

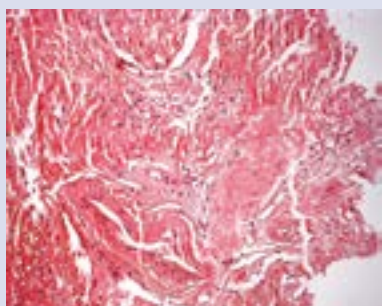
# The paramount importance of repeated left ventricular endomyocardial biopsy during the diagnosis of restrictive cardiomyopathy due to AL cardiac amyloidosis

Kluczowe znaczenie powtórnej biopsji lewej komory w diagnostyce kardiomiopatii restrykcyjnej na tle AL amyloidozy serca

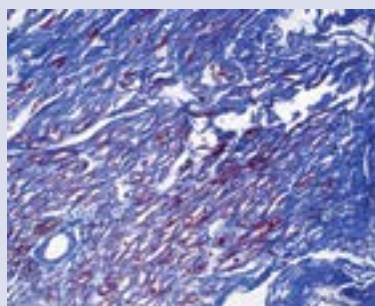
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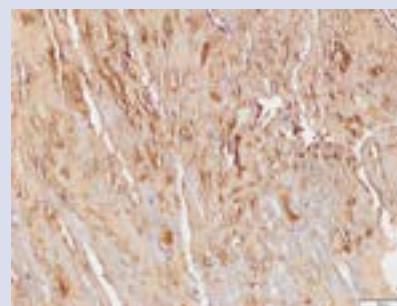
Amyloidosis is a group of disorders characterised by extracellular deposition of insoluble fibrillary proteins known as amyloid fibrils. Light chain amyloidosis (AL) is the most aggressive form and is caused by the accumulation of monoclonal immunoglobulin light chains secondary to B-cell dyscrasia. The heart is affected in up to 90% of cases, and more than half of patients present with heart failure (HF) symptoms. Accumulation of amyloid fibrils causes the myocardial wall to thicken and stiffen leading to the development of restrictive cardiomyopathy (RCM). Despite treatment with chemotherapy, the median survival rate in AL amyloidosis and HF is less than six months. A 57-year-old female without previous cardiac history sought medical attention due to rapid and progressive dyspnoea and signs of right ventricular (RV) congestion (ascites, peripheral oedemas, hepatomegaly). Prior medical history included: chronic kidney disease advanced to the 3<sup>rd</sup> stage (creatinine 158  $\mu\text{mol/L}$  [44–80], eGFR-CKD 39 L/min [ $> 60$ ]), stroke (ischaemic injury of the thalamus confirmed with magnetic resonance), and Graves-Basedow disease, currently in euthyrosis on Thiamazole 5 mg t.d.s. (TSH 0.134  $\mu\text{IU/mL}$  [0.27–4.2], FT3 5.1 pmol/L [3.1–6.8], FT4 25 pmol/L [12–22]). On electrocardiogram characteristic low voltages ( $< 0.5$  mV) of QRS complexes at the limb leads were observed. Laboratory tests showed normal blood morphology, grossly elevated NT-proBNP to 7889 pg/mL ( $< 125$ ), mildly elevated CK-MB 34 U/mL ( $< 25$ ) and hs-troponin T 0.045 ng/mL ( $< 0.014$ ), and on electrophoresis additional gamma-globulin signal. Free light chain ratio of lambda and kappa in serum was abnormal. Urine electrophoresis was negative. Echocardiogram revealed normal left ventricular (LV) and RV diameter, both atria grossly enlarged (left and right atrium area 32 cm<sup>2</sup> [ $< 20$ ] and 28 cm<sup>2</sup> [ $< 20$ ], respectively), mildly depressed ejection fraction to 50% [ $> 60$ ]), restrictive physiology of the mitral inflow (E/A 3.2 [ $< 1.5$ ], E' lateral 2.5 cm/s [ $> 7$ ], E/E' 37 [ $< 13$ ]), high suspicion of pulmonary hypertension (estimated pulmonary artery systolic pressure 60 mm Hg [ $< 35$ ]), distended and non-compliant inferior vena cava, and thickened inter-atrial septum (approximately 10 mm [ $< 3$ ]). The diagnosis of RCM was made and she underwent RV endomyocardial biopsy (EMB), which revealed massive fibrosis but was otherwise unpecific. Similarly, bone marrow biopsy was negative. Conventional HF treatment with beta-blockers, angiotensin converting enzyme-inhibitors, and diuretics did not improve the patient's status and she was sent to our centre. Despite non-diagnostic RV-EMB, the rapid course, laboratory findings, and imaging convinced us to undertake LV-EMB. The histopathology revealed a large amount of amorphous substance between tightly squeezed myocytes (Fig. 1) and widespread fibrosis (Fig. 2). Characteristic apple-green birefringence of the samples, stained with Congo red, were seen under a polarising microscope, which was diagnostic for cardiac amyloidosis. In order to determine the amyloid precursor protein, the immunohistochemistry (anti-bodies against immunoglobulins light chains) has been performed, which confirmed kappa and lambda free light chains (Fig. 3). Systemic chemotherapy with bortezomib, melphalan, and dexamethasone was initiated. However, due to toxicity, the therapy was changed to low-dose thalidomide, cyclophosphamide, and dexamethasone. Unfortunately, the patient's clinical status gradually deteriorated leading to death five months after the onset of symptoms.



**Figure 1.** Left ventricle endomyocardial biopsy sample (haematoxylin + eosin staining) — large amount of amorphous substance (pale pink) compressing surrounding myocytes



**Figure 2.** Widespread areas of replacement fibrosis (trichrome staining, intense blue)



**Figure 3.** Immunohistochemistry — deposition of kappa and lambda free immunoglobulin light chains (patchy areas of intense brown colour)

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**Conflict of interest:** none declared

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