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CLINICAL CASE OF WILLEBRAND DISEASE COMBINED WITH CROHN'S DISEASE IN AN ADOLESCENT SAKHA

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The article presents an interesting clinical case of Willebrand's disease in combination with Crohn's disease and congenital heart disease in a 17-year-old Sakha teenager. Such clinical cases are rare in the public literature, since the combination of these diseases is practically not found. The onset of Crohn's disease at the age of 16 significantly affected the development and severity of clinical manifestations. Therapy with a genetically engineered biological drug and substitution therapy made it possible to achieve clinical and laboratory remission.

Keywords: Willebrand,s disease, Von Willebrand,s factor, homeostasis, Crohn,s disease, congenital heart disease.

Introduction. Von Willebrand disease (WD) is an inherited disease that occurs with quantitative or functional von Willebrand factor deficiency. Willebrand factor is a glycoprotein involved in hemostasis, synthesized in endothelial cells and megakaryocytes. After transcription and translation, it binds to form dimers and then the von Willebrand factor propetide is cleaved and secreted into the vessel lumen. Willebrand factor functions as a factor VIII carrier and aids in platelet adhesion and binding to endothelial components after vascular injury. Any qualitative deficiency leads to bleeding and this syndrome is called von Willebrand disease [7,8,11].

Hereditary phenotypic forms of von Willebrand disease are: Type 1: Autosomal – dominant disease caused by partial quantitative deficiency of von Willebrand factor; type 2: Autosomal – dominant disease caused by several qualitative defects of the Willebrand factor. It has four subtypes – 2A – AD (AR), 2B – AD, 2N – AD, 2M – AD. Of there, the most common is 2A; type 3: Autosomal recessive disease caused by a complete defect of the von Willebrand factor, where the levels of the factor are not detected, and is manifested by a severe bleeding disorder [4, 9].

The incidence of von Willebrand disease is 1% in the population, the prevalence is 1 – 2 people per 10,000 population, while the severe course of the disease is observed in 125 patients per 1 million people [3, 10].

Diagnosis of BV is complex and often requires evaluation with bleeding assessment tools, family history, and in – depth laboratory testing. Bleeding symptoms do not always correspond to levels of von Willebrand factor or factor VIII activity, and may also vary depending on type, age and sex, which complicates both diagnosis and treatment [6].

The tendency to bleed is usually proportional to the degree of Willebrand factor deficiency, since Willebrand factor is a carrier of factor VIII in circulating blood [5]. Thus, in BV, the goal of treatment is to correct the double defect of hemostasis – impaired internal coagulation due to low levels of factor VIII.

Crohn's disease is a chronic inflammatory bowel disease, with predominant damage to the ileum and colon, any part of the gastrointestinal tract can also be affected. It is characterized by the formation of granulomas in the affected area of the intestine, later it captures the deep layers, affecting the entire thickness – transmural lesion. The disease is complicated by systemic organ damage [1, 2].

The combination of von Willebrand disease and Crohn's disease is rare in the literature, and since both diseases affect the hemostasis system in different directions, the management of patients should be carried out by a multidisciplinary team of doctors [1].

The purpose of the study: to describe a clinical case of the course of von Willebrand disease, Crohn's disease and congenital heart disease in a 17 – year – old teenager.

Anamnesis: a child from 8 years old is registered with a hematologist with a diagnosis of von Willebrand disease. 1 type. At the onset of the disease, heavy nasal bleeding was noted, followed by severe anemia (hemoglobin level up to 40 g/l). The diagnosis was first made in March 2014, based on medical history, typical clinical manifestations, characteristic laboratory data (activated partial prothrombin time (APTT) – 51 seconds, Willebrand factor – 1%, VIII and IX clotting factors – 100%). Replacement therapy was prescribed: 500 IU of coagulation factor VIII; 1200 IU von Willebrand factor in the prophylaxis regimen 2 times a week. At the age of 12 in 2018 an episode of severe iron deficiency anemia (hemoglobin 40 g/l) was detected, stopped by the administration of perenteral iron intravenously by drip. At 16 years old in 2022 again profuse nasal bleeding, decreased appetite, paraclinically – hemoglobin 43 g/l. He was hospitalized at the place of residence, received EMOLT replacement therapy (erythrocyte mass depleted of leukocytes and platelets) with a positive clinical and laboratory effect.

To determine the cause of anemic syndrome and to correct therapy for von Willebrand disease in august 2023, was sent to the oncohematological department of the Pediatric Center of National Center of Medicine named after M.E. Nikolaev.

Complaints upon admission: according to the mother, they noticed dark feces, dizziness, tremors of the hands. The child did not receive replacement therapy for the underlying disease due to complex venous access.

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On examination: moderate condition due to anemic and asthenic syndromes. Height – 161cm, weight – 55.4 kg. Respiratory rate – 20 per minute. Saturation – 99%. Heart rate – 77 per minute. BP – 120/65. Appetite is broken. Sleep is calm. The consciousness is clear. The physique is correct. The throat is not hyperemic. The mucous membranes of the mouth and pharynx are clean, pale in color. Nasal breathing is free. Osteoarticular system without features. Lymph nodes are not enlarged. The chest is of regular shape. Percussion – clear pulmonary sound is all fields. Vesicular breathing, no wheezing. Heart tones are clear, rhythmic. The abdomen is soft, painless. Liver and spleen were not enlarged. Urination is free, painless. No peripheral edema.

He was examined by otolaryngologist and pediatric surgeon to exclude acute surgical pathology.

Paraclinically:

Complete blood count from 22.09.2023: Hb-60g/l; RBC-2,4x10^{12}/l; PLT-250x10^{9}/l; WBC-16.8x10^{9}/l; lymphocytes – 12%; monocytes – 0.4x10^{9}/l; stab neutrophils-8%, eosinophils-3%, ESR to Panchenkov-20mm/h. Conclusion: decreased hemoglobin, erythrocytes, lymphocytosis, leukocytosis, neutrophil shift of the leukocyte formula, increased ESR.

Clotting time – 13min, Activated Partial Prothrombin Time – 51sec.

Biochemistry analysis of the blood from 22.11.2023: ALT-10U/L; AST-8.9U/L; C-reactive protein-114.9mg/L; total protein-65.8g/L; urea-4.00mmol/L, glucose-5.75mmol/L; creatinine-49.4mmol/L. Conclusion: creatinine, C-reactive protein increased.

Abdominal ultrasound from 26.09.2023: Liver not enlarged. Intrahepatic bile ducts are not dilated. Vascular pattern preserved. Hepatic veins are not dilated.

Echocardiography from 28.09.2023: Congenital heart disease. Perimembranous ventricular septal defect. Open oval window-0,24cm. Additional trabecula in the left ventricular cavity.

Computed tomography from 06.10.2023: Focal and infiltrative changes in the lung parenchyma were not detected.

Colonoscopy from 22.09.2023: The lumen of the cecum is narrowed by 1/3 due to edema of the bauginium shutter, the mucous membrane of the bauginium shutter is sharply edematous and hyperemic, with multiple ulcers up to 2.0cm, with fresh undercut edges, the crater is covered with fibrin. The mouth of the flap is spasmed, not passable. The rest of the examined areas of the colonic mucosa are undistinguished. Intestinal mucosa fragments were taken for histological examination. Microscopic description: foci of lymphoid infiltration with single lymphoid follicles were found in the material of the small intestine mucosa. Conclusion: Terminal ileitis. Crohn's disease. Active stage with ulcers and strictures.

Based in complaints, medical history, clinical symptoms and laboratory and instrumental data, the patient was given the main clinical diagnosis: von Willebrand disease. Type1. Concomitant diagnosis: Crohn's disease. Active stage with ulcers and strictures. Congenital heart disease.

Perimembranous ventricular septal defect. Open oval window. Additional trabecula in the left ventricular cavity. Anemia of mixed genesis, severe. Iron deficiency and vitamin V12 – deficiency anemia. Clinically, the combination of these diseases is manifested by a pronounced asthenic syndrome.

Treatment was prescribed: replacement therapy – clotting factor VIII – 500IU, Willebrand factor – 1200IU, intravenous drip pulse therapy with methylprednisolone succinate – 500mg in sodium chloride solution. Against the background of therapy, clinical and laboratory positive dynamics is noted. Additional examination in the federal center is recommended.

In January 2024 the patient was examined at the National Medical Center for Childrens Health of the Ministry of Health of the Russian Federation. Clinical diagnosis: Hereditary deficiency of factor VIII, von Willebrand disease. Type1. Crohn's disease 1b. Ileite and colitis (L3). Stenotic form (B20), no growth retardation (GO). Congenital heart disease. Ventricular septal defect – 0.27cm. Perimembranous ventricular septal defect. Open oval window – 0.24cm. Additional trabecula in the left ventricular cavity. Bilateral deafness. Iron deficiency anemia. Vitamin V12 – deficient anemia. High – grade myopia.

Therapy with Adalimumab (Humira) 40mg 1 every 2 weeks (every 2 weeks) was initiated continuously. As replacement therapy, the patient was recommended to continue replacement therapy: Coagulation factor VIII 500IU+Willebrand factor (Gemate) at a dose of 1200IU 3 times a week.

Over time, improvement – in the complete blood count of 26.01.2024: Hb – 124g/L; RBC – 5.35x10^{12}/L; PLT – 343x10^{9}/L; WBC – 6.21x10^{9}/L; LYMF – 1.46%; monocytes – 7.4x10^{9}/L; stab neutrophils – 3%; segmented neutrophils – 62%; eosinophils – 0.04%; determination of ESR by Panchenkov – 9mm/h.

Treatment follows clinical guidelines for two major diseases (Crohn's disease and hereditary deficiency of clotting factor VIII and von Willebrand disease). Combination therapy with Adalimumab and blood coagulation factor VIII+von Willebrand factor (Gemate) improved the patient's condition and normalized peripheral blood counts.

Conclusion. This clinical case of a child with von Willebrand disease is aggravated by the onset of Crohn's disease at the age of 16, which was clinically manifested by the development of severe hypochromic anemia against the background of ulcers of the large intestine. Against the background of therapy of Crohns disease with a genetically engineered biological drug and replacement therapy of Willebrand disease, the child has a persistent clinical and laboratory remission. The management of this child requires a multidisciplinary team: pediatrician, hematologist, gastroenterologist, cardiologist

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INTRADURAL LIPOMA IN A NEWBORN

Intradural lipoma (spinal cord lipoma) is a rare benign tumor in the spinal cord consisting of white fatty tissue. The article presents a clinical case of intradural lipoma in a newborn.

Keywords: newborn, intradural lipoma, spinal cord, tethered spinal cord syndrome, skin appendage, surgical treatment.

Introduction. Intradural lipoma is a rare benign tumor of white fatty tissue inside the spinal cord. This formation of dysembryogenetic genesis is located in the lumbar-sacral region, originating from the conus of the spinal cord. The clinical picture of intradural lipoma includes: rudimentary appendages (tail), hypertrichosis, subcutaneous formation in the lumbar region of a soft-elastic consistency. Intradural lipomas limit the mobility of the spinal cord, which is called tethered spinal cord syndrome [5;6].

Tethered spinal cord syndrome (TSCS) is a complex of pathological symptoms that is caused by tension of the spinal cord due to fixation of its caudal part [1]. Received widespread publicity in 1976, neurologist Hoffman published observations of typical symptoms in 31 patients. In children, the true incidence is unknown. According to some data, 0.8-1.4 cases per 1000 live births [9;11]. Risk factors include folic acid deficiency in the first trimester of pregnancy. TSCS is manifested by impaired sensitivity and motor function of the lower extremities, dysfunction of the pelvic organs, and skin symptoms in the lumbar region [8]. Surgical treatment consists of eliminating fixation factors: removal of pathological tissue (lipomas, dermal sinus), excision of the pathologically altered filament terminale. The earlier the surgery is performed, the lower the patient's risk of developing severe neurological deficits in the future.

Clinical case. Below is a clinical case of a newborn with a congenital malformation of the musculoskeletal system and tethered spinal cord syndrome at the State Institution of the Republic of Sakha (Yakutia) Republican Hospital No. 1 - National Center of Medicine named after M.E. Nikolaev, Perinatal Center.

The child was born to a 26-year-old woman from the first pregnancy, which occurred in the 1st trimester цшер grade 1 anemia (she took Maltofer), and in the 2nd trimester with shortness of breath. She was observed by a cardiologist with cardiac arrhythmias - frequent single extrasystole with episodes of bigeminy, trigeminy, quadrigeminy. Rare single supraventricular extrasystole, no treatment was carried out. Taking into account the Rh negative blood type - blood group AB(IV) Rh(-), Rh immunization was carried out at 30 weeks. Prenatal ultrasound diagnostics carried out within the screening period without any special features. The boy was born from the first spontaneous labor at 39.1 weeks in a cephalic presentation, after medical preparation of the birth canal with mifepristone. The condition of the child at birth is satisfactory, the Apgar score is 8/10 points. Physical parameters correspond to gestational age: birth weight 3300 g, body length 54 cm, head circumference 34 cm, chest circumference 33 cm. Among the features of the course of labor is a long anhydrous period of 12 hours, the waters are light. From the first hours of life, the child is breastfed. During the initial examination on the mother's abdomen in the delivery room, special attention was drawn to a soft tissue formation (dimensions 1.5x1.5 cm) in the sacral region, from the top of which a "tail" up to 2.0 cm long extends.

From the medical history of the child's mother it is known: she has been registered with the antenatal clinic since the early stages of pregnancy, and has regular visits. Denies bad habits, injuries, surgeries, blood transfusions. Gynecological diseases - ovarian cyst, cystectomy in 2022. Common diseases - chicken pox, rubella, acute respiratory infections, chronic bronchitis. The epidemiological history is calm. In a registered marriage, the husband is 25 years old, healthy, not burdened by heredity.

At the age of 3 days of life, a newborn boy was transferred from the neonatal department to the pathology department of newborns and premature infants for further examination and treatment with a diagnosis of: Q 79.9 Congenital malfor-

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