on the competence approach, a certain dependence between knowledge and skills, subordination of acquired knowledge to professional skills is established. This, in turn, contributes to the fact that education becomes personally significant for the student [1,2,3,4].

Special attention in teaching the discipline «Vaccinal prevention in pediatrics» issues of post-vaccination complications and vaccination reactions. Teachers developed lectures with a detailed presentation of the educational material. In accordance with this, methodical recommendations and instructions for students were prepared and approved for publication. Special attention was paid to the organization of independent work of students, which is one of the most important components of the educational process and a condition for the development of students ' competence. Working independently, students not only firmly and deeply assimilate the subject educational material, but also develop skills of research and professional activity, ability to work with educational and scientific literature, ability to make responsible and constructive decisions in various crisis situations.

In the course of discipline training, great attention is paid to the calendar of preventive vaccinations. At the end of the training, students should be free to navigate the timing of vaccinations.

Organization of independent work of students is carried out taking into account didactic principles that reflect the specifics of this area of pedagogical activity in high school. These include the following principles: unity of educational (classroom) and independent (extracurricular) activities of students; individualization and differentiation; professional orientation, contributing to the transfer of educational and cognitive activity of students in the professional and pedagogical; consciousness and creative activity of students; possible difficulties of tasks for independent work, taking into account the time for their implementation; systematic, sequence and continuity of the organization of independent work. Independent work involved the use of situational tasks and tests developed for each lesson in preparation of students for classes.

Offset on discipline included control of the acquired practical skills.

Conclusion:

1. Changing the educational process is a necessary condition for the formation of students ' clinical competence.

2. The introduction of new clinical disciplines contributes to their acquisition of professional knowledge and skills.

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The author:

Olga Ivanova – Doctor of medical Sciences, Professor, Department of Pediatrics and pediatric surgery of the medical Institute M. K. Ammosov North-Eastern Federal University, Oyunsky str., 27, Yakutsk, Russia, e-mail:olgadoctor@list.ru.

CLINICAL CASE

Kh.A. Kurtanov, T.N. Alexandrova, N.I. Pavlova, I.I. Mulina, I.E. Solovyeva, M.A. Varlamova, L.M. Neustroeva, A.T. Dyakonova

CLINICAL CASE OF ACUTE MYOCARDIAL INFARCTION IN THE ONSET OF CHRONIC MYELOPROLIFERATIVE DISEASE

ABSTRACT

The main clinical problem of patients with chronic myeloproliferative diseases are thrombotic complications causing death and invalidism. Possible long-term latent course of these diseases, comorbid cardiovascular pathology increases the risk of fatal complications. This article presents a clinical case of chronic myeloproliferative disease in a 57-aged man, who first manifested with acute Q-positive myocardial infarction. The patient successfully underwent recanalization, transluminal balloon angioplasty with stenting of the anterior descending coronary artery. Based on thrombocytosis and bone marrow examination he fulfill the diagnosis of essential thrombocythemia. During follow-up of three years, the progression of disease is observed with the development of secondary myelofibrosis. The diagnosis is confirmed by bone marrow histology and taking into account high risk of recurrent thrombotic complications, he administered with cytoreductive and antiplatelet therapy.

Keywords: chronic myeloproliferative diseases, thrombosis, cardiovascular complications, myocardial infarction.

Introduction

Chronic myeloproliferative diseases are clonal diseases that affect hematopoetic stem cells. The trigger mechanism of diseases is a point somatic mutation in the 14 exon of the JAK2 gene, leading to the replacement of valine by phenylalanine in codon 617 (JAK2V617F) of the polypeptide chain. As a result of this mutation, JAK2 tyrosine kinase, a key enzyme of the JAK2/STAT kinase pathway, leads to uncontrolled proliferation of myeloid precurcors [3]. Prevalence of JAK2V617F mutation among patients with polycythemia vera (PV) is 97%, essential thrombocytopenia (ET) is 55% and primary myelofibrosis (PMF) is 65% [10].

The main cause leading to disablement and a decrease in survival of patients with ET and PI is the tendency to thrombosis [4]. In case of ET, arterial thrombosis is more common than venous, which is more often seen in PV patients. ET commonly manifest with symptoms of microcirculatory disorder such as erythromelalgia and transient neurologic

disorders. Hemorrhagic complications caused by a decrease of von Willebrand factor concentration in plasma as a result of its binding with platelet glycoprotein IIb/IIIa [1].

Chronic myeloproliferative diseases affect mainly elderly people (mean age 55 years), whose somatic status is complicated by cardiovascular risk factors. Such comorbid conditions as atherosclerosis, hypertension, metabolic syndrome, and lifestyle increase the risk of cardiovascular complications in this cohort of patients [2, 8]. Often there are cases of latent course of myeloproliferative disease, when the only clinical presentation of disease is thrombosis. At the time of diagnosis, thrombosis of various localizations occur in 31,2% of patients with ET [11]. Polycythemia or thrombocytosis may be masked by an increased volume of plasma and/or hypersplenism, which makes it difficult to interpret laboratory findings and diagnose chronic myeloproliferative diseases. Delayed diagnosis of these diseases can lead to the development of fatal complications, such as myocardial infarction, strokes, thrombosis of the veins of the portal system.

Objective: to demonstrate the clinical case of myeloproliferative disease, presented with acute myocardial infarction at the onset.

Material and methods of investigation. A retrospective analysis of the medical records of patient B., followed-up by hematologists of Yakutsk since 2014, was carried out.

Clinical case

*Patient B., a man of 57 years, had become acutely ill in December 2013 when he complained of angina pectoris that are not managed with nitroglycerin. He was administered to emergency cardiology department, where a Q-positive myocardial infarction was diagnosed based on ECG, Echocardiography, dynamics of cardiospecific enzymes. Complete blood count demonstrated moderate thrombocytosis (421*109/l), mild anemia (erythrocytes 3,49*109/l, hemoglobin 107 g/l), ESR 13 mm/h, leukocytic formula is unchanged. In biochemistry hyperglycemia (blood sugar 6.1 mmol/l), dyslipidemia (total cholesterol 5.4 mmol/l, triglycerides 0,9 mmol/L, low density lipoproteins (LDL) 3,8 mmol/l, lipoproteins high density (HDL) 1,2 mmol/l) were identified. Patients denied any history of angina, he has been smoking for over 20 years for 5-7 cigarettes a day. He has a history of 3rd degree arterial hypertension without medications, varicose veins of legs which are managed by phlebectomy 2011. In hospital, selective coronary angiography (SCAG) was performed, where an occlusive thrombosis of the proximal segment of the anterior descending artery (PNA) of the left coronary artery (LCA) was detected. Recanalization, transluminal balloon angioplasty (TBCA) with PNA stenting was carried out and medical treatment – anticoagulants, antiplatelets, angiotensin converting enzyme inhibitors (ACE inhibitors), beta-blockers, statins were prescribed. During inpatient care, the platelet count increased to 864*109/l for the first time. He was discharged from hospital on the 15th day in a satisfactory condition with recommendations to continue double antiplatelet therapy (acetylsalicylic acid 125 mg + clopidogrel 75 mg), metoprolol 25 mg, ivabradine 5 mg, rosuvastatin 10 mg.*

*Patient visited hematologist in January 2014 with complaints of general weakness. In examination the skin and visible mucous membranes are of a normal color, clean. The body mass index is 26 kg/m2. Peripheral lymph nodes are not palpable. Vesicular breathing, no wheezing. Breathing rate is 16 per min. Heart rhythm sounds are muffled, heart rate is 66 min. Blood pressure is 130/80 mm/Hg. The abdomen is mild, painless, the liver and spleen are not enlarged. No signs of peripheral edema. At the examination: complete blood count – erythrocytes 4,09*109/l, leukocytes 8,5*109/l, hemoglobin 116 g/l, platelets by smear 1104.8 * 109/l, stab neutrophils 3%, segmented neutrophils 61%, eosinophils 5%, lymphocytes 24%, monocytes 7%, ESR 7 mm/h. Biochemical blood test – albumin 44,5 g/l, total protein 76,9 g/l, bilirubin total 9,9 µmol/l, direct bilirubin 2.9 µmol/l, ALT 31,7 U/l, AST 26,1 U/l, urea 7,3 mmol/l, creatinine 107,6 µmol/L, glucose 5,06 mmol/l, total cholesterol 6,06 mmol/l. Bone marrow morphology demonstrated one megakaryocyte with numerous small nuclei, platelets aggregations and giant platelets. Bases on clinical presentation, examination and laboratory findings patient was diagnosed with essential thrombocythemia and antiplatelet therapy was prescribed.*

*The patient returned to hematologist in March 2017 for routine check-up. He does not have any complaints. During examination, mild thrombocytosis 682*109/l, progression of anemia (erythrocytes 3,53, hemoglobin 85 g/l, hematocrit 29,5%), normoblastosis 2:100, hyper-segmentation of neutrophils and acceleration of ESR up to 29 mm/h were revealed. Blood biochemistry demonstated a high LDH level 822,6 U / L, hyperuricemia 511,3 µmol/l, other indices were within reference ranges. According to abdominal ultrasound there was a moderate splenomegaly (63,5 cm2). Additional studies was erformed to exclude other hematological diseases: chimeric BCR-ABL transcript - 0%, trepanobiopsy – bone marrow is hypercellular marrow (relatively to age). The erythroid lineage is represented by normoblasts. The granulocyte lineage is represented by all forms of differentiation with a predominance of maturing forms. The number of megakaryocytes is increased, with hyperchromic hypo- and hyperlobular nuclei, also present with cloud-shaped, dysmorphic, isolated nuclei in the form of reindeer antigens, located in large groups, up to 14 cells, near the bony beams. Van Gieson, Masson coloring showed collagen fibrosis proliferation in bone marrow stroma. Stroma contains of lymphocytes, eosinophils. Conclusion: The histological picture does not exclude the presence of chronic myeloproliferative disease, primary myelofibrosis. Immunohistochemical study was not conducted due to the lack of specific reagents. Histologic study is allowed to comfirm clinical diagnosis – chronic myeloproliferative disease: an essential thrombocythemia with an outcome in secondary myelofibrosis. Patient was prescribed with cytoreductive therapy – hydroxyurea is 500 mg/day and antiplatelets.*

Discussion

The clinical presentation of ET is characterized by the absence of pathognomonic symptoms and is depend on disease stage and rate of progression. Disease onset is usually asymptomatic, it proceeds slowly over a several years. Patients usually come to hospital because of microcirculation disorders – acrocyanosis, erythromelalgia, headaches, secondary Raynaud's syndrome. In a significant part of patients, blood count abnotmalities are detected during routine examination or when examined for other co-existing pathologies [1, 4]. In this clinical case disease manifested first with acute myocardial infarction. Duration of disease is unknown, since the patient has not previously visited ambulance. Probably, there was a latent course of the disease, because progression to postthrombocythemic myelofibrosis is commonly occur after long-term history of ET. The frequency of progression to secondary myelofibrosis, according to the literature, is 3-10% during the first 10

years, and 6-30% after disease duration of more than 10 years [1].

Vascular accidents at the moment of diagnosis are not rare – myocardial infarction in 10,2% of patients, strokes – in 13,0% [11]. The international prognostic risk scale for thrombosis in essential thrombocythemia (IPSET-thrombosis) includes age over 60 years, diabetes mellitus, hypertension, smoking, history of thrombosis and the presence of JAK2V617F mutation [6]. Despite the high diagnostic and prognostic significance of the determination of the mutational status of JAK2V617F, it is not always possible to perform molecular genetic studies in routine clinical practice. Additional risk factors associated with thrombogenic risk are leukocytosis and dyslipidemia [3, 9]. In this patient, the risk factors are presented by smoking, arterial hypertension and dyslipidemia.

When stratifying the risk of recurrent thrombotic complications, it should be noted that patients with history of thrombosis are at high risk and require a complex approach to the treatment of disease, as well as secondary thrombotic prevention. To correct leukocytosis and thrombocytosis in older people, hydroxyurea (Hydrea) is commonly used [5,8]. Prevention of thrombotic complications includes measures to correct lifestyle, arterial hypertension, smoking cessation and drug therapy [1]. The gold standard of long-term therapy after myocardial infarction is a double antiplatelet therapy with acetylsalicylic acid and clopidogrel. Acetylsalicylic acid is not recommended for patients taking anagrelide due to increased risk of bleeding [7].

Conclusion

Presented clinical case demonstrates the possibility of a long latent ET course that first manifested with myocardial infarction. The absence of pathognomonic symptoms makes it difficult to diagnose chronic myeloproliferative diseases. The high risk of developing fatal complications and disease progression determine the need for regular medical examinations and the introduction of molecular diagnostic methods for the detection of JAK2V617F mutation in routine clinical practice.

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The authors:

1. Kurtanov Khariton Alekseevich – PhD, Chief scientific officer - Head of the Department of Molecular Genetics. Tel.: +7 (914) 106 00 30. E-mail: hariton_kurtanov@mail.ru;

2. Aleksandrova Tuiara Nikonovna – junior researcher of the laboratory of heritable pathology alexandrova_tuyara@mail.ru;

3. Pavlova Nadezhda Ivanovna – PhD, temporary acting chief scientific officer - head of the laboratory of heritable pathology E-mail: solnishko_84@ inbox.ru;

4. Mulina Inna Ivanovna – Head of the Department of hematology National Centre of Medicine;

5. Solovieva Irina Eremeevna – hematologist of National Centre of Medicine;

6. Varlamova Marina Alekseevna – junior researcher of the laboratory of heritable pathology;

7. Neustroeva Lena Mikhaylovna – junior researcher of the laboratory of the Laboratory of Population Genetics;

8. D'yakonova Aleksandra Timofeevna – junior researcher of the laboratory of heritable pathology.