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CLINICAL CASE OF MEGALOBLASTIC ANEMIA IN A TEENAGER WITH NEW CORONAVIRUS INFECTION

This article presents a clinical case of newly diagnosed megaloblastic anemia in a 15-year-old teenager girl from the Republic of Sakha (Yakutia), in combination with intercurrent disease COVID-19. The new coronavirus infection occurs rapidly on the background of of suppressed hematopoiesis, with the development of complications in the form of community-acquired bilateral severe polysegmental pneumonia and bilateral exudative pleurisy, which required observation and treatment in a hospital. The performed standard complex therapy for megaloblastic anemia and pneumonia caused by SARS-CoV-2 made it possible to achieve clinical and laboratory improvement in the patient and restore the function of the red bone marrow.

Keywords: megaloblastic anemia, cobalamin deficiency, folic acid deficiency, COVID-19, new coronavirus infection, pneumonia.

Introduction. Megaloblastic anemia (MA) encompasses a heterogeneous group of macrocytic anemias characterized by the presence of large red blood cell precursors called megaloblasts in the bone marrow [2]. Megaloblastic anemia is ubiquitous, regardless of gender and age.

This condition is due to impaired DNA synthesis, which inhibits nuclear division. Cytoplasmic maturation, mainly dependent on RNA and protein synthesis, is less impaired. This leads to an asynchronous maturation between the nucleus and cytoplasm of erythroblasts, explaining the large size of the megaloblasts [2].

The main diagnostic criteria for megaloblastic anemia are the detection of macrocytic, hyporegenerative anemia, thrombocytopenia, a decrease in the level of vitamin B12 and folic acid in the blood serum, Jolly bodies and Cabot rings, granulocytic hypersegmentation can be detected in a peripheral blood smear.

The main cause of megaloblastic anemia is a deficiency of vitamin B12 (cyanocobalamin) and folic acid. Folic acid is found in foods such as green vegetables, fruits, meat, and liver. The daily requirement for children is: for newborns - 65 mcg, for children up to a year - 85 mcg, from 1 to 3 years - up to 300 mcg, from 4 to 8 years - up to 400 mcg, from 13 years - 18 years - 400-500 mcg [2]. The main sources of cobalamin/vitamin B12 are meat, fish, eggs and dairy products. The daily requirement for children is: 0.3 to 1.4 mcg/day [2]. Vitamin B12 deficiency may be due to the refusal to consume animal products, which is currently an urgent problem among children and adolescents. The most dangerous is the development of vitamin B12 deficiency in newborns and infancy, since there is a high risk of developing irreversible complications, including delayed physical and psychomotor development, but this can be prevented by preventing vitamin B12 and folic acid deficiency during pregnancy [4].

Although safe and effective therapy is available and treatment of anemia is simple, diagnosis can be extremely difficult due to the many and varied clinical manifestations, often coexisting diseases, and the limitations of currently available diagnostic tests [3]. Megaloblastic anemia is most often detected during routine laboratory tests, since anemia develops gradually, and symptoms are present only in patients with severe anemia [2].

In this regard, we would like to share our own clinical observation.

Clinical case: patient A., 15 years old. entered the oncology department of the Pediatric Center of Republic Hospital №1 – National Center of Medicine, named after M.E. Nikolaev 17.01.22

From the history of life: a girl from the fourth pregnancy, which proceeded against the background of anemia of mild severity in the mother. Giving birth naturally at a period of 39 weeks. Birth weight is 3600 g, birth length is 54 cm. Apgar score 8/9 points. Breast feeding to the age of 12 months. The mental and physical development of girl age-appropriate. Vaccination of girl, According to the national vaccination schedule in Russia. Heredity: on the maternal side - diseases of the cardiovascular system, on the father's side - strokes. Earlier diseases: acute respiratory infections (ARI), COVID-19. Allergic anamnesis: to the vaccine "Grippol" in the form of a rash. There were no surgeries, no injuries.

Anamnesis of the disease: since the autumn of 2022, the girl began to be disturbed by epistaxis, which became more often in winter, her parents noticed paleness of cutaneous integuments, the child complains about fatigue.

At the beginning of December 2021, the girl got sick with the ARI: the body temperature rises to C39.3C, a sore throat and general weakness. The parents consulted a doctor, was prescribed treatment. On the background of the therapy, there was an improving the health.

At the beginning of January 2022 the body temperature rises to 39-40C, dry cough. Parents lowered the temperature with paracetamol. On January 7, 22, was called district pediatrician at home, were recommended taking antibiotics, a swab was taken from the pharynx and nose for the diagnosis of COVID-19. From 08.01.2022 Polymerase chain reaction - the result is positive. 01/10/22 was prescribed treatment: azithromycin. On January 13, 22 her health deteriorated, increased cough and shortness. The girl was hospitalized in an emergency at infectious department of Central District Hospital.

Based on the investigation results: total blood count: there was a pronounced three-growth aplasia, ESR 79 mm/h, MCV 112 fl, MCH 39.1 pg, hemoglobin 27 g/l, thrombocytopenia 29*10*9/l, leukopenia 0.9* 10*9/l, biochemical blood test: increased transaminases, inflammatory reaction, total protein - 54.4 g/l; total bilirubin - 166.2 μmol/l; ALT- 277 U/l; AST-153 U/l; LDH 1605.34 U/l, CRP - 74 g / l. According to the results of the coagulogram - hypocoagulation, PTI 58.6%; INR - 1.7; APTT - 42 sec. CT scan of the chest - Conclusion: Polysegmental pneumonia, high probability of covid-19, CT2 (48%).

The child received the following therapy: the antibacterial drug Ceftriaxone at a daily dose of 2 g, 4 procedures of hemotransfusion with washed erythrocytes, two transfusions of fresh frozen plasma.

On January 17, 22, a PCR test of COVID-19 was taken: the result was negative. The child was delivered by emergency aircraft to the The Pediatric Center of National Centre of Medicine The Republic of Sakha (Yakutia), the Medical Commission held a meeting. The decision of the council: for emergency indications she was moved into intensive care on. after stabilization of state, the patient was transferred to the pediatric oncology department.

An objective examination on admission: Height-163cm. Weight-58.5kg. Objectively, the condition is grave, caused by anemic syndrome. The child is conscious. Body temperature is 36.0C. The state of health is reduced, sluggish. Appetite is selective (eats more white meat, snacks, sweets, starchy foods). Stature is correct, normosthenic. The skin is very pale, with an icteric tint, dry, hemorrhagic rash on the arms and legs and at the injection sites on the elbow bend. Visible mucous membranes are pale, clean. Pharynx unchanged from the tonsils. Nasal bleeding from the left nasal passage has stopped by wicking. Regular peripheral lymph nodes aren't enlarged. Breathing is weakened with the medium and sonorous fine bubbling rales. Respiratory rate – 28/min. Saturation - 95%. Heart sounds are rhythmic, clear. Heart rate – 85/min. BP 119/66 mm Hg. Abdomen is soft and painless in palpation. Liver and spleen are regular in size. Fecal retention for 2 days. Urination is regular and painless. Urine is deep yellow.

Paraclinically: total blood count: leukocytes - 1.7 thousand / μl, erythrocytes - 1.7 million / μl, MCV 96.9 fl, MCH 34.8 pg, Hb - 53 g / l, platelets - 12 thousand / μl, myelocytes - 1%, reticulocytes-1, ESR - 68 mm/h Biochemical blood test: total protein - 43.8 g/l; albumin - 27.7 g/l; total bilirubin - 34.8 μmol / l; direct bilirubin - 12.7 μmol/l; ALT - 67.5 U / l; AST - 43.9 U/ l; sugar - 5.08 mmol/l; LDH - 928.8 U / l; alkaline phosphatase - 29.6 U / l. Coagulogram: PTI - 13.6 sec; INR - 1.2; APTT - 39.7 sec; fibrinogen - 5.99 g/l. Blood serum from 01/18/22: folic acid - 0.6 ng / ml (3.10-20.50); vitamin B12 - 8.8 pmol / l (20.60 - 196.70).

A bone marrow puncture was performed from 4 points (anterior and posterior iliac crests). Myelogram: Blast cells 0.4%; 0%; 0.2%; 0%. Puncture of varying degrees of cellularity with increased proliferation of erythroid germ with impaired maturation with signs of megaloblastoidity. The morphological picture of megaloblastic anemia.

CT scan of the chest organs: CT-signs of bilateral polysegmental pleuropneumonia, average risk of covid-19, CT-2. Bilateral pleural effusion. Ultrasound of the pleural cavities: Free fluid in the pleural cavities: on the right, the approximate volume is 64 cm3, on the left, the approximate volume is 78 cm3.

In order to identify the pathology of the gastrointestinal tract, the patient was prescribed an examination:

Urea1 breath tests for Helicobacter pillory - the result is negative;

Esophagogastroduodenoscopy - Superficial gastritis, duodenitis. A biopsy was taken.

Biopsy results: Fragments of the gastric mucosa without pathology. HP has not been identified.

Fragments of the mucosa of the duodenum, the ratio of the lengths of the villi and crypts ~2-2.5:1. Enterocytes are high. The number of MELs is 10 per 100 enterocytes. Own plate with infiltration by lymphocytes, plasmocytes, single granulocytes.

Ultrasound of abdominal cavity organs: Hepatosplenomegaly, sediment in the gallbladder, diffuse changes in the liver parenchyma are visualized;

Feces on helminth eggs: negative.

Results of laboratory and instrumental studies confirms the clinical diagnosis of the patient.: Megaloblastic anemia, severe severity (cobalamin and folic acid deficiency). Comorbidities: Community-acquired bilateral polysegmental pneumonia, viral-bacterial, severe. Respiratory failure 3 stage. Bilateral exudative pleurisy. Status after COVID19 dated 08.01.22. CT2.

Treatment was carried out: antibacterial, antifungal and symptomatic therapy. With a pathogenetic purpose, it was prescribed: Cyanocobalamin (Vitamin B12) at a dosage of 400 mcg x 1 time per day in / in drip, folic acid 5 mg, 1 tab x 3 times a day [1]. Hemotransfusion therapy was carried out with blood components: washed erythrocytes according to individual selection, hardware thrombus suspension.

At discharge: total blood count: leukocytes - 4.95 thousand / μl, erythrocytes - 3.47 million / μl, MCV 98.6 fl, MCH 31 pg, HGB - 102 g / l, thrombus - 334 thousand / μl, reticulocytes-15. Biochemical blood test dated 01/31/22: total protein - 64.8 g/l; total bilirubin - 20.1 μmol/l; ALT - 74.8 U / l; AST- 42.9 U / l. According to the results of CT of the chest organs in comparison with the CT scan of 01/18/2022, positive dynamics, CT-1, lesion volume 15%, regression of effusion in both pleural cavities.

Against the background of the therapy, there was an improvement in the condition and normalization of blood counts. Clinically, the girl became more active, her general condition improved, pallor and yellowness of the skin decreased, due to the improvement in her condition, on the 15th day the girl was discharged, with recommendations: dispensary observation for 2 years with a pediatrician at the place of residence; include in the diet foods rich in folate, vitamin B12, vegetables, fruits, gray-grinded cereals, meat products; continue drug treatment with vitamin B12 preparations at a dosage of 400 mcg s / c once a week for 2 months; then 2 times a month for 6 months and folic acid 5 mg, 1 tab x 3 times a day, 1 month; control of the KLA and a biochemical blood test 1 time in 2 weeks - 1 month, then 1 time per month.

Conclusion. In the case described by us, anemia was hyperchromic, hyporegenerative, macrocytic, in combination with an increase in transaminase activity, there was a pronounced three-line aplasia, a decrease in the level of vitamin B12 and folic acid in the blood serum, erythroid proliferation with impaired maturation with signs of megaloblastoidity, aplastic anemia was excluded, acute leukemia. Based on the medical history of the girl, the probable cause of the disease was established: inadequate, poor nutrition, with the exception of animal products. Against the background of the girl's habitual diet and lifestyle, the anemic syndrome developed slowly. The deterioration of the condition was gradual, the first signs of anemia in the girl were still in the fall of 2022, but did not attract the attention of her parents, and only an infectious intercurrent disease forced her to see a doctor. In connection with the identified megaloblastic anemia in a child, it is necessary to conduct a differential diagnosis with other types of anemia, such as aplastic anemia, autoimmune pancytopenia, Marchiafava-Micheli disease. The combination in the clinical picture of severe anemic syndrome, abdominal pain and dyspeptic disorders, icterus of the skin and sclera requires a targeted diagnostic search to exclude oncopathology of the abdominal organs. In all cases of vitamin B12 deficiency, broad tapeworm invasion should be excluded. It is important to find out the features of previous operations on the patient's digestive organs (gastrectomy, resection of the stomach, anastomosis with the presence of a blind loop of the intestine).

Early diagnosis of megaloblastic anemia, timely initiation of treatment and adequate follow-up after the elimination of anemia provide a favorable outcome of the disease and avoid the development of irreversible complications.

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