

# Heart affected by amyloidosis – a case study (RCD code: III-3A.2)

**Katarzyna Ptaszyńska-Kopczyńska\*, Włodzimierz Jerzy Musiał, Karol Adam Kamiński**

Department of Cardiology, Medical University of Białystok, Poland

## Abstract

We present a case of a 65-year old woman, who was admitted to hospital due to recurrent pulmonary oedema. Patient's history included chronic obstructive pulmonary disease. Echocardiography revealed concentric hypertrophy of the left ventricle walls without narrowing of the outflow tract, accompanied by the mild/moderate mitral stenosis, preserved systolic and mildly impaired diastolic function of the left ventricle. Those comorbidities were not severe but their coexistence contributed to rapid heart failure progression. During another admission for pulmonary oedema the patient had cardiac arrest in the mechanism of the pulseless electrical activity, which triggered the diagnostics of amyloidosis. Right heart catheterization was performed showing an unusually high wedge pressure. Histological analysis confirmed the diagnosis of amyloid light-chain (AL) amyloidosis, so the patient was scheduled for the first course of chemotherapy. Unfortunately, shortly after discharge, the patient developed pulmonary oedema and died before admission to hospital. This case shows the adverse course of the disease, fast progression of unspecific symptoms that may attribute to multiple comorbidities. JRCDC 2015; 2 (5): 156–160

**Key words:** amyloidosis, heart failure, pulmonary oedema, chronic obstructive pulmonary disease

## Introduction

Heart failure (HF) is one of the main death causes from cardiac reasons and the success of treatment is largely dependent on the etiology. An increased attention is paid to the diastolic HF, which incidence is comparable to the systolic dysfunction. Diastolic HF in the course of the cardiac form of amyloidosis is a rare disease that can often be undiagnosed. This pathology is associated with rapid progression and poor prognosis despite the use of the targeted therapy. In this article we present a case of a patient with amyloidosis, who was also affected by COPD.

## Case presentation

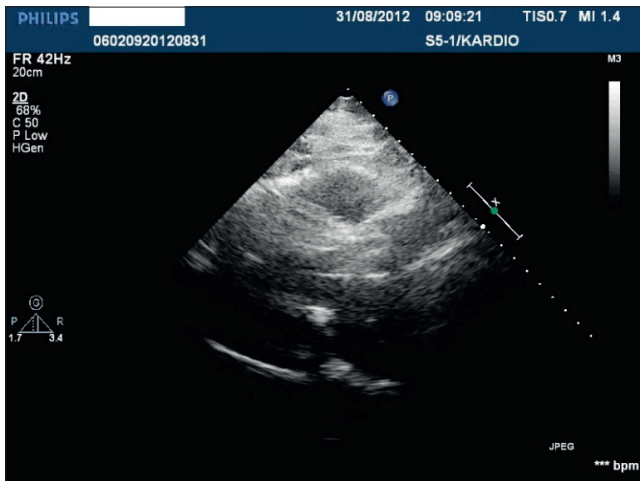
A 65-year-old woman was hospitalized on January 2012 at the Intensive Care Unit due to acute respiratory failure, which was a consequence of cardiac arrest of an unknown etiology (pulmonary oedema was suspected). In the subsequent days of stable hemodynamic and respiratory condition, the patient was transferred to the Cardiology Department for further diagnosis and

treatment. The patient had a history of HF (NYHA III class), hypertension, type 2 diabetes and chronic obstructive pulmonary disease (COPD) (non-smoker for 7 years). Moreover, the patient underwent inferior wall infarction treated pharmacologically in 1989, an episode of pulmonary embolism in 1998 and had a DDD pacemaker implantation because of an atrioventricular Mobitz II block with a periodic complete atrioventricular block with syncope in 2011. The physical examination revealed obesity (BMI – 34 kg/m<sup>2</sup>), congestive and inflammatory auscultation findings at the base of the lungs and irregular heart rate. Electrocardiography (ECG) showed atrial fibrillation (AF) with ventricular rate of about 90/min. Echocardiography revealed a left ventricle (LV) with concentric hypertrophy (18 mm interventricular septum), without evidence of narrowing of the outflow tract (Figure 1, 2). It was accompanied by mild mitral stenosis, enlarged left atrium (65 mm), impaired contractility of the inferior and low-lateral wall with preserved systolic function (ejection fraction – 50%) and mildly impaired diastolic function (Figure 3). The mean pressure in the pulmonary artery was approximated in echo for 20.3 mm Hg. Moreover, additional structures at the posterior mitral valve leaflet and of the posterior part of the mitral annu-

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\* Corresponding author: Department of Cardiology, Medical University of Białystok, M. Skłodowskiej-Curie str. 24A, 15-276 Białystok, Poland; tel.: 0048 85 7468 656, fax 0048 85 7468 604; e-mail: fizklin@wp.pl

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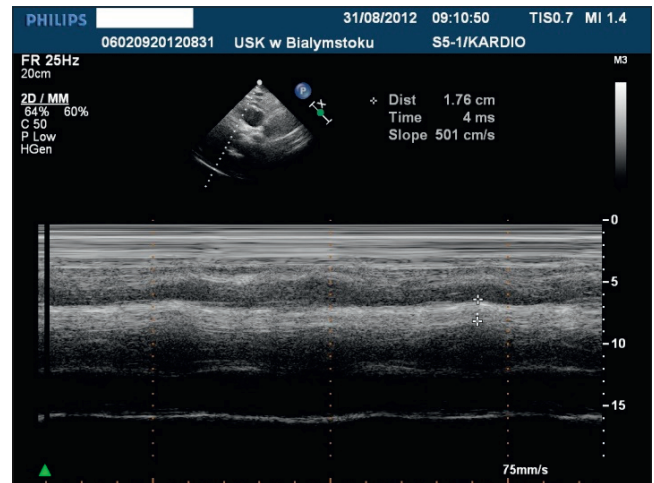
**Figure 1.** Transthoracic echocardiography, the long-axis parasternal projection. The left ventricle concentric hypertrophy revealed during the first hospitalization

lus were observed (Figure 4). The transesophageal echocardiography (TEE) described these structures as massive calcifications, that gently impaired the flow into the LV with the outflow surface assessed for 1.9 – 2.2 cm<sup>2</sup>. Biochemical analysis revealed high concentration of brain natriuretic peptide (BNP), normocytic anemia, subclinical hyperthyroidism and hypokalemia. To exclude the ischemic etiology of the cardiac arrest, coronary angiography was performed and showed no significant changes in the coronary arteries. The 48-hour Holter ECG monitoring recorded few episodes of non-sustained ventricular tachycardia (approximately 200/min) lasting up to 11 seconds.

## Patient management and follow-up

During the first hospitalization because of a high risk of life-threatening arrhythmia recurrence, right ventricular electrode was removed and subsequently cardioverter-defibrillator was implanted. The pharmacotherapy included a large dose of a beta-blocker (bisoprolol), angiotensin converting enzyme inhibitor, aldosterone antagonist, statin, low-molecular-weight heparin followed by oral anticoagulant, bronchodilators and glucose-lowering drugs. Due to large swelling of the lower extremities, the patient received a loop diuretic. In the following days of hospitalization a sinus rhythm with a frequency 60–70/min and intraventricular conduction disturbances in the form of a right bundle branch block related to the pacemaker stimulation were observed [Fig. 5].

After discharge, the patient remained stable for 4 months, then was hospitalized twice in a month at another department due to a pulmonary oedema. Later, the patient was hospitalized because of pulmonary oedema associated with slightly elevated blood pressure (max. 160/100 mm Hg in home measurements). The ECG showed AF with ventricular frequency 90/min. The blood pressure was 190/100 mm Hg at admission. Laboratory analysis registered leukocytosis and boundary markers of myocardial necrosis. Due to increasing signs of respiratory failure the patient required

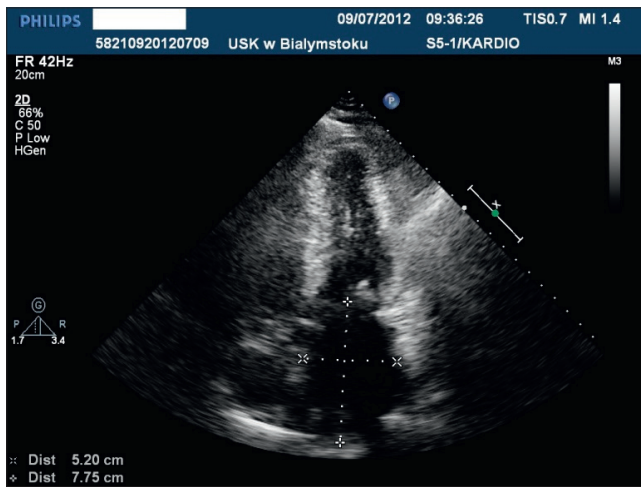


**Figure 2.** Transthoracic echocardiography, the parasternal long-axis M-mode projection. The interventricular septum measurement of 1.76 cm

a two-day respiratorotherapy, which was complicated by pneumonia. The targeted antibiotic was applied after cultures showed *Pseudomonas aeruginosa* in the bronchial aspirate. In pharmacotherapy the antihypertensive treatment, including a diuretic, was intensified. The persistent AF was treated with amiodarone infusion and on the second day the return of sinus rhythm was observed. In the following days, despite the improvement of hemodynamics, the patient reported rest dyspnoea. The spirometry test showed a high degree of obstruction (GOLD 3), which was the basis for intensification of the bronchodilator pharmacotherapy. After 2 weeks of hospitalization the patient was discharged home in stable condition.

Another hospitalization took place after a month. This time the cause of HF decompensation was the attack of paroxysmal atrial tachycardia with ventricular rate 144/min. Furthermore, in the course of the pharmacotherapy with non-selective beta-blocker – sotalol – which was used for the prevention of arrhythmias, cardiac arrest with electrical activity without pulse was observed. During cardiopulmonary resuscitation episodes of ventricular tachycardia/ventricular fibrillation effectively interrupted by the ICD were observed. After this incident the patient required one day of respiratorotherapy.

After patients stabilization, for better understanding of hemodynamics, right heart catheterization (RHC) was performed. The thermodilution method showed reduced cardiac index (2.06 l/min/m<sup>2</sup>) and elevated pulmonary vascular resistance (3.4 Wood units). Moreover, elevated pulmonary artery pressure (58/28 mmHg, mean 41 mm Hg) with high pulmonary artery wedge pressure (28 mm Hg) and elevated central venous pressure (17 mmHg) were observed. Laboratory results revealed significantly reduced TSH concentration (previously normal) with normal FT3 and FT4 levels. In pharmacotherapy the dose of selective beta-blocker was reduced and an antithyroid drug was added. After exclusion of sarcoidosis by pulmonologist, samples for histopathological analysis because of the amyloidosis suspicion were taken. After four weeks the patient was hemodynamically stable and discharged home. His-



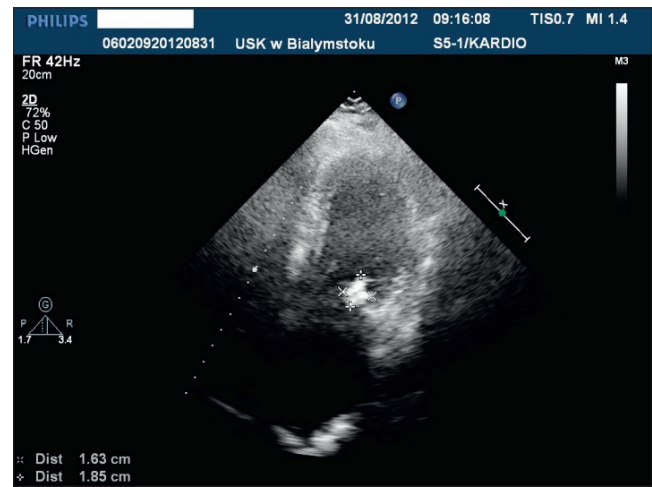
**Figure 3.** The four-chamber apical view. The left atrial measurement of  $5.2 \times 7.75$  cm

tological analysis confirmed the diagnosis of amyloid light-chain (AL) amyloidosis, so the patient was scheduled for the first course of chemotherapy. Unfortunately, shortly after, the patient developed pulmonary oedema and died before admission to the hospital.

## Review of literature

The coexistence of heart amyloidosis and COPD is a very rare condition and there is lack of data regarding treatment of such patients. The most reports concentrate on hypertrophic cardiomyopathy coexisting with lung disease. The restrictive cardiomyopathy in the course of amyloidosis is a uncommon condition, that entails diagnostic and therapeutic difficulties. Typical echocardiographic image of amyloidosis is not always observed. This disease in the echocardiography as well as clinically can mimic restrictive cardiomyopathy. The problem, that is encountered in this case, is the co-occurrence of the cardiovascular and respiratory system dysfunction, which requires deliberate therapy, especially on the adrenergic system. The coexistence of these diseases with mitral stenosis additionally impaired the left ventricular filling. A reflection of this problem was observed during RHC in an elevated PAWP.

Amyloidosis is a group of primary or secondary diseases characterized by an extracellular deposition of an insoluble protein (amyloid) in various organs, whose symptoms may mimic many diseases [1]. This pathology is the rarest HF cause and it is connected with many diagnostic and therapeutic problems. The standard diagnostic tools are mostly insufficient and the final diagnosis is available only after the histological analysis. The clinical picture varies depending on the amyloidosis type and on the cardiac involvement itself which presents a wide spectrum of pathological changes. The first most common presentation is the decrease of an exercise tolerance, atrial arrhythmias and pericardial effusions, followed by pulmonary congestion or pulmonary oedema [2,3]. These symptoms may be accompanied by elevated levels of BNP and troponin, even in the early stage of the disease. The feature that could over-

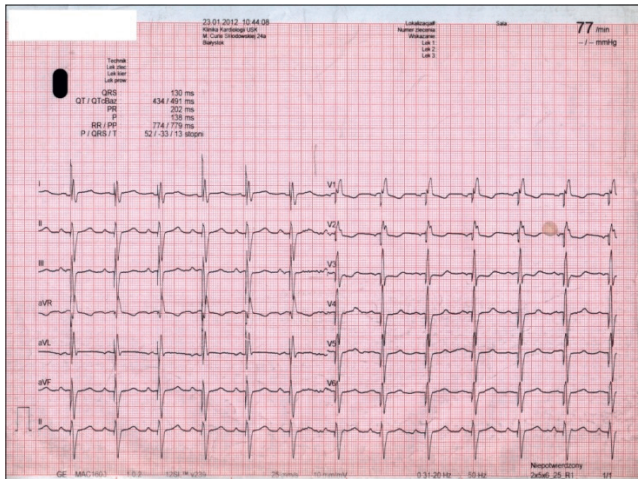


**Figure 4.** Transthoracic echocardiography, the four-chamber apical view. The calcification on the posterior mitral valve leaflet and on the posterior part of the mitral annulus of  $1.65 \times 1.83$  cm diameter

take the clinical manifestation of the disease, is diastolic dysfunction observed in the echocardiography [4,5]. In the advanced stages disproportionate accumulation of amyloid within the septum mimicking hypertrophic cardiomyopathy with dynamic narrowing of left ventricular outflow tract (LVOT) can be observed [6, 7]. The predominant ECG change is low QRS voltage and intraventricular conduction disturbances, often in the form of a left-bundle branch block. During 24-hour ECG monitoring, a non-sustained supraventricular and ventricular tachyarrhythmia can be observed in the majority of patients [3].

One of the HF symptoms observed in this case was the right ventricular pressure overload, which by the interventricular septum affected left ventricular function. Numerous experimental and clinical studies showed that the right ventricular pressure overload, as a consequence of increased pulmonary vascular resistance, can affect via a common septum on the left ventricular filling profile by reducing its diastolic susceptibility [8,9]. There were no observable direct abnormalities of the LV caused by COPD [10]. The effect of volume or pressure overload of the right ventricle on the left ventricular function is defined as the inverse Bernheim phenomenon and is explained by the common wall (the interventricular septum) and the common cavity of the pericardium covering the heart [9,11]. In chronic right ventricular pressure overload, a phenomenon that plays a dominant role is the movement of the septum towards the LV cavity. That results in reduction of the LV volume, contractility and, consequently, in the increase of the LV diastolic pressure [12]. Diastolic dysfunction, which increases in proportion to the pressure in the right ventricle, is intensified under the influence of physical exertion or infection [13–15]. According to this, the clinical picture of COPD beyond the capacity of the right ventricle, may be indirectly created by a left ventricular diastolic dysfunction. Potential increase in left ventricular filling pressure, passively transferred to the pulmonary capillary system, can be applied to the already elevated precapillary pressure and contribute to the severity of dyspnea in these patients.





**Figure 5.** ECG registered during the first hospitalization

## Treatment

There are a few targeted therapies depending on the type of amyloidosis, however, the systemic form of the disease is associated with a poor prognosis. The annual mortality reaches 40% even after application of treatment [16]. The presented case shows how difficult challenge is to treat such patients. Some data of patients affected by hypertrophic cardiomyopathy and pulmonary disease is available, but there is still lack of knowledge on patients with amyloidosis. It appears that in these patients the use of cardioselective beta-blockers will result in less exacerbation of COPD. In summary of the Cochrane Database Systemic Review there were no adverse effects of the use of selective beta-blockers on FEV1 or exacerbations of COPD [17]. However it was found, that treatment with these drugs in cardiac patients with concomitant COPD should be intensified very carefully [17]. A subsequent study revealed that the use of non-selective beta-blockers turns out to be beneficial in reducing the incidence of hospitalization [18].

In this case primary or secondary nature of amyloidosis was not specified. Location and course of the disease suggests its primary character. Isolated cardiac amyloidosis is very rare and additional patient tests did not suggest this disease, that further hampered appropriate diagnostic evaluation. This resulted in a delay of a direct therapy. So far, an effective direct therapy for primary amyloidosis hasn't been found. The recommended treatment is based on the reduction or elimination of a number of plasma cells producing a monoclonal amyloid deposition [19]. Another treatment method is an autologous stem cell transplantation. In addition to pharmacological treatment in patients with isolated cardiac amyloidosis, heart transplantation is possible, but it is associated with a high risk of disease recurrence [20,21]. The standard symptomatic pharmacotherapy of the HF in amyloidosis may have limited or even harmful effects, especially related to beta-blockers. Digitalis and calcium channel blockers may accumulate in the tissues with accumulated amyloid, and therefore these drugs are relatively contraindicated due to increased toxicity [22,23]. The recommendations related to implantation of a pacemaker and cardioverter-defibrillator in preventing sudden cardiac death in patients with hypertrophic

cardiomyopathy do not work in those with amyloidosis [24, 25]. Limitations arise from the belief that sudden cardiac death in these patients is the result of electromechanical dissociation [25]. However biventricular pacing may be beneficial in prevention of cardiac decompensation resulting from ventricular dyssynchrony [26].

## Summary

This case shows how complex problem is the coexistence of the heart and lung diseases. The impairment of left ventricular filling was related to the amyloidosis, mitral stenosis and COPD. Heart catheterization allowed for a better understanding of the hemodynamic abnormalities in such a complex etiology of HF. Despite the well-preserved systolic function, cardiac index was reduced mainly due to elevated left ventricular filling pressure, that was illustrated by high PAWP with slightly elevated central venous pressure. Moreover, hyperthyroidism, which increased the incidence of arrhythmia, had its share in the destabilization of the patient's condition. The application of adequate pharmacotherapy was delayed because of an improper diagnosis. However, despite the possible induction of targeted therapy, the patient's prognosis remained poor.

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