A difficult diagnosis: right unilateral cardiogenic pulmonary edema. Usefulness of biochemical markers of heart failure for the correct diagnosis

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We describe a case of unilateral pulmonary edema occurring in a young woman affected by hypertrophic cardiomyopathy complicated by acute worsening of mitral regurgitation. The relevant role of biochemical markers of heart failure, such as brain natriuretic peptide and carbohydrate antigen 125, in clarifying the final diagnosis of cardiogenic pulmonary edema and modifying treatment accordingly is emphasized.

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Introduction

Unilateral cardiogenic pulmonary edema is a rare clinical and radiological presentation of acute dyspnea and it is often confused with other most common causes of unilateral alveolar and interstitial infiltrates such as infection, lung cancer, lung infarction, atelectasis, aspiration and bronchial obstruction. We describe a case of right pulmonary edema in a young woman with hypertrophic cardiomyopathy in whom the unilateral distribution of the lung involvement caused a delay in the correct diagnosis and in the appropriate treatment. The rapid determination of two biological markers, such as brain natriuretic peptide (BNP) and carbohydrate antigen 125 (CA-125), frequently resulted elevated in heart failure[1,2], was helpful for the final diagnosis of cardiogenic pulmonary edema.

Case report

A 27-year-old woman affected by non-obstructive hypertrophic cardiomyopathy was admitted to the emergency room of our hospital for severe dyspnea associated with atrial tachycardia lasting for several hours.

Hypertrophic cardiomyopathy was diagnosed when she was 14 years old and her previous medical history was characterized by recurrent syncopal episodes and consequent automatic cardioverter-defibrillator implantation. In the last years she reported recurrent episodes of atrial tachycardia, and she has been treated with metoprolol (200 mg/day), propafenone (600 mg/day) and amiodarone (200 mg/day).

On admission the patient complained of palpitation and dyspnea at rest. Heart rate was 130 b/min, blood pressure 105/70 mmHg, without fever.

Examination of the chest was normal and heart evaluation revealed tachycardia and mild apical systolic murmur. Electrocardiography showed atrial tachycardia with heart rate of 140 b/min, without any significant signs of left ventricular hypertrophy. Normal sinus rhythm occurred 12 hours after admission, after successful overdrive pacing.

Hemoglobin, D-dimer, renal and hepatic function, serum electrolytes, creatine kinase-MB and troponin levels were within normal ranges. Chest roentgenography documented cardiomegaly and the presence of the implanted automatic cardioverter-defibrillator, without signs of pulmonary congestion.

Echocardiography, performed on hospital admission, showed left ventricular asymmetric hypertrophy mainly affecting the interventricular septum (end-diastolic thickness 22 mm, left ventricular end-diastolic diameter 49 mm, left ventricular end-systolic

diameter 28 mm), anterior and lateral free walls; the left atrium was markedly enlarged (50 × 90 mm, area 40 cm^2). Left ventricular systolic function was normal (ejection fraction > 60%). There was a mild mitral valve prolapse and moderate mitral regurgitation; there was no sign of intraventricular dynamic obstruction at basal conditions. Left ventricular filling pressure was typical of abnormal relaxation (E/A wave ratio < 1, deceleration time > 220 ms); indirect estimate of pulmonary systolic artery pressure was within the normal range.

Thirty-six hours later the patient suffered from worsening dyspnea, fever (38°C), anxiety, hypotension, and severe respiratory failure.

Chest roentgenography showed diffuse interstitial infiltrates in the right lung (Fig. 1) in presence of leukocytosis (white blood cell count 12 000/mm^3) and C-reactive protein level elevation. A chest computed tomography confirmed the presence of interstitial infiltration of the right lung and initial involvement of the left upper lobe (Fig. 2).

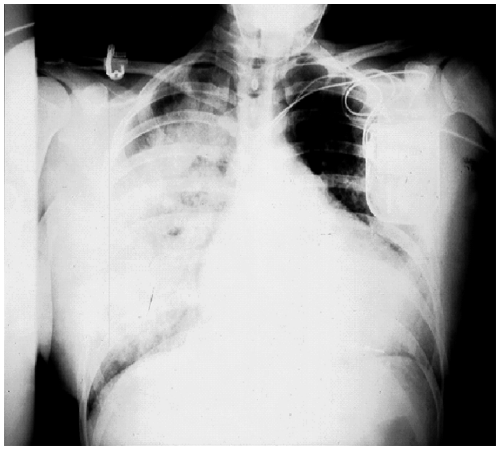

Figure 1. *Chest X-ray performed on the day of acute dyspnea revealing the presence of a right-sided pulmonary edema with a diffuse infiltrate.*

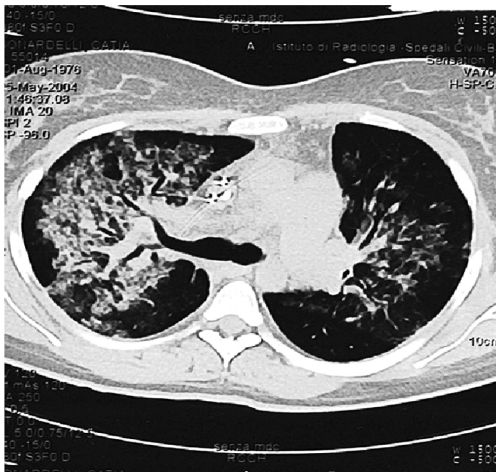

Figure 2. *Chest computed tomographic scan confirming the presence of a unilateral interstitial infiltrate.*

Based on clinical (particularly fever), biochemical (abnormal white blood cell count) and imaging data, a diagnosis of pneumonia was presumed and, accordingly, broad-spectrum antibiotic therapy was started. Detailed microbiological and serological investigation was performed and resulted negative.

Three days later, due to persistence of a continuous state of severe respiratory failure and monolateral right infiltrates at the second chest X-ray and computed tomographic scan, with no evidence of infections or sepsis and with antibiotic therapy inefficacy, serum levels of BNP and CA-125 were determined: BNP was 1352 pg/ml (normal values < 100 pg/ml) and CA-125 was 95 U/ml (normal values < 30 U/ml) suggesting the presence of heart failure.

Echocardiographic examination was then repeated and showed, compared to that performed on admission, a more evident systolic anterior motion of the mitral anterior leaflet with a 30 mmHg late-peaking intraventricular gradient. Furthermore, there was a worsening of mitral regurgitation, which was severe, with a color Doppler flow jet directed toward the right pulmonary veins (Fig. 3); left ventricular filling pattern was restrictive (early filling to atrial systole ratio 2.5; deceleration time of early filling 140 ms), indicating high values of mean left atrial pressure, and systolic pulmonary hypertension was recorded (echocardiographic indirect estimation of pulmonary systolic pressure was 55 mmHg, confirmed by right heart catheterization). According to the serum levels of biochemical markers of heart failure and the Doppler echocardiographic data a diagnosis of cardiogenic unilateral pulmonary edema caused by acute worsening of mitral regurgitation was hypothesized and therapeutic approach modified. The clinical picture of the patient improved promptly after intravenous administration of diuretics and vasodila-

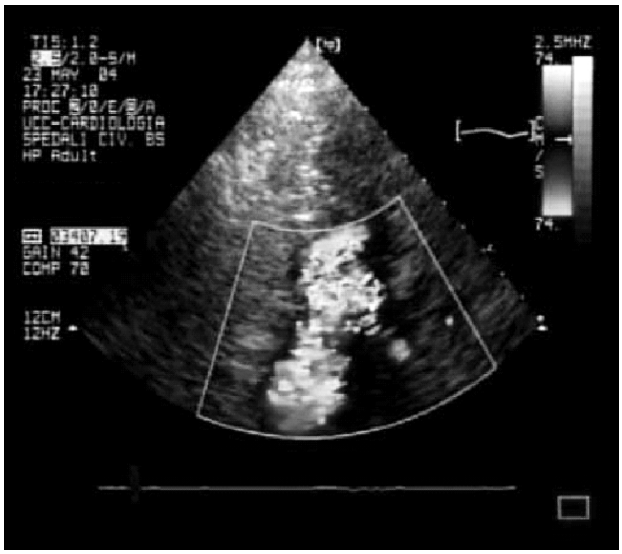

Figure 3. *Echocardiographic examination showing severe mitral regurgitation with a high velocity jet directed toward the right pulmonary vein.*

tors; also the radiological picture of the lung edema resolved (Figs. 4 and 5) together with a marked fall in BNP (506 pg/ml), and CA-125 (30 U/ml) values, assessed 24 hours after appropriate treatment.

Discussion

Asymmetric pulmonary edema is caused by local alteration of vascular homeostasis and it can be explained by local imbalance of the Starling equation for increased pulmonary venous pressure (cardiogenic edema), less frequently, by decreased oncotic pressure, by impaired lymphatic drainage or disruption of alveolar epithelial-endothelial integrity (non-cardiogenic edema)[3].

Unilateral cardiogenic pulmonary edema is an unusual clinical condition reported as a manifestation of left heart failure, mostly affecting the right lung. As described by Calenoff et al.[4] pulmonary edema can be classified as ipsilateral or contralateral with respect to lung abnormalities. Ipsilateral pulmonary edema is usually due to acute alterations in the components of the alveolar-capillary complex in one lung only. Contralateral pulmonary edema refers to an edema occurring on the side opposite to the lung with a major perfusion abnormality (Table I).

Table I. Causes of ipsilateral and contralateral pulmonary edema.

Ipsilateral cardiogenic pulmonary edema
Left ventricular failure (acute mitral regurgitation)
Unilateral veno-occlusive disease
Extrinsic pulmonary venous compression (neoplasm)
Ipsilateral non-cardiogenic pulmonary edema
Lung re-expansion
Aspiration
Pneumonitis
Surgical or traumatic injury (evacuation of hydrothorax or pneumothorax)
Contralateral pulmonary edema
Unilateral pulmonary thromboembolism
Congenital absence/hypoplasia of a pulmonary artery
Swyer-James syndrome
After pneumonectomy at the contralateral side
Acute bronchial obstruction by a foreign body or tumor

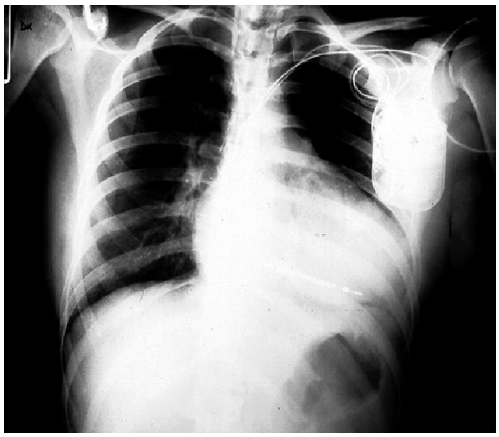

Figure 4. *Chest X-ray demonstrating the complete resolution of the right-sided pulmonary edema after medical treatment.*

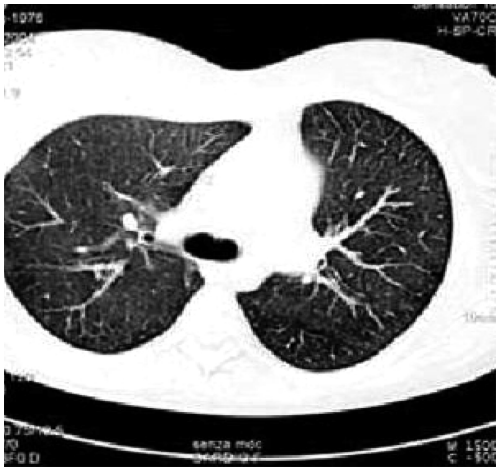

Figure 5. *Chest computed tomographic scan confirming complete resolution of the interstitial infiltrate.*

Unusual mechanisms have also been reported: left to right shunts (for example, septal rupture)[5], extrinsic compression of a pulmonary vein by aneurysmal dilation of adjacent aorta or pulmonary artery[6-9], acute mitral insufficiency secondary to paravalvular leak of a prosthetic mitral valve[10-12], and gravitational edema.

Asymmetric pulmonary infiltrates of cardiac origin are rare. In the majority of cases they are misdiagnosed because the likelihood of cardiac disease is not considered and diagnosis of one of the more common causes of focal lung disease (such as pneumonitis, hemothorax, atelectasis or neoplasia) is often incorrectly made.

When pulmonary edema occurs in a patient with severe mitral regurgitation, it is usually cardiogenic. Rare cases of a regurgitant jet oriented toward the origin of the right pulmonary veins has been documented by transesophageal echocardiography using color flow Doppler imaging in patients with asymmetric right-sided[10-13] and, in one case, left pulmonary edema[14].

The predilection of edema formation in the right side is explained by the anatomy of the pulmonary veins in relation to the mitral valve apparatus. The plane of the mitral valve is inclined postero-superiorly and to the right, and the regurgitant jet penetrates the origin of the pulmonary vein in the right upper lobe.

Isolated or predominantly right upper lobe edema has been reported in 9% of cases with severe mitral valve regurgitation[4]; these data underline the importance to consider acute mitral regurgitation for the differential diagnosis of unilateral pulmonary involvement in patients with known or suspected mitral valve disease.

In our patient the presence of a worsening mitral insufficiency (severe) was probably due to valve abnormalities typical of hypertrophic cardiomyopathy, and to the presence of systolic anterior movement of the mitral apparatus with variable degree of septal contact determining an inconstant mild left ventricular outflow tract obstruction associated with severe left ventricular diastolic dysfunction. Finally, in this case the use of Doppler echocardiographic examination and the determination of biochemical markers of heart failure, such as BNP and more recently CA-125, allowed both to demonstrate, respectively, the retrograde flow of blood mainly into the right pulmonary veins as a pathogenetic mechanism of unilateral pulmonary involvement, and to confirm the cardiac origin of respiratory distress, although elevated levels of BNP may be associated with sepsis and pneumonia without primitive heart failure[15]. In our case report the rapid disappearance of dyspnea and of monolateral pulmonary infiltrates with cardiac marker reduction after diuretic therapy confirm the cardiac etiology of the clinical picture.

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