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A CLINICAL CASE OF BRUTON AGAMMAGLOBULINEMIA IN A CHILD OF THE REPUBLIC SAKHA (YAKUTIA)

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Bruton's disease is a genetic disease associated with impaired synthesis of serum immunoglobulins and B cells. The disease refers to primary immunodeficiency.

This article is devoted to the description of the clinical course of Bruton's disease in a child. The child has a history of 6 episodes of pneumonia. Primary immunodeficiency is suspected in the Pediatric center. Then the child is sent to the leading scientific institution of pediatric Oncology and immunology and the diagnosis is clarified. Clinical diagnosis: Primary immunodeficiency. Bruton's Disease. All patients with Bruton's disease require lifelong replacement therapy with intravenous immunoglobulins. Early diagnosis of primary immunodeficiency in children will avoid the risk of life-threatening conditions. Primary care pediatricians should be wary of the disease.

Keywords: immunodeficiency, immunoglobulins, patient, hereditary disease.

Introduction. Bruton agammaglobulinemia is a hereditary disease, associated with synthesis of serum immunoglobulin and B-cells. The disease is referred to the primary immunodeficiency diseases. It was first described by Dr. Ogden Bruton, an American pediatrician, in 1952. He reported of an 8-year old boy, suffering from different infectious diseases. The boy was 14 times infected by pneumonia from the age of 4, besides he had otitis, sinusitis, sepsis and meningitis. In the blood analysis no antibodies were found out.

A molecular mechanism was first performed in 1993, when two groups of the scientists independently demonstrated that X-linked agammaglobulinemia resulted from mutation at non-receptor tyrosine kinase gene, which was later named as Bruton's tyrosine kinase [1,2].

The disease is manifested by frequent viral infectious diseases complicated by bacterial ones. Genetic defect is present on the long arm of the X-chromosome resulting in mutation of cytoplasmic protein kinase gene. Thymus gland size and structure are within the norm, the number and function of T-lymphocytes in peripheral

blood are not changed. No germinal centers and plasmatic cells are present in lymph nodes. Low concentration of B-cells and immunoglobulins of all isotypes are defined [3,4].

Bruton agammaglobulinemia is transmitted by X-linked recessive inheritance; the disease is common only for males (with XY sex-determination system). Females do not develop Bruton agammaglobulinemia, even if they are heterozygous a recessive gene of an X-chromosome is compensated by normal gene homologous X-chromosome. The disease is common for males with 1:25000 of prevalence.

Objective: A clinical case of a boy with Bruton agammaglobulinemia is described in the article.

Materials and methods: We have analysed a case report of the patient made by the Consultative polyclinic, the Pediatric Center of Republican hospital #1 under National Center of medicine. The boy has been examined there for 2 years.

Clinical description of Bruton agammaglobulinemia. Anamnesis: A second pregnancy boy was born on the 40 week of gestation by operative delivery. The boy was breast-fed until he was 1 year and two months. He lives in a village. His psychomotor development was according to his age. From the very first days after delivery he suffered from the infection of the upper respiratory system once a month, by the age of 3 he developed acute pneumonia 6 times, he had chronic otitis and sinusitis. When he was 4 he developed pains in the joints, the child could not walk. In November 2018 the child was referred to the cardiorthromatology department of the Pediatric center of the Republican hospital #1, National health center.

On admission he complained of the pains in joints, a stuffy nose and purulent nasal discharge.

The condition was estimated as grave. Skin surface was moderately moist and swarthy. Mucous membrane of the oral cavity was rose and moist. The pharynx was not hyperemic. The tonsils were not enlarged, without coating. Nasal breathing was complicated, and there was nasal discharge of purulent origin. On auscultation the respiration was vesicular, no crackling sounds were present. There was no cough and dyspnea. Heart sounds were loud and rhythmic. The abdomen showed no pain on palpation. Stool was regular and formed. The liver was on the costal margin and painless. The spleen was impalpable. Urine was unchanged, no dysuria. No signs of meningeal and focal disorder were noticed.

Laboratory findings: tests for rheumatoid disorders were within the norm: rheumatoid factor – 10 mUn/ml, C-reactive protein – 2.1 mg/ml, antistreptolysin O 120 Un/l. Immunogram data reveal impaired humoral immunity. The immunogram shows absence of immunoglobulin A, and reduced level of immunoglobulin M and G.

On admission (12.11.2018) total blood analysis showed: hemoglobin (120 g/l); erythrocytes 4.77×10^{12} /l, leucocytes 10.76×10^9 /l, sedimentation rate 15 mm/hr.

In 13.09.2019 the electrocardiogram revealed a sinus rhythm. The electrical axis shows vertical position. The ultrasound investigation of the organs of the abdominal cavity revealed no abnormalities.

In 13.09.2019 the boy was examined by an otolaryngologist. The examination revealed chronic otitis of both ears, dry anterior rhinitis.

The child is hereditary complicated by his mother side. The patient's mother said that her brother died of acute pneumonia at the age of 5.

As a result of examination at the con-

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Indices of immune status, 12.11.2018

Index	Result	Reference interval
IgA total	0.00mg/ml	(0.7-3.00)
IgM total	0.07 mg/ml	(0.6-2.00)
IgG total	4.9 mg/ml	(8.00-16.00)
Complement C4	29.16 mg/dl	(9.00-36.00)
Complement C3	113.80 mg/dl	(75.00-135.00)
CD3+	94.00%	(62.00-69.00)
CD16+CD56+	2.17%	
CD4CD8	4.00%	
CD4+	63.00%	(30.00-40.00)
CD8+	29.00%	(25.00-32.00)
CD19+	2.00%	
CD3+HLA-DR+	6.00%	(8.00-12.00)
CD25+	6.00%	
IgE total	1.5 IU/ml	(0.00-100.0)
Circulating immune complex	35 IU	

sultative polyclinic of the Republican hospital #1, National health center, the boy was diagnosed with primary immunodeficiency, chronic otitis of the both ears, dry anterior rhinitis. In January 2019, the child was referred to the department of immunology at the National research medical center of children hematology, oncology and immunology. After profound examination he was diagnosed with primary immunodeficiency, Bruton agammaglobulinemia, chronic bilateral otitis, and dry anterior rhinitis.

There were the following recommendations:

1. Regular follow-ups at a local immunologist, pediatrician, and otolaryngologist.
2. Life-long replacement therapy with immunoglobulin – Ig Vena.
3. In a case of infectious process not less than 2-week of intravenous antibiotics of wide spectrum (like cephalosporins of the 3rd-4th generation, macrolids, and aminoglycosyds) therapy should be recommended.
4. Total blood analysis with leukogram, biochemical blood analysis and immunogram once in 3 months.
5. Preventive inoculations are not recommended as they are ineffective in that

case. Mantoux test (Diaskin test) should be annual.

6. In a case of next pregnancy the mother is recommended to carry out prenatal genetic screening between 9 and 10 weeks.

7. Molecular-genetic investigation of inheritance through the female line, and immunological examination of (IgA, IgG, IgM) of males through the female line.

8. Taking into account that primary immunodeficiency is genetically determined disease with inevitable breakdown of the immune system functions and with high risk of life-threatening bacterial infections, autoimmune processes; it requires life-long replacing therapy with IV-introduced immunoglobulins; replacement therapy refuse results in life-threatening conditions with infectious and autoimmune complications. Thus, for the reasons given that the child has a severe breakdown with stable disturbance of the functions of the body resulting in limited life-style and necessity of social support (including rehabilitation), in accordance with the Government order of the Russian Federation 20.02.2006 #95 "On order and recognition of the disability of the individual" it is recommended to refer the patient to the local medical

and social disability examination. In accordance with the Government order of the Russian Federation #339 29.03.2018 "On introduction of changes in the Rules of disability acknowledgement" disability is acknowledged by the age of 18 for the patients with primary immunodeficiency.

Since February 2019 the child is regularly examined by the immunologist, the otolaryngologist, and the pediatrician of the Consultative polyclinic of the Republican hospital #1, National health center.

From February 2019 to September 2019 the patient took IV immunoglobulin (Ig Vena 10 gr) 6 times. The patient is examined monthly: he is taken blood analysis, biochemical blood examination, immunogram, and immunoglobulin of peripheral blood. For the time mentioned the child suffered from acute respiratory viral infection once and there were no recurrent cases of otitis. The child is considered as disabled.

Thus, IV immunoglobulin introduction is necessary for the patients with Bruton agammaglobulinemia to prevent life-threatening complications.

Conclusions:

1. All the patients with Bruton agammaglobulinemia should have life-long IV-immunoglobulin therapy.
2. Early diagnosis of primary immunodeficiency among children can prevent life-threatening conditions afterwards.

References

1. Галактионов В.Г. Иммунология. Изд-во МГУ, 1998;480. [Galaktionov V. G. Immunology. Izd-vo MGU, 1998;480. (In Russ.).]
2. Ковальчук Л.В. Клиническая иммунология и аллергология с основами общей иммунологии. ГЭОТАР-Медиа, 2011;640. [Kovalchuk L. V. Clinical immunology and allergology with the basics of general immunology. GEOTAR-Media, 2011;640. (In Russ.).]
3. Ройт А., Бростофф Дж., Мейл Д. Иммунология. Мир, 2000;592. [Roit A., Brostoff J., Mail D. Immunology. Mir, 2000;592. (In Russ.).]
4. Ярилин А.А. Иммунология. ГЭОТАР-Медиа, 2013;321. [Yarilin A. A. Immunology. GEOTAR-Media, 2011;321. (In Russ.).]