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## THE ROLE OF IRON DEFICIENCY ANEMIA IN PATIENTS WITH CHRONIC HEART FAILURE IN THE EXAMPLE OF A CLINICAL CASE

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Anemia is common comorbidity in patients with heart failure. In Europe one in two patients with chronic heart failure has iron deficiency. Iron deficiency anemia is associated with a worse prognosis in the heart failure patient population and is an independent risk-factor for mortality, poor exercise capacity and low quality of life.

**KEY WORDS:** anemia, comorbidity, iron deficiency, heart failure

## РОЛЬ ЗАЛІЗОДЕФИЦИТНОЇ АНЕМІЇ У ПАЦІЄНТІВ З ХРОНІЧНОЮ СЕРЦЕВОЮ НЕДОСТАТНІСТЮ НА ПРИКЛАДІ КЛІНІЧНОГО ВИПАДКУ

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Анемія – найбільш поширений коморбідний стан у хворих з хронічною серцевою недостатністю. В Європі більш ніж у половини пацієнтів, які страждають на хронічну серцеву недостатність, діагностовано дефіцит заліза. Залізодефіцитна анемія пов'язана з гіршим прогнозом у хворих з хронічною серцевою недостатністю і є незалежним фактором ризику смертності, зниження толерантності до фізичних навантажень та зниження якості життя.

**КЛЮЧОВІ СЛОВА:** анемія, коморбідність, дефіцит заліза, серцева недостатність

## РОЛЬ ЖЕЛЕЗОДЕФИЦИТНОЙ АНЕМИИ У ПАЦИЕНТОВ С ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ НА ПРИМЕРЕ КЛИНИЧЕСКОГО СЛУЧАЯ

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Анемия – наиболее частое коморбидное состояние у пациентов с хронической сердечной недостаточностью. В Европе, более чем у половины пациентов, страдающих хронической сердечной недостаточностью, диагностируют железодефицит. Железодефицитная анемия ассоциируется с худшим прогнозом у пациентов с хронической сердечной недостаточностью и является независимым фактором риска смертности, снижения толерантности к физическим нагрузкам и снижения качества жизни.

**КЛЮЧЕВЫЕ СЛОВА:** анемия, коморбидность, железодефицит, сердечная недостаточность

## INTRODUCTION

Anemia has been frequently observed in patients with chronic heart failure (CHF) and has been associated with increased mortality [1–2]. Increased mortality as well as increased rates of hospital admissions and decreased quality of life or exercise tolerance increased

attention from the medical societies around the world. Estimates of the prevalence of anemia in patients with CHF and low ejection fraction range widely from 4 % to 61 % [3–4].

Causes of anemia in patients with CHF, possibility of anemia contributing to more severe CHF, forms of anemia prevalent in CHF populations, recommended treatment to

improve anemia and the general condition of patients with CHF, as well as a Clinical Case demonstrating the role of anemia in the developing heart failure will be further discussed [5].

Anemia is the most common disorder of the blood, affecting about a quarter of the people globally. It is a reduction in the total amount of red blood cells (RBCs) in the blood [2]. Reduction in the number of RBCs transporting O<sub>2</sub> and CO<sub>2</sub> impairs the body's ability for gas exchange leading to even more detrimental effects starting from the nervous system to the other systems of the body [6–7].

Heart failure (HF), also known as congestive heart failure (CHF) occurs when the heart fails to pump blood at the rate needed by the body. HF is a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function [5–6]. More than 20 million people have HF worldwide with men having a higher incidence than women. In the year after diagnosis the risk of death is about 35 % after which it decreases to below 10 % each year.

Anemia now occupies an important place in our present understanding of the pathogenesis of heart failure. In Europe, one in two patients with CHF has iron deficiency (ID) [8]. ID is associated with a worse prognosis in the HF patient population and is an independent risk-factor for mortality, poor exercise capacity and low quality of life [9–10].

Anemia has been found to be more prevalent in heart failure patients with a higher NYHA functional classification, greater degree of renal dysfunction, advanced age, female sex, and African-American race. The relationship between anemia and CHF is mutual, the former produces or worsens the latter and vice versa [1–2].

Anemia depends nearly exclusively on hemorrhage, which sets in motion an integrated response with actions in different regions, which include vasoconstriction and thrombosis, fluid retention, stimulation of erythropoiesis, and vascular repair. All these as a result of the human adaptive mechanisms induced to maintain perfusion, O<sub>2</sub> supply to tissues, but also to preserve volume [11]. As a consequence, left ventricular dilation and hypertrophy can occur, with the next result

being the production or worsening of CHF [11–12].

Potential causes for anemia in heart failure patients are likely to be a multifactorial. Routine diagnostic evaluation includes:

- complete blood count with reticulocyte count and index serum iron and total iron binding capacity transferrin saturation ferritin serum B12 and folate,

- thyroid stimulating hormone fecal occult blood test red blood cell distribution width (RDW) is a numerical measure of the variability in the size of circulating erythrocytes, taken during a standard blood count test.

Ineffective erythropoiesis causes heterogeneity in erythrocytes size and a higher RDW. RDW has recently emerged as a new prognostic marker of HF, regardless of Hb levels [12].

## **CLINICAL CASE**

### **Patient medical profile**

Female Patient N., 58-y old, retired, resident of urban area, was admitted to the hospital on 14<sup>th</sup> of November 2016

### **Chief complaints**

Patient complains of general weakness, palpitations, stabbing chest pain, without any radiation, that is relieved without medications, dyspnea during physical activity, absent at rest numbness of fingertips, attention deficit disorder.

### **History of present illness**

These complaints were felt by Patient N. 1 year ago. Last exacerbation was 3 days ago, she didn't take any drugs. After consulting with the physician, she was thus admitted to the hospital (14.11.2016) for further observation and tests.

### **Past medical history**

For over 5 years, Patient N. suffered from essential hypertension. Her therapist prescribed medications such as diuretics and B-blockers (name not specified), but she did not comply with the proper dosing and as such, her BP level was unstable (she recalled it rising up to 150–170/100 mm Hg). Patient N. also suffered from chronic gastritis since year 2000. Patient N. has had no history of viral hepatitis, Diabetes Mellitus. She also denied any history of easy bruisability, menorrhagia. No surgical history.

### **Family/social history**

Patient's mother and sister suffer from essential hypertension. No family history of

anemia or any other hematologic disorder, no family history of kidney and liver diseases. Patient N. denied any illicit drug history, alcohol use, smoking and allergic reactions both to environmental factors and to drugs. She is married, has 2 children.

#### **General examination**

Vital signs: temperature 36,7C<sup>0</sup>; blood pressure (BP) – 150/80 mm Hg; heart rate(HR) – 82 beats per minute; respiratory rate(RR) 19 breaths per minute; height 160 cm; body weight 57 kg; body mass index(BMI) – 22,2 kg/m<sup>2</sup>.

#### **Physical examination**

Elderly female, had correct orientation in space and surroundings, mild depressed. Skin was pale with the absence of rashes and hemorrhages. Mucous membranes were pale and wet. Tongue is clear and wet. Turgor and elasticity of the skin were decreased. There were koilonychias. Subcutaneous fat tissue is normal. There were no any chest variations and surgical incision sites. Edema of the lower limbs was observed (2+). Joints were normal, active and passive movements were painless. The rest general inspection was unremarkable.

#### **Objective examination**

Percussion of the lungs was normal. Heart borders extended to the left on 1,5 cm of midclavicular line. Heart sounds were decreased in all points of auscultation. It was observed an accentuation of S2 on aorta point. Systolic murmur was auscultated on the 1st point of the heart auscultation (apex of the heart). Auscultation of the lungs was normal. No abdominal bruits or rubs were observed. The kidneys were not palpable. Stool and urination were normal.

#### **Laboratory and instrumental methods**

Complete blood count: (16.11.2016) Hb – 40 g/l; RBCs – 1.6\*10<sup>12</sup> /l; WBCs – 3.9\*10<sup>9</sup> /l; Segmented neutrophils – 79 %; Lymphocytes – 16 %; ESR – 18 mm/h

Complete blood count: (22.11.2016) Hb – 55 g/l; RBCs – 2.2\*10<sup>12</sup> /l; WBCs – 4.2\*10<sup>9</sup> /l; Segmented neutrophils - 74%; Lymphocytes - 19%; ESR-17 mm/h

Complete blood count: (29.11.2016) Hb-70 g/l; RBCs – 2.4\*10<sup>12</sup> /l; WBCs-4.1\*10<sup>9</sup> /l; Segmented neutrophils – 73 %; ESR – 17 mm/h

Conclusion: remarkable decrease in Hb, RBC indicated a severe form of anemia. An increase in segmented neutrophils could be a result of an infection or inflammation process. A slight decrease in lymphocytes was observed. The rest results were unremarkable.

Biochemical blood test (16.11.2016): AsAT – 0,59 U/l; AlAT – 0,7 U/l. All parameters except AsAT, AlAT were normal.

Blood lipid profile (16.11.2016): LDL – 127 mg/dL; HDL – 55mg/dL; Total cholesterol – 5.5 mmol/L; Triglycerides – 58 mg/dL. All parameters except LDL were normal. There was a slight increase in low density lipoprotein (LDL).

Biochemical blood test (17.11.2016): Serum iron – 2.3 mkmol/l; total iron-binding capacity (TIBC) – 35.7 mkmol/l; Transferrin saturation – 6.4 %; serum ferritin – 28 ng/mL; Vitamin B12 – 85 ng/L. There was no vitamin deficiency anemia. Remarkable decrease in iron levels in the blood indicated Iron deficiency (ID) anemia.

Urinalysis (16.11.2016) was normal.

Esophagogastroduodenoscopy (16.11.2016): The mucosa of the esophagus was normal. Gastric mucosa was reddened and swollen. The structure of the folds was not changed.

Abdominal ultrasound (19.11.2016): Liver and gallbladder was normal. The spleen was enlarged (size 133×60 mm (N – 110×60 mm)).

Chest X-Ray (21.11.2016): There were no infiltrative or local changes in the lung. The sinuses were without liquid. Left heart border displaced sinisterly, inferiorly and posteriorly. There was rounding of the cardiac apex.

ECG (21.11.2016): Sinus rhythm, regular. Heart rate – 82 bts/min. Left ventricular hypertrophy.

Heart echocardiography (22.11.2016): End-DV LV – 120 ml; End-SV LV – 34 ml; mitral valve – regurgitation I degree; posterior wall of the LV – 13 mm; interventricular septum – 12 mm; ejection fraction – 40 %. Concentric left ventricle hypertrophy, decreased ejection fraction.

Upper gastrointestinal tract radiography (23.11.2016): There were signs of gastritis.

Six Minute Walk Test (6MWT) (25.11.2016): Patient N. walked 425 feet in 6 minutes. The test result complied with functional class II chronic heart failure.

#### **Final diagnosis**

*Main Disease:* Iron deficiency anemia, stage 2, severe degree, mixed genesis

*Concomitant Diseases:* Essential arterial hypertension II stage 2<sup>nd</sup> grade. Chronic heart failure (CHF) 2<sup>nd</sup> class according to the NYHA classification with reduced ejection fraction, chronic gastritis (unspecified).

### **Hospital treatment**

RBCs transfusion BIII Rh+ 368,0 ml (16.11.16); tardyferon (ferrous sulfate) 80 mg 1 tablet twice a day; sufer 20 mg/ml IV; bisoprolol 2,5 mg 1 tablet once a day; perindopril 5 mg 1 tablet once a day.

### **Recommendation**

1) Lifestyle modification.

Diet:

– Meat: beef, pork, or lamb, especially organ meats such as liver;

– Poultry: chicken, turkey, and duck, especially liver and dark meat;

– Fish, especially shellfish, sardines, and anchovies;

– Legumes, including lima beans, peas, pinto beans, and black-eyed peas;

– Iron-enriched pastas, grains, rice, and cereals.

Patients should be strictly warned against a «tea and toast diet» as tea strongly blocks iron absorption.

Activity restriction: patients with moderately severe iron deficiency anemia and significant cardiopulmonary disease should limit their activities until correction of the anemia with iron therapy.

2) Drug therapy: tardyferon (ferrous sulfate) 80 mg 1 tablet twice a day 3–4 months, perindopril 5 mg 1 tablet once a day.

### **CONCLUSIONS**

The goal of this clinical case was to bring awareness to the prevalence of anemia and CHF, and influence of iron deficiency anemia in the progression of CHF while also focusing on diagnostic testing and treatment strategies [11].

The origins of anemia in heart failure are multifactorial. Its pathways are complex and not well understood.

There is no single treatment that will suit all patients, because of treatment must be based on an understanding of the causes of anemia in each patient.

According to last recommendation, the 2016 European Society of Cardiology guidelines, IV iron therapy is recommended for patients with Heart Failure with reduced Ejection Fraction and absolute or functional ID in order to alleviate HF symptoms and improve exercise capacity and quality of life [12].

The role of anemia in developing of HF should be researched and recognized more to understand the target levels of ferritin and iron in patients with or without anemia and CHF to reduce mortality and improve quality of life [13].

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