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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INTRODUCTION

Amyloidosis is a group of diseases with a variety of clinical manifestations characterized by extracellular 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 08.01.2018.

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.

Table 1.

| Laboratory parameters | 12.12.2017 | Normal |
|-----------------------|------------|--------|
| Blood test            |            |        |
| 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  |
| LVES, 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/m²            | 1.9                         | 1.7–4.5|
| Interventricular septum | 16                          | 6.4–9.2|
| LV posterior wall, mm   | 16                          | 6.4–9.2|
| Myocardial mass, g      | 200                         | <146   |
| Myocardial mass index, g/m² | 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, mm         | 12    | –    | –      |
Случай из клинической практики

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REFERENCES

1. Kozlovskaya L.V., Rameev V.V. Draft clinical recommendations on diagnosis and treatment of systemic amyloidosis (AA, AL). Society of Nephrologists of Russia. 2014: 30 (in Russ.).
2. Nonka T.G., Repin A.N. Diagnostic and treatment opportunities for cardiac amyloidosis. Clinical Medicine. 2015; 93 (4): 66–73 (in Russ.).
3. Kozlov V.A., Sapozhnikov S.P., Sheptuhkina A.I., Golencov A.V. Comparative analysis of different amyloidosis models. Bulletin of RAMS. 2015; 70 (1): 5–11 (in Russ.). DOI: 10.15690/vramn.v70i1.1225.
4. Martinez-Naharro A., Hawkins P.N., Fontana M. Cardiac amyloidosis. Clinical Medicine. 2018; 18 (2): s30–s35 (in Russ.). DOI: 10.7861/clinmedicine.18-2s-s30.
5. Smirnova E.A., Abdurakhmanova E.K., Filonenko S.P. Systemic AL amyloidosis: difficulties in diagnosis (literature review and findings of the study). I.P. Pavlov Russian Medical Biological Bulletin. 2016; 24 (3): 141–153 (in Russ.).
6. Kozyrev K.M., Tsutsaev A.K., Kozyreva S.M., Kontaev R.V., Panagov Z.G., Lalieva Z.E. Structural and functional characteristics of senile cardiac amyloidosis and multi-organ amyloidosis (literature review). Bulletin of Advanced Medical Technology. 2017; 24 (1): 229–236 (in Russ.).
7. Blagova O.V., Nedostup A.V., Sedov V.P., Kogan E.A., Pasha S.P., Garagarina N.V., Alieva I.N., Sedov A.V., Tsaregorodtsev D.A., Kulikova B.A., Shepeleva N.E., Sarkisova N.D. Clinical masks of amyloidosis with cardiac damage: features of diagnosis at the modern stage. Russian Journal of Cardiology. 2017; 22 (2): 68–79 (in Russ.). DOI: 10.15829/1560-4071-2017-2-68-79.
8. Nikiforov V.S., Nikishchenkova Yu.V. Current opportunities of speckle tracking echocardiography in clinical practice. Rational Pharmacotherapy in Cardiology. 2017; 13 (2): 248–255 (in Russ.). DOI: 10.20996/1819-6446-2017-3-2-248-255.
9. Promislow S.J., Ruddy T.D. The evolving landscape of nuclear imaging in cardiac amyloidosis. Journal of Nuclear Cardiology. 2018; 27: 210–214. DOI: 10.1016/j.jncm.2012.10.006.
10. Luciani M., Troncone L., Monte F.D. Current and future circulating biomarkers for cardiac amyloidosis. Acta Pharmacologica Sinica. 2018: 1–9. DOI: 10.1038/aps.2018.38.

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