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The clinical case of cardiac amyloidosis associated with multiple myeloma

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ABSTRACT

This clinical case demonstrates the difficulty of timely intravital diagnosis of cardiac amyloidosis and the prescription of adequate drug therapy which is associated not only with the limited possibilities of establishing a correct diagnosis and the absence of specific treatment in most cases, but also with a delay in seeking medical care. Thus, development and improvement of non-invasive screening methods of examination will allow to identify this pathology at earlier stages with a possibility of prescribing effective drugs and performing heart transplantation in some cases.

Key words: amyloidosis, multiple myeloma, restrictive cardiomyopathy, endomyocardial biopsy.

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Клинический случай амилоидоза сердца, ассоциированного с миеломной болезнью

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РЕЗЮМЕ

Данный клинический случай демонстрирует сложность своевременной прижизненной диагностики амилоидоза сердца и подбора адекватной медикаментозной терапии, что связано не только с ограниченными возможностями установления точного диагноза и отсутствия в большинстве случаев специфического лечения, но и с поздним обращением пациентов за медицинской помощью. Таким образом, разработка и усовершенствование неинвазивных скрининговых методов обследования позволит выявлять патологию на более ранних этапах с возможностью подбора эффективных препаратов, а в ряде случаев – трансплантации сердца.

Ключевые слова: амилоидоз, миеломная болезнь, рестриктивная кардиомиопатия, эндомиокардиальная биопсия.

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INTRODUCTION

Amyloidosis is a group of diseases with a variety of clinical manifestations characterized by extracelalular deposition of insoluble pathological fibrillar proteins [1]. The pathology was first described by T. Bonet in the 17th century. In the mid-19th century, R. Virkhov applied the term “amyloid”, and in 1937, F.R.B. Atkinson discovered amyloidosis in patients with myeloma [1, 2].

Currently, 4 theories of amyloidogenesis are known: G. Teilum’s theory of local cell genesis, Loeschke-Letterer’s immunological theory, V. Cagli’s theory of dysproteinosis and the mutation theory, but none of them explains the organospecificity and localization of the lesion [3]. The classification of amyloidosis is based on determination of the type of amyloid (A) and precursor protein (A is amyloid A-protein, L is immunoglobulin light chains, TTR is transthyretin, etc.). Clinically, generalized and local forms of the disease are distinguished [1, 3]. The most common type of amyloidosis involving the heart is AL [4]. Idiopathic AL amyloidosis and the one associated with various kinds of monoclonal plasma cell dyscrasias, including multiple myeloma and some other monoclonal gammopathies, are distinguished [5].

Due to late manifestation of the disease, clinical signs are very diverse and may be often disguised as an accompanying pathology (ischemic heart disease, Alzheimer’s disease, renal failure, etc.), which causes late diagnosis and lack of necessary treatment especially in the old age [6, 7]. Common symptoms are the following: hypotonia with syncopal events, chronic heart failure with signs of congestion in both circulations, and heartburn [7]. Currently, along with routine methods of investigation, it is possible to detect amyloidosis more frequently due to introduction of non-invasive screening method, such as speckle tracking echocardiography and magnetic resonance imaging of the heart [8, 9]. Although methods of determining biomarkers of amyloidosis in peripheral blood are being investigated, endomyocardial biopsy followed by histochemical examination is the only method of identifying the type of amyloidosis which allows to timely prescribe adequate drug therapy [10].

The case below is a clinical case of heart amyloidosis associated with myeloma and confirmed by a morphological study.

CLINICAL CASE

Patient S., 67 years old, was hospitalized in the Department of Emergency Cardiology of the Cardiology Research Institute, Tomsk National Research Medical Center in 12.2017 with complaints about shortness of breath of a mixed nature upon exertion, which remits at rest. Thyroidectomy for diffuse toxic goiter in 2007, euthyroidism (L-tyroxine 100 μg). Episodes of non-rhythmic heartbeat and atrial fibrillation were not recorded. Alopecia areata for 3 years. Chronic bronchitis. Loss of body weight by 13 kg in the last 6 months.

In history: 11.2017 she was urgently hospitalized in the district hospital with suspicion of acute coronary syndrome with atypical clinical manifestations and reduction of QRS voltage complexes on ECG. Laboratory diagnosis did not confirm myocardial infarction, but a transthoracic echocardiogram (TTE) revealed hypokinesia of the lower segments. The condition was complicated by pulmonary edema, bilateral hydrothorax, IIB chronic heart failure. Standard drug treatment did not lead to positive dynamics; the patient was transferred to the Cardiology Research Institute. Parameters of blood and urine are presented in Table 1; TTE, ultrasonography of kidneys – in Table 2. Objective clinical examination: BP 90/60 mmHg, hepatomegaly, leg edema. ECG showed sinus tachycardia (HR 104 bpm) and reduction of QRS voltage complex. Myeloma was revealed in laboratory tests. In order to verify the previously diagnosed myocardial infarction, invasive coronary angiography was performed and coronary atherosclerosis was not detected. Given the available restrictive pattern of transmitral blood flow, structural condition of the left ventricle, and minor response to drug treatment, storage disorder was suspected. Magnetic resonance imaging was

carried out, which allowed to visualize both ischemic and non-ischemic (amyloidosis/glycogenosis) damage against the background of myocardial dystrophy (Fig. 2). Endomyocardial biopsy of the right ventricle was performed: PAS-positive substance in the interstitium and endocardium and amyloid deposits were determined.

On the basis of all the data, it was possible to verify the diagnosis of secondary amyloidosis of the heart, probably AL type, associated with myeloma. Against the background of therapy with beta-blocker, inhibitor of ACE, and diuretics, hydrothorax was relieved; however, persistent hypotonia, pronounced fatigue, insomnia, and decreased appetite were preserved. The patient was transferred to the Department of Nephrology and Chronic Hemodialysis, where bone marrow trepanobiopsy was performed and myeloma and kidney amyloidosis were confirmed. Hydrothorax and hydropericardium in the intensive care unit recurred, fatigue increased, cachexia, hypotonia, and pulmonary edema recurred. The patient died on 8.01.2018.

This clinical case demonstrates the difficulty of timely intravital diagnosis of amyloidosis and selection of adequate drug therapy, which is associated not only with limited possibilities of establishing an accurate diagnosis and absence of specific treatment in most cases, but also with a delay in seeking medical care. Thus, the development and improvement of non-invasive screening methods will allow to detect the pathology at earlier stages with the possibility to select effective drugs and perform heart transplantation in some cases.

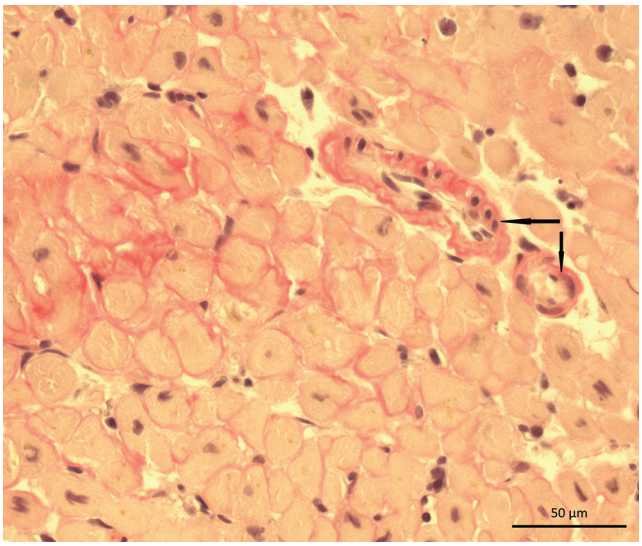

Figure. Myocardial biopsy

Table 1.

Laboratory parameters		
Blood test		
	12.12.2017	Normal
White blood cells, 10^9/L	6.8	4.0–9.0
Red blood cells, 10^{12}/L	5.03	3.9–4.7
Hemoglobin, g/L	163	120–140
ESR, mm/h	6	2–20
Blood biochemistry		
CPK-MB, U/L	22	0–25
Creatinine, µmol/L	72	53–97
Urea, mmol/L	5.9	2.2–7.2
Cholesterol, mmol/L	5.9	3.5–5.2
Total protein, g/L	49	64–83
CRP, mg/L	4.0	0–10.0
Potassium, mmol/L	3.8	3.5–5.1
Urinalysis		
White blood cells	10–12	0–3
Protein, g/L	5	0–0.08
Bence – Jones protein	+++	
Daily protein excretion, g/day	4.98	0–0.14

Table 2

Instrumental parameters		
Echocardiography 12.12.2017		
		Normal
Left atrium, mm	50x64	43 × 49
Right atrium, mm	47x61	43 × 49
LAV, ml	100.8	20–59
RAV, ml	97	19–64
LVED, ml	41	50–112
LVES, ml	18	12–41
RVED, mm	33	36–51
RVES, mm	21	21–34
EF LV (B), %	60	55–78
SV LF, ml	27	39–74
CI, L/min/m^2	1.9	1.7–4.5
Interventricular septum, mm	16	6.4–9.2
LV posterior wall, mm	16	6.4–9.2
Myocardial mass, g	200	< 146
Myocardial mass index, g/m^2	136	44–100
RVSP, mmHg	52	20–32
Vena cava inferior, mm	23	< 21
E/A	2	0.62–1.39
E/ e`	21	< 8

Ultrasound of the kidneys 18.12.2017			
	Right	Left	Normal
Length, mm	107	101	90–120
Width, mm	60	52	45–60
Parenchymal thickness, mm	13.7	12	12–20
Cyst	12 mm	–	–

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