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СИСТЕМНЫЙ АМИЛОИДОЗ С ПОРАЖЕНИЕМ СЕРДЦА: ОСОБЕННОСТИ ТЕЧЕНИЯ И ТРУДНОСТИ ДИАГНОСТИКИ

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Systemic Amyloidosis with Cardiac Involvement: Features of Course and Diagnostic Difficulties

Резюме

Разнообразие клинических форм амилоидоза связано с различиями амилоидогенных белков-предшественников. Вовлечение сердца характерно для AL- и ATTR-амилоидоза, при этом поражение сердца развивается у подавляющего большинства больных с AL-амилоидозом и у 50 — 60 % пациентов с ATTR-амилоидозом. ATTR- (транстиретиновый) амилоидоз — один из вариантов системного амилоидоза; белком-предшественником является транстиретин при наличии мутаций в его молекуле (семейные формы) или возрастных нарушениях секреции его тетрамеров. До недавнего времени считалось, что на территории России транстиретиновый амилоидоз не встречается. Однако внедрение в практику методов молекулярно-генетической диагностики мутаций транстиретина продемонстрировало встречаемость ATTR-амилоидоза в России с частотой, близкой к среднеевропейской для не эндемичных зон. В статье представлено клиническое наблюдение системного амилоидоза у пациентки среднего возраста. Заболевание дебютировало в возрасте 54 лет карпальным туннельным синдром. В последующем доминирующим проявлением заболевания стала рефрактерная к лечению хроническая сердечная недостаточность. Выявленные в динамике неоднородность структуры и значительное утолщение миокарда при сохранной фракции выброса в сочетании с новыми симптомами (диарея, ортостатическая артериальная гипотензия, периорбитальная пурпура, протеинурия) были расценены как инфильтративное поражение сердца в рамках системного амилоидоза. Развившаяся асистолия послужила причиной летального исхода. По результатам аутопсии диагноз системного амилоидоза был подтвержден. В статье обсуждаются вопросы дифференциальной диагностики AL- и ATTR-амилоидоза, основанной на анализе анамнестических и клинических данных. Дебют заболевания с синдрома карпального канала, прогрессирующая дистальная невропатия в сочетании с автономной дисфункцией, доминирующее поражение сердца, отсутствие амилоидоза почек по данным аутопсии, длительность заболевания с момента клинической манифестации до летального исхода 43 месяца в большей степени указывает на ATTR-амилоидоз. В статье также обсуждаются современные подходы к диагностике амилоидного поражения сердца в клинической практике, указывается на возникающие при этом трудности, подчеркивается важность ранней диагностики амилоидоза сердца, что позволяет реализовать возможности современных методов лечения амилоидоза.

Ключевые слова: *системный амилоидоз, ATTR-амилоидоз, амилоидоз сердца, хроническая сердечная недостаточность, полиневропатия*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

The diversity of clinical forms of amyloidosis is related to differences in amyloidogenic precursor proteins. Cardiac involvement is characteristic of AL- and ATTR-amyloidosis, with cardiac involvement developing in the vast majority of patients with AL-amyloidosis and in 50-60 % of patients with ATTR-amyloidosis. ATTR- (transthyretin) amyloidosis is one of the types of systemic amyloidosis, the precursor protein of which is transthyretin in the presence of mutations in its molecule (familial forms) or age-related disorders of its tetrameric secretion. Until recently, it was believed that transthyretin amyloidosis did not occur in Russia. However, the introduction of molecular genetic diagnostic methods for transthyretin mutations has demonstrated the occurrence of ATTR amyloidosis in Russia with a frequency close to the European average for non-endemic areas. The article presents the case report of systemic amyloidosis in a middle-aged woman. The disease presented at the age of 54 years with carpal tunnel syndrome. Subsequently, chronic heart failure refractory to treatment became the dominant manifestation of the disease. Heterogeneity of structure and significant myocardial thickening with preserved ejection fraction detected in dynamics in combination with new symptoms (diarrhea, orthostatic arterial hypotension, periorbital purpura, proteinuria) were considered as an infiltrative heart lesion within the framework of systemic amyloidosis. The result was a fatal asystole. Autopsy findings confirmed the diagnosis of systemic amyloidosis. The article discusses the issues of differential diagnosis of AL- and ATTR- amyloidosis based on the analysis of anamnestic and clinical data. The onset of the disease with carpal tunnel syndrome, the progressive distal neuropathy combined with autonomic dysfunction, the dominant cardiac involvement, the absence of renal amyloidosis according to autopsy data, and the duration of the disease from the time of clinical manifestation to death of 43 months are more indicative of ATTR amyloidosis. The article also discusses modern approaches to diagnostics of amyloid heart lesion in clinical practice, points out the difficulties arising in this case, emphasizes the importance of early diagnosis of cardiac amyloidosis, which allows to realize the possibilities of modern methods of amyloidosis treatment.

Key words: *systemic amyloidosis, ATTR-amyloidosis, cardiac amyloidosis, chronic heart failure, neuropathy*

Conflict of interests

The authors declare no conflict of interests

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BP — blood pressure, BMI — body mass index, EDD — end-diastolic dimension, LV — left ventricle, IVS — interventricular septum, PH — postural hypotension, RV — right ventricle, PASYS — pulmonary artery systolic pressure, EF — ejection fraction, CCF — chronic cardiac failure, ECG — electrocardiography/electrocardiogram, echoCG — echocardiography, NTproBNP — N-terminal pro B-type natriuretic peptide

Systemic amyloidosis is a group of diseases caused by extracellular deposits of insoluble fibrillar protein masses — amyloid, having a common physical (crystal-like) structure. A regular structure of amyloid fibrils ensures homogeneous behaviour when stained for morphological examinations, in particular congophilic properties, where the colour changes to apple-green in polarised light. Diverse clinical forms of amyloidosis are caused by differences in amyloid precursor proteins, the number of which currently exceeds thirty [1, 2].

The most common form of systemic amyloidosis in therapeutic practice is AA-amyloidosis, where the precursor protein is acute phase protein of chronic inflammation SAA, and AL (AH)-amyloidosis, where the precursor protein is light (L) or heavy (H) immunoglobulin chains in plasma cell dyscrasia, including multiple myeloma. ATTR-(transthyretin) amyloidosis is also a systemic form of amyloidosis; the precursor protein is transthyretin (a protein transporting thyroxine and retinol) with mutations in its molecule (family form) or age-related abnormalities in secretion of its tetramers [1, 2].

Until quite recently, it was believed that transthyretin amyloidosis does not affect the citizens of Russia. However, after the introduction of routine molecular genetic methods to diagnose transthyretin mutations, staff at E. M. Tareev clinic demonstrated cases of ATTR-amyloidosis in Russia, with the incidence close to the Central European rates for non-endemic regions (8 % vs. 10 %, respectively). Taking into account the time from first signs of the disease to diagnosis (median: 69 months), the authors conclude that in Russia ATTR-amyloidosis is under-diagnosed [3]. The presented case study can illustrate this observation.

Patient P., 58 years old, ethnicity: Russian, first noticed the signs of weakness, rapid fatigability, shortness of breath when walking at a moderate speed in November 2021, after the past coronavirus infection. During the next 4 months, exercise tolerance reduced, shortness of breath started appearing after walking 50–100 m and at

night; the patient noticed palpitations, swelling of her feet and shins, episodes of hypotension. An examination in the central district hospital in March 2022 showed pulmonary hypertension: pulmonary artery systolic pressure (PASYS) of 60 mm Hg, tricuspid regurgitation, D-dimer elevation to 900 ng/mL (normal range: 0–550 ng/mL). The patient was diagnosed with pulmonary embolism of small branches and prescribed rivaroxaban 20 mg, bisoprolol 2.5 mg, spironolactone 25 mg, torasemide 5 mg. The therapy was ineffective, and in May 2022 the patient was admitted to the Regional Clinical Hospital (Saratov). History taking showed that, prior to coronavirus infection, the patient did not have any cardiovascular disease; in 1995 she underwent cholecystectomy; in 2019 the patient underwent surgery for carpal tunnel syndrome (on the left); birth: 1, menopause from 56 years. Her father died at the age of 74 years old from a heart disease (no details are known); her mother was diagnosed with DM2 at the age of 82 years old. Upon admission, the patient had symptoms of congestion in the two circulations: shin swelling, positive hepatojugular reflux, bubbling rales in the lower sections of the lungs. Heart tones are muffled; heart rate is 72 bpm, blood pressure is 120/70 mm Hg. Computed tomography showed interstitial changes in the lungs, signs of venous stasis, bilateral hydrothorax. Echocardiography (echoCG) showed the following results: left ventricle ejection fraction (LV EF) — 66 %, left ventricular mass index (LVMI) — 97 g/m^2 (M-mode), PASYS — 55 mm Hg. Holter ECG monitoring recorded rare supraventricular and single polymorphous premature ventricular complexes. Duplex Doppler ultrasound of veins in the lower extremities did not show any pathologies. Laboratory test results, including troponins, creatine phosphokinase MB, C-reactive protein, D-dimer, total protein, were normal; N-terminal pro B-type natriuretic peptide (NTproBNP): 156.4 pg/mL. For more details, please refer to Table 1.

In the absence of clinical and instrumental signs of pulmonary embolism, myocarditis, ischaemic heart disease, which could cause chronic cardiac failure (CCF), unspecified cardiomyopathy was diagnosed. The therapy with perindopril 4 mg, bisoprolol 2.5 mg, spironolactone 100 mg, torasemide 5 mg yielded positive results. In August 2022, the patient was admitted to the Regional Clinical Hospital again. With the regular therapy for

Table 1. *Dynamics of complete blood count and the biochemical blood test*

Parameters / Date	May 2022	August 2022	March — April 2023
Red blood cells RBC, 10^{12}/L	4,3	5	4,0
White blood cells WBC, 10^9/L	6,6	10,6	9,2
Hemoglobin HGB, g/L	131	151	124
Platelets PLT, 10^9/L	294	341	323
Red blood cell sedimentation rate, millimeters/hour	13	15	18
Blood serum protein, g/L	60,3	61,7	53,8
Serum albumin, g/L	37	38,1	37,7
Creatinine, μmol/L	72,4	87,1	101
C-reactive protein, mg/L	1,9	17,32	21,7
Cortisol, nmol/L N 150-660	study not performed	study not performed	659
NTproBNP, пг/мл	156,4	study not performed	2259,9
ALT, units per liter	18,3	19,8	11,3
AST, units per liter	27	21,4	16,3
Glucose, mmol/L	4,5	6,0	5,4
Cholesterol, mmol/L	5,4	5,0	4,1
Sodium, mmol/L	141,9	135,2	134,1
Potassium, mmol/L	3,95	4,3	4,5
Calcium, mmol/L	1,22	1,24	1,22

Note. ALT — alanine aminotransferase, AST — aspartate aminotransferase

2.5 months, the patient did not have peripheral oedema; she did not have shortness of breath at rest, but it appeared with moderate exercise; however, one month before hospitalisation, the patient noted aggravation of shortness of breath (when walking 100 m), as well as chill feet, burning sensation in her fingers and toes, pain in calf muscles during walking. It is worth mentioning that lower pain and tactile sensitivity (like "gloves" and "socks"), paresthesia were observed for the past three years, but were less pronounced. Laboratory and instrumental test results are presented in Tables 1 and 2. Repeated echoCG showed that LVMI had increased from 97 to 122 g/m^2 (M-mode) and the anterior wall of the right ventricle (RV) slightly thickened to 0.55 cm. The neurologist diagnosed dysmetabolic sensory and motor polyneuropathy. The patient was discharged with recommendations to continue ACE inhibitors, diuretics, b-blockers. The neurologist recommended taking alpha-lipoic acid, gabapentin, vitamins B, bencyclane. After discharge in September 2022, the patient noted diarrhoea (3–4 times a day). Symptomatic therapy with Smecta, loperamide was inefficient. In November, the patient was diagnosed with chronic gastritis, chronic gallstone pancreatitis, dolichosigmoid, sigmoid diverticles, haemorrhoids in outpatient settings.

In January 2023, progressive CCF was observed, and the diuretic therapy was updated: spironolactone 200 mg and torasemide 40 mg were added. In April 2023, the patient was admitted to the Regional Clinical Hospital with shortness of breath with minimal exercise, shin swelling, blackouts when standing up from horizontal position, weight loss (30 kg in one year), burning sensation in her fingers, progressive weakness, loose stool (2–4 times a day). Examination revealed a new symptom — periorbital skin purpura (Fig. 1).

BP in prone position was 120–110/85mm Hg; when the patient stood up, systolic BP dropped to 85 mm Hg, diastolic BP — to 60 mm Hg. Non-rhythm pulse of 68–75 bpm. Holter ECG monitoring showed transient grade 2 atrioventricular block, type 1 and 2.

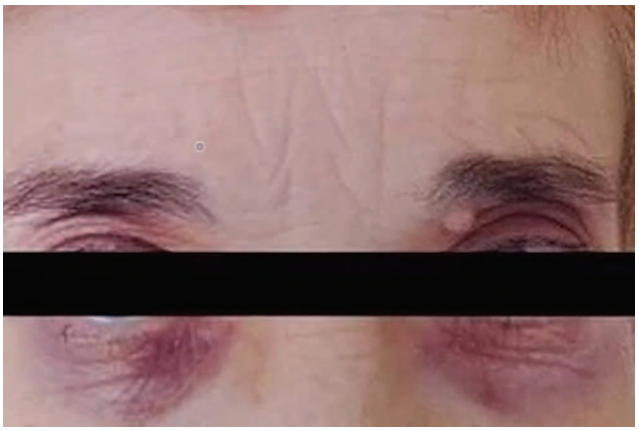

Figure 1. *Periorbital cutaneous purpura (the «raccoon eye» symptom)*

Laboratory test results demonstrated a clinically significant rise in NTproBNP values to 2259.9 pg/mL, moderate hypoproteinemia with normal blood albumin (Table 1), proteinuria (1.0 g/L).

Negative echoCG changes were observed: LVMI increased to 201 g/m^2 (M-mode), LV posterior wall thickness reached 1.8 cm, interventricular septum thickness — 2.0 cm, RV anterior wall thickness — 0.83 cm, right and left atria dimensions reached 4.46 and 4.05 cm, respectively. Thicker interventricular septum and ventricle and atria walls were not associated with ECG signs of myocardial hypertrophy and were interpreted as possible infiltrative heart damage. Also, during examination, reduction in LV end-diastolic dimension (EDD) from 5.1 to 3.9 cm, non-homogeneous myocardium structure, preserved EF (68.7 %) with progressive CCF (Table 2) were of interest.

Table 2. *Dynamics of echocardiography indicators*

Parameters / Date	May 2022	August 2022	March — April 2023
Left ventricular mass index, g/m^2	97	122	201
Ejection fraction left ventricular, %	66	62	68
Systolic pressure in the pulmonary artery, mm Hg	55	44	58
Left ventricular end diastolic size, mm	5,1	4,9	3,9
Thickness of left ventricular posterior wall, cm	1,0	1,1	1,8
Thickness of the interventricular septum, cm	1,0	1,1	2,0
Thickness of right ventricular anterior wall, cm	0,5	0,55	0,83
Left atrium, cm	3,7	3,8	4,05

EchoCG signs of restrictive cardiomyopathy and high grainy myocardium reflectivity were additional information pointing out to possible heart amyloidosis. In our observation, low ECG complex voltage (an additional sign) was absent. However, of note, currently low-voltage ECG is not a reliable sign, because it is recorded only in 20 % of ATTR cases and 29 % of AL-amyloidosis cases [3].

Restrictive cardiomyopathy with non-homogeneous myocardium structure and preserved EF with refractory CCF, combined with bilateral carpal tunnel, postural hypotension (PH), motor diarrhoea with weight loss, renal impairment (proteinuria), periorbital skin purpura (raccoon eyes) underlied a conclusion on systemic amyloidosis. To rule out AL-amyloidosis with multiple myeloma, blood and urine M-gradient was examined (result: negative), and a sternal puncture was performed: normocellular bone marrow, plasmatization — 1 %. However, no blood and urine tests were performed for the presence of free light immunoglobulin chains, therefore, it was impossible to reliable rule out AL-amyloidosis, including together with multiple myeloma. No amyloid was found in rectum mucous biopsy material. Given significant proteinuria, a renal biopsy was scheduled. On day 2 of hospitalisation to the nephrology unit, when the patient was standing up in the morning, she suddenly collapsed with cardiac arrest; ECG results showed asystole. Resuscitation was inefficient; the patient was pronounced dead.

Final clinical diagnosis.

Primary disease. Primary amyloidosis with involvement of the heart, GIT, somatic and sympathetic nervous system, kidneys (chronic renal disease, stage C3A2). Relative mitral and tricuspid incompetence with regurgitation, grade 3. Pulmonary hypertension, stage 2.

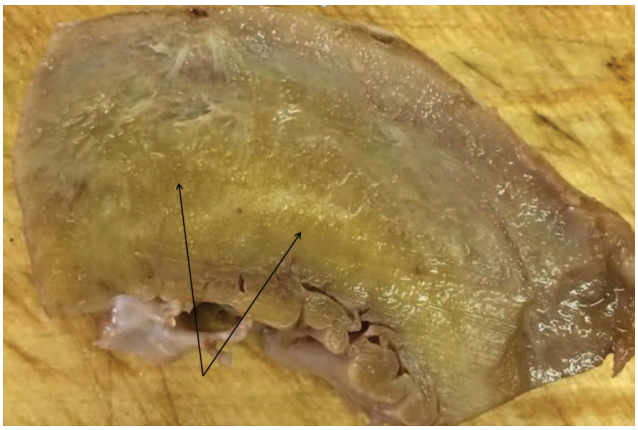

Figure 2. *Heart. Multiple yellowish layers (deposits of amyloid masses)*

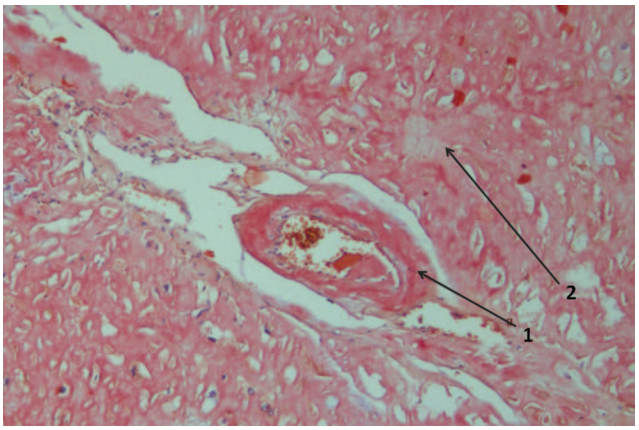

Figure 3. *Myocardium*
Note. 1 — deposits of amyloid masses in the wall of small myocardial artery; 2 — deposits of amyloid masses in myocardium. Congo red stain; magnification ×20

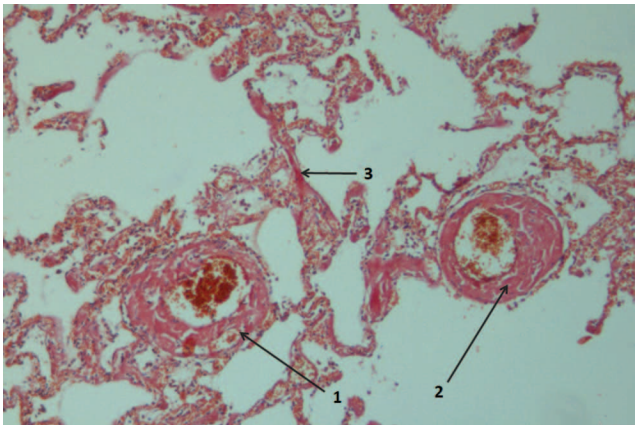

Figure 4. *Lung*
Note. 1,2 — deposits of amyloid masses in the walls of small arteries; 3 — amyloid deposits in the interalveolar septum. Congo red stain; magnification ×20

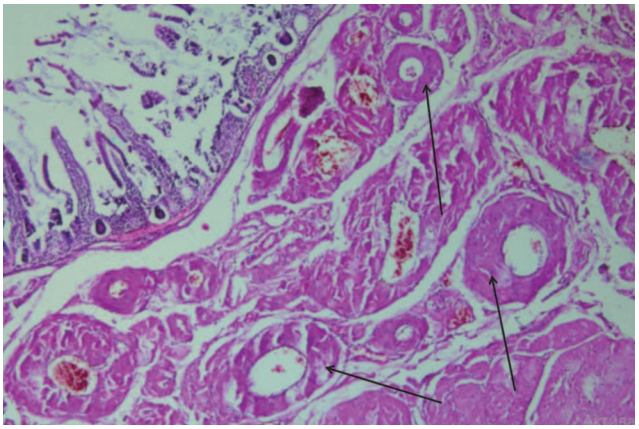

Figure 5. *Small intestine*
Note. Arrows indicate deposits of amyloid masses in many vessels of submucosa. Hematoxylin and eosin stain; magnification ×20

Primary disease complications. CCF with preserved left ventricle ejection fraction, functional class 4 (NYHA). Ascites, bilateral hydrothorax. Transient stage II atrioventricular block, type 1 and 2. Asystole on April 20, 2023. Condition after resuscitation on April 20, 2023.

Comorbidities. Dorsopathy, cervical osteochondrosis. Chronic gallstone pancreatitis. Chronic gastritis. Dolichosigmoid. Sigmoid diverticles. Haemorrhoids.

Postmortem diagnosis.

Primary disease. Primary amyloidosis, involving mostly the heart, with areas of complete replacement of myocardial tissue with amyloid masses in the posterior wall of the left ventricle; with involvement of the atria, valves, coronary and intramural artery walls; with involvement of vessels and walls of pulmonary alveoli, submucosal and muscular GIT layers, mesostenium, extraorganic arteries and renal veins.

Thus, postmortem examination confirmed the diagnosis of systemic amyloidosis. Severe heart damage seen on postmortem data is of utmost interest. Figure 2 shows a gross specimen with areas of complete replacement of the myocardium with amyloid masses. Also, a slide of the heart tissue shows an area of total replacement of the myocardium with amyloid masses, amyloid deposits in myocardial artery walls (Fig. 3). The systemic nature of the damage is illustrated with slides of the lung and small intestine tissue (Fig. 4 and 5, respectively). Kidney damage manifested as amyloid deposits in walls of extraorganic renal arteries and veins; however, no amyloid was found in renal parenchyma. The structure of the renal tissue showed some CCH-associated changes: acute dystrophy-like changes and necrosis of individual tubule cells, interstitial tissue sclerosis of 30 %.

Amyloid was verified using Congo red and dichroism in polarised light. Amyloidosis typing was not performed due to technical reasons.

Discussion

In this case study, the possibility of timely clinical diagnosis of amyloidosis and differential diagnosis of the type of amyloidosis require unconditional discussion. The absence of chronic inflammatory diseases, cancer, involvement mostly of the heart and nervous system rule out secondary AA-amyloidosis. Therefore, the differential diagnosis should include the concept of AL- and ATTR-amyloidosis.

In this patient, the disease started with a neurological pathology — progressive distal symmetric polyneuropathy, which included carpal tunnel syndrome. Over a long time the nervous system pathology was treated as a comorbidity; however, in the absence of diabetes mellitus, excessive alcohol consumption, absence of occupational stress for the wrist, genesis of this pathology was unclear and could be a reason for a deeper examination at the earlier stages of the disease. According to the literature, nervous system involvement is observed in 17 % to 35 % of AL-amyloidosis patients and almost in all patients with various hereditary amyloid polyneuropathies, including ATTR; while bilateral carpal tunnel syndrome is typical for ATTR-amyloidosis [3-5].

In AL-amyloidosis and especially in ATTR-amyloidosis, PH is a common event; this is a circulatory insufficiency, where vessels are no longer able to maintain normal blood pressure during orthostatic loads. Usually, this symptom is associated with dysfunctional sympathetic nervous system (amyloidosis of vessel nerve plexus); it manifests as sickness and blackout during orthostasis with an abrupt rise in BP. In severe cases, postural hypotension is associated with syncope, sometimes it causes an acute cerebrovascular accident. This sign is one of the most important factors of unfavourable prognosis [3, 4]. In this case study, during hospital admission in April 2023, PH was one of the symptoms to assume amyloidosis in this patient. PH was underestimated in the prehospital phase.

An autonomous dysfunction manifests not only as PH. Intestinal wall infiltration with amyloid involvement of intestinal nerve plexus presents as motor diarrhoea with secondary malabsorption, which results in weight loss. True malabsorption is significantly rarer (4–5 %) in amyloidosis [3]. When discussing the causes of significant weight loss, seen in this case study during the last year of the patient's life, impaired muscle trophism in patients with peripheral amyloid polyneuropathy should be taken into account as well.

According to the literature, kidney damage (proteinuria and renal insufficiency) is observed in 80–90 % of AL-amyloidosis patients and only in 20–23 % of patients with ATTR-amyloidosis; and often it is diagnosed after the heart and peripheral nervous system have been damaged [4]. This sequence of symptoms was observed in this clinical case: proteinuria was diagnosed just several weeks before death, during hospitalisation in April 2023. The cause of proteinuria is another topic for discussion. According to postmortem study results, the patient did not have amyloid damage to her renal parenchyma, but had amyloid deposits in extraorganic renal vessels, which is another argument for ATTR-amyloidosis. Proteinuria was likely to be a result of renal congestion because of progressive CCF, confirmed by morphological changes in renal parenchyma

in the form of protein degeneration and necrosis of tubule cells and interstitial tissue sclerosis.

Heart damage develops in a majority of patients with AL-amyloidosis and in 50–60 % of patients with ATTR-amyloidosis. In the clinical presentation of ATTR-amyloidosis, heart damage can be the most important symptom [3,4,6]. Patients with ATTR are known to have significantly thicker myocardium (median value: 17 mm, interquartile range: 16–18 mm) vs. AL patients (median value: 15 mm, interquartile range: 13–16.5 mm) [7]. The association between the life expectancy after first signs of the disease and the amyloid type has been confirmed. In AL-amyloidosis, the median survival rate with the natural course is less than 12 months. If left untreated, usually it takes ATTR-anyloidosis 5–15 years to progress to the terminal damage to the heart or nervous system; the median survival rate is 57 months [8]. In this case study, myocardial involvement was prevailing; myocardium was 20 mm thick, disease duration from onset of clinical symptoms (carpal tunnel syndrome) to death was 43 months.

When discussing differential diagnosis of AL- and ATTR-amyloidosis, a possible observation is that in this case study, the clinical data together with postmortem examination results are a very strong evidence of ATTR-amyloidosis. This conclusion is based mostly on the presence of some signs typical for ATTR-amyloidosis and unusual for AL-amyloidosis, such as bilateral carpal tunnel syndrome, absence of renal involvement and life expectancy of 43 months after onset of the disease. It is worth noting that pronounced cardiomyopathy, where the myocardium was 20 mm thick, is also typical for ATTR-amyloidosis. PH is reported in both forms of amyloidosis and is, therefore, irrelevant. Periorbital skin purpura, which was observed at the end stage of the disease and which is most typical for AL-amyloidosisa, cannot be the primary differentiating symptom.

In this case study, it is only at the late stage when echoCG showed a myocardium pathology typical for amyloidosis: high grainy myocardium reflectivity, significantly thicker myocardium, restrictive impairment of the LV diastolic function with preserved EF, dilated atria. Interestingly, in the presence of refractory CCF and systemic pathology, dynamic echoCG is advisable (in this case, the interval between echoCG examinations was 8 months). Of note, the role of echoCG in the diagnosis and evaluation of cardiac amyloidosis prognosis is much higher with the emergence of highly informative modes of tissue Doppler examinations (strain, strain rate and speckle-tracking) [3]. The use of strain and strain rate methods in patients with systemic amyloidosis demonstrates that despite prevalence of diastolic cardiac insufficiency in amyloid cardiomyopathy and relatively late reduction in LV ejection fraction, the most early sign of heart involvement is reduced global LV longitudinal strain [9].

At present, the diagnosis of heart amyloidosis includes two important stages: suspicion phase and definite diagnosis phase. Myocardial amyloidosis should be suspected when the left ventricle wall is at least 12 mm thick in combination with red flags of amyloidosis: at least one extracardiac (polyneuropathy, bilateral carpal tunnel syndrome, standalone dysfunction, macroglossia, skin bruising, proteinuria, renal insufficiency) and cardiac signs (cardiac failure with disproportionately high NT-proBNP levels, unexplained right-side heart failure with preserved ventricle and valve ejection fraction, idiopathic pericardial effusion, persistently high troponin levels, disproportionately low QRS voltage or early conduction abnormalities) [5].

The definite diagnosis phase is based on detection of diagnostic criteria of amyloidosis, which can be both invasive and non-invasive. Invasive diagnostic criteria (detection of amyloid fibrils in cardiac tissue or non-cardiac amyloid together with the typical signs on echoCG or heart MRI) can be used in any form of heart amyloidosis, whereas non-invasive criteria are used only for ATTR [5]. Non-invasive criteria include heart MRI with delayed Gd contrasting, which allows diagnosing heart amyloidosis in 47 % of patients, even with normal myocardium wall thickness [6]. Also, heart amyloidosis can be diagnosed using scintigraphy with 99mTc-pyrophosphate and 99mTc-3,3-diphospho-1,2-propanodicarboxylic acid (99mTc-DPD). Intensive imaging agent accumulation in the myocardium together with unspecified myocardium thickness is an indication of highly probable ATTR-amyloidosis, if AL-amyloidosis has been ruled out [4]. The diagnostic algorithm also includes amyloid typing, which is essential for specific therapy.

In this case study, the full algorithm for amyloidosis diagnosis was not implemented. The diagnostic experience in this observation was limited to suspicion of this pathology. On the one hand, the untimely diagnosis of heart amyloidosis was due to the late onset of cardiac symptoms. On the other hand, non-cardiac signs of the disease, a wide array of clinical manifestations were evaluated only at the advance stage of the disease, and no active timely diagnostic search was performed. Besides, diagnostic challenges can be associated with inadequate awareness of doctors of the signs of ATTR-amyloidosis, the distinctive feature of which is renal non-involvement in 80 % of cases.

Conclusion

Nowadays, clinicians are able to timely diagnose amyloidosis with heart damage. Despite the advancements and better availability of instrumental methods of examination, timely initiation of diagnostic search is still very relevant.

The totality of clinical symptoms, primarily a combination of progressive neuropathy and signs of unspecified cardiopathy and progressive CCF, allows suspecting amyloidosis and initiating diagnosis verification, including amyloidosis typing. Only early diagnosis can ensure that the new therapies are efficient. The recent years have been remarkable for significant success in the therapy of both AL- and ATTR-amyloidosis, which is a result of clinical introduction of proteasome inhibitor bortezomib in the therapy of AL-amyloidosis, primarily as part of multiple myeloma patient care [4], as well as transthyretin stabilisers, particularly tafamidis. Efficacy and safety of tafamidis in polyneuropathy progression inhibition have been confirmed, especially at early stages, as well as for better survival rates in patients with hereditary myocardial ATTR-amyloidosis [10]. It imposes specific requirements to early diagnosis of myocardial amyloidosis, where the key factor is adequate doctor awareness of this pathology.

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Волошинова Е.В.: разработка концепции и дизайна, обоснование и написание рукописи, анализ и интерпретация данных; согласие автора быть ответственным за все аспекты работы.

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Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Voloshinova E.V.: conceptualization and design, justification and writing of the manuscript, analysis and interpretation of data; author's agreement to be responsible for all aspects of the work.

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Yakovleva E.V.: data analysis and interpretation, manuscript writing, verification of critical intellectual content, and final approval of the manuscript for publication.

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