n.v. 0-500.0 ng/ml), troponin (0.211 ng/ml, n.v. 0-0.045 ng/ml) and NT-pro-BNP (2435 ng/l, n.v. 0-125 pg/ml). This symptom together with pleuritic chest pain and tachycardia drew our attention to the possibility of thromboembolism.

### Diagnosis

Transthoracic echocardiography showed the presence of hypoechoic masses in both right and left atria moving over the interatrial septum (Video 1).

Contrast-enhanced chest CT scan showed a saddle embolus at the bifurcation of the main pulmonary artery, multiple opacification defects in main branches, lobar and segmental branches of pulmonary arteries, and the presence of bilateral basal subpleural thickening (Figure 2 a-b-c). No masses or venous thrombosis in the abdominal CT-scans. Brain CT scan documented a hypodense area of ischemic significance in the left occipital lobe near tentorium (Figure 3). Doppler ultrasonography of lower extremities was negative for thrombus. Anticoagulation with enoxaparin was started and the patient was evaluated and underwent emergency cardiac surgery.

![Figure 1 A-B. Chest X-ray showing thin and circumscribed bilateral basal opacities.](image-url)
Paradoxical embolism with thrombus stuck in a patent foramen ovale

Treatment: Surgical Procedure

Through a median sternotomy and extracorporeal circulation, a right atriotomy was performed, and a big fresh thrombus was visualized inside the right atrium, crossing, via a patent foramen ovale, inside the left atrium. The thrombus was removed, and the patent foramen ovale was occluded by direct suture (Figure 4). Left atrium was opened and explored: no further thrombotic lesions were identified. Pulmonary artery was opened: inside the main pulmonary artery and the left pulmonary trunk, up to left lobar arteries, a huge amount of coarse thrombotic material was identified and removed.

Outcome

Screening for thrombophilic state showed high homocysteine levels and methylene tetrahydrofolate reductase (MTHFR) homozygous mutation. Thus, it is conceivable that a transient minor infection acted as pro-thrombotic cause in an active smoker with hyperhomocysteinemia due to the homozygous mutation of MTHFR. The patient was discharged on the seventh post-operative day with a 6-months edoxaban prescription, folic acid supplementation and indication to quit smoking.

Discussion

The present case shows the occurrence of neurological symptoms in a patient admitted for fever and chest pain. The diagnosis of paradoxical...
embolism was based on clinical features and CT evidence of both stroke and pulmonary embolism, together with the echocardiographic evidence of a thrombus stuck in PFO. The choice was to treat patient by emergency cardiac surgery, in order to reduce the risk of massive re-embolism, with subsequent anticoagulation. However, there are some aspects that deserve further discussion and clarification.

First of all, the patient came to ED mainly for non-specific symptoms, fever and arthralgia. Their acute onset could be attributed to an infection or to COPD exacerbation, in an active smoker. However, worsening of pre-existing dyspnea, cough with productive sputum and wheezing at chest examination were lacking. Subsequently, chest pain with pleuritic features (e.g. elicited by breathing and poorly responding to analgesics) appeared. Thus, at ED, a chest-X-ray showing thin and circumscribed bi-basal thickening (Figure 1) was performed, and the patient was admitted to our Internal Medicine ward with diagnosis of bronchopneumonia. It should be underlined that the diagnosis of pneumonia requires suggestive clinical features of respiratory system infection, demonstrable infiltrate by chest radiograph or other imaging technique, with or without supporting microbiological data. Raised inflammatory indexes (e.g., leukocytosis), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), are not helpful to differentiate bronchopneumonia from pulmonary embolism. However, leukocytes and ESR are modestly increased in pulmonary embolism, while significantly higher in patients with bronchopneumonia. Moreover, in our patient, procalcitonin levels were normal. The diagnosis of pneumonia could also be supported by the presence of opacities at bilateral basis of the lungs, which may also indicate infarcted pulmonary areas (Hampton hump sign). In our case, the small opacities observed at X-ray, could be attributable to pulmonary embolism complicated with lung infarction, as showed by chest CT-scan (Figure 2c). The patient had no known risk factor for, nor history of, thromboembolism. According to Well’s score, the patient should be considered at low-risk for pulmonary embolism. D-dimer, troponin and NT-pro-BNP have not been performed in ED. D-dimer could be elevated in presence of inflammatory state, and probably could not be helpful to discriminate the diagnosis. However, elevated troponin and NT-pro-BNP, associated to electrocardiographic findings of sinus tachycardia could support the suspicion of PE. Probably, hemodynamic stability, fever, leukocytosis, cough, chest pain and the absence of risk factors for thromboembolism directed towards a typical bronchopneumonia picture. After admission, the association between chest/respiratory symptoms, tachycardia and hemianopsia drew our attention to the possibility of systemic and pulmonary embolism, in other words paradoxical embolism. Besides the evidence of stroke and massive pulmonary embolism, a thrombus entrapped in a PFO was found. This is a rare and life-threatening condition and no treatment guidelines are available due to the lack of randomized trials. Possible treatment strategies include medical (e.g. anticoagulation or thrombolysis), surgical, or a combination of the two treatments. Each of them has its own advantages and disadvantages. The rationale for thrombolysis is the dissolution of pulmonary artery thrombus, with consequent drop in pulmonary pressure and increase of cardiac index, in order to prevent the occurrence and/or worsening of right heart failure and to decrease the chance of recurrent large pulmonary embo-

Figure 4. Picture of the thrombus stuck in the patent foramen ovale and removed from the right atrium during surgical procedure.
lism or stroke. On this connection, according to European Society of Cardiology guidelines, systemic thrombolysis in patients with intermediate or high-risk PE should be performed only if clinical signs of hemodynamic decompensation are present. Thrombolysis leads to clinical and echocardiographic improvement within 36 hours in more than 90% of patients, especially if performed within 48 hours onset. The choice of thrombolysis in patients with mobile right heart thrombus is doubtful, given the risk of a short-term mortality higher than 20%. Anticoagulation represents a valid and reasonable option for patients with comorbidities, high bleeding and surgical risk. However, both thrombolysis and anticoagulation can be associated with complications such as bleeding, fragmentation of the thrombus resulting in additional embolism (pulmonary and systemic), hemodynamic deterioration and massive stroke. Therefore, according to Erkut et al., thrombolysis and anticoagulation could not represent the best option for patients with large and mobile intracardiac thrombi. In these patients, cardiac surgery could be the first option, because it allows to remove thrombi and close the PFO, preventing recurrent paradoxical embolism especially in patients without comorbidities. According to the available literature, when compared with anticoagulation alone, surgical thrombectomy is associated to a significant reduction of systemic embolism and to a trend toward improved survival. A recent systematic review of the literature by Myers et al. including 154 studies, there is no difference in terms of survival between thrombolysis, anticoagulant therapy or thrombectomy, even if surgery significantly reduces the odds of systemic embolism. In any case, thrombolysis, at least catheter directed interventions, are generally effective and well tolerated, with a low rate of adverse events. In the present case, surgical treatment allowed to solve multiple problems: to perform PFO closure, to remove the fluctuating stuck thrombus and embolism in pulmonary arteries, particularly the one in the main pulmonary trunk.

Conclusions

Although rare, the evidence of a thrombus stuck in a patent foramen ovale represents a clinical emergency. Surgical correction seems to be a safe and effective option, at least for patients with low surgical risk.

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Conflict of Interests

The authors declare that they have no conflicts of interest.

References


