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A CLINICAL CASE OF WISKOTT-ALDRICH SYNDROME

DOI 10.25789/YMJ.2020.70.31

УДК616.8-008.6

Wiskott-Aldrich syndrome is a disease, characterized by combined insufficiency of both humoral and cellular immunity, it is inherited by X-chromosome recessive linkage and is expressed by the following triad of signs: recurring chronic microbial inflammations, hemorrhagic syndrome, and eczema [3]. The syndrome was first described by A. Wiskott in 1937, he described a case of three boys from the same family suffering from thrombocytopenia combined with severe eczema and secondary infections, while their four sisters did not show any of these symptoms. The prevalence of Wiskott-Aldrich syndrome is 4 : 1 000 000. It mostly affects boys. Molecular defect results in absence of WASP protein (Wiskott-Aldrich syndrome protein), coded by WASP gene, it is localized in the short arm of X-chromosome [1, 4]. The objective of the article is to describe clinical and laboratory characteristics of Wiskott-Aldrich syndrome in a 2-month-infant. We represent a clinical case of the Russian infant having triad of signs characteristic to Wiskott-Aldrich syndrome. It is the first case in the department of oncohaematology of the Pediatric center, Republican hospital №1, National health center for medical examination.

Keywords: immunodeficiency, inheritance, survey, immunology, genetics.

Wiskott-Aldrich syndrome is a disease, characterized by combined insufficiency of both humoral and cellular immunity, it is inherited by X-chromosome recessive linkage and is expressed by the following triad of signs: recurring chronic microbial inflammations, hemorrhagic syndrome, and eczema [3]. The syndrome was first described by A. Wiskott in 1937, he described a case of three boys from the same family suffering from thrombocytopenia combined with severe eczema and secondary infections, while their four sisters did not show any of these symptoms. The prevalence of Wiskott-Aldrich syndrome is 4: 1 000 000. It mostly affects boys. Molecular defect results in absence of WASP protein (Wiskott-Aldrich syndrome protein), coded by WASP gene, it is localized in the short arm of X-chromosome [1, 4].

The **objective** is to describe the clinical and laboratory characteristics of Wiskott-Aldrich syndrome in a 2-month infant.

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We describe a clinical case of Wiskott-Aldrich syndrome in a 2-month Russian infant experiencing a triad of signs characteristic to such inherited disease as Wiskott-Aldrich syndrome. The boy had been hospitalized to the department of oncohaemotology from September to November of 2019.

On the 30th of November 2019 a two-month male infant was hospitalized to the department of oncohaemotology of the Pediatric center, Republican hospital #1, National health center for medical examination. He was referred from the regional hospital with the complaints of periodical scarlet streak of blood in stool, conjunctival hemorrhage, decreased level of platelets in common blood count. The entrance diagnosis was vertically transmitted infection of the viral or bacterial origin, vertically transmitted secondary thrombocytopenia, unconfirmed immunodeficiency, and anal abscess.

The anamnesis showed that the child was born from the first pregnancy, the pregnancy ran smoothly. The mother gave a natural childbirth at the 39th week of pregnancy. At the moment of hospitalization the infant was breastfed. After the childbirth hemorrhagic discharge from the anus and subconjuctival hemorrhage of the left eye were noticed. The complete blood count showed decreased level of platelets.

On admission the infant was examined by a haemotologist and a pediatrician. The condition of the infant was assessed as grave and poor. The skin surface was swarthy and moderately moist. The mucous membranes of the oral cavity were pink and moist. The pharynx was not hyperemic. The tonsils were not enlarged, no coating was noticed. Peripheral lymph nodes were not enlarged. The nasal breathing was not complicated. No cough and breathlessness were present. The auscultation showed vesicular breathing with no rales. The heart sounds were rhythmic and loud. On palpation the abdomen was soft and painless. The stool was regular and solid. The liver was enlarged (1 cm below the costal margin). The spleen was not enlarged. No dysuria, the urine did not change. No meningeal and focal signs were noticed. The stool was with scarlet streak of blood.

The blood test for clotting time detection and complete blood count were administered. The blood test showed that the clotting time was within the normal rate: the Duke method of clotting time: 1 minute; blood coagulation time according to Sukharev: 3,20 min.

The complete blood count of the blood corpuscles revealed reticulocytosis and thrombocytopenia. The reticulocytes were 35.0. Thrombocytes were 36.0% (normally it is 100-420). Thrombocrit value was 0.04% (normally it is 0.15% - 0.4%). The results showed expressed anemia and activation of hemopoiesis.

The biochemical analysis of the blood test revealed high level of the total bilirubin and direct bilirubin.

The PCR test for infection did not reveal mycoplasma, ureaplasma and cytomegalovirus infections.

The immunoglobulin results were IgM – 0.01 gr/l; IgG – 6.9 gr/l, IgA – 0.00 gr/l; IgE total – 0.00 gr/l. Total absence of M immunoglobulin, A and E immunoglobulins, and low level of G immunoglobulin were reported. These results indicated a possible initial immunodeficiency case.

Immunogram shows CD+46%; CD4+43%; CD8+3%; CD19+31%; CD-HLA-DR+2%; CD 25+8%; CIC (circulating immune complexes) 14%. The immunogram revealed low level of T-supressors, and B-cells.

Fecal occult blood test was positive.

No HIV for 11.01.2019.

The child underwent several instrumental procedures.

The colour Doppler ultrasound imaging revealed oval window (0.26cm), enlarged right atrium cavity (1.83cm), right ventricle (1.0cm), tricuspid valve regurgitation, ectopic attachment of mitral valve chords, and additional left ventricular trabeculae.

The colonoscopy revealed total hemorrhagic colitis. Distally the dorsal part was not accessible because of the mucous membranes hemorrhage when they came into contact with the apparatus. The walls of large intestines were elastic and air could stretch the walls. The lumen of sigmoid, ascending, transverse and descending colons seemed normal, the folds were of the normal height, there was greenish substance in the curves of the colon. The mucous membrane of the transverse and descending colons was unevenly hyperemic with the signs of hemorrhagic erosions. A great number of erosions with size from 0.25 to 0.5 cm was scattered, the vesicular pattern was clear. Mucous membrane of the sigmoid colon was hyperemic with hemorrhagic erosions, the vesicular pattern was unclear. The rectal lumen was normal, the mucosa was unclear with scattered hemorrhagic erosions (0.2cm). Perianal examination revealed a scar of paraproctitis.

Esophagogastroscopy revealed no abnormalities.

According to the results of the investigation further consultation with gastroenterologist and allergist-immunologist was recommended.

The consultations of the specialists revealed a case of early childhood death in the maternal anamnesis. The mother told that her own brother had died at early age. For the following 20 years only girls were born in this family. The immunogram determined absence of M immunoglobulin, A and E immunoglobulins, low level of G immunoglobulin, low level of T-suppressors, and B-cells. There was marked decrease of platelet count in a peripheral blood and platelets count by Fonio method, thus revealing protein molecule destruction. These molecules participate in the process of platelet formation. The results showed the decrease of the quantity of platelets and quality of the cells, which is characteristic to the initial immunodeficiency, i.e. Wiskott-Aldrich syndrome.

The clinical diagnosis, based on the results of the investigations, examination and family history taking, was: initial immunodeficiency, Wiskott-Aldrich syndrome, infantile atopic dermatitis in the restricted form.

Gastroenteric visual and instrumental examinations revealed hemorrhagic intestinal erosion. The consultation of the specialists could help specify the diagnosis and it was decided to refer the biological material of the whole blood with further molecular genetic test (WaSP) to the National medical research center of childhood hematology, oncology and immunology. The PCR-diagnosis of the genetic locus was positive [1].

The final diagnosis was Wiskott-Aldrich syndrome, initial immunodeficiency, immune thrombocytopenia, infantile atopic dermatitis, in the restricted form with mild severity.

Concomitant diseases were non-infectious gastroenteritis, unconfirmed colitis, erosive hemorrhagic colitis, postsurgical condition after operated abscess in perianal area, normochromal anemia of mixed genesis.

During the period of hospitalization at the department of oncohematology of the Pediatric center of the National health center the patient was administered: the ward nursing by the mother, special diet #15, breastfeeding, pankreatin ¼ tablets 3 times a day, fenistil 2 drops 2 times a day lasting for 5 days, and elidel cream externally.

The patient was referred to the immunological department of the National medical research center of childhood hematology, oncology and immunology for further examination, a substitutive therapy was administered [2, 4, 5]. At the moment the patient is treated with immunovenin 0.1-0.4 gr/kg each month.

The following scheme of inpatient examination was recommended:

1. Regular check-up at the following specialists: a pediatrician, an immunologist, and a hematologist.

2. Laboratory investigations: complete blood count (with obligatory leucocyte count) once every 2-3 months. Biochemical blood test with hepatic enzymes activity detection, protein C-reactivity – every 6 months, urine analysis every 6 months, and in cases of intercurrent diseases.

3. Instrumental investigations: electrocardiogram – once a year, ultrasonic imaging of the abdominal cavity – once a year, X-Ray examination of the chest – once a year.

4. Consultations: immunologist every 3 months during the first year of examination, then every 6 months; surgeon – once a year, oculist – every 6 months; dentist – once a year, and otolaryngologist – once a year.

5. Vaccinations are contraindicated.

Conclusion. We have described a clinical case of Wiskott-Aldrich syndrome in a 2-month infant. Microbial inflammation in the form of paraproctitis, hemorrhagic syndrome in the form of erosive hemorrhagic colitis and eczema, which was later diagnosed as atopic dermatitis, was revealed clinically [3]. Thus we have described a classic triad of Wiskott-Aldrich syndrome. A detailed family history taking became a key moment in the diagnosis of the congenital disease. The anamnesis revealed high mortality rate of the male infants at early childhood, which possibly could be connected with microbial inflammation associated with initial immune deficiency. The diagnosis of the congenital disease is undoubtedly due to molecular-genetic investigations [1]. A due time diagnosis, substitutive therapy and competent clinical examination can predict and prolong the life for Wiskott-Aldrich syndrome patients [2, 4, 5].

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