CLINICAL CASE

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A CLINICAL FOLLOW-UP OF A 5-YEAR OLD CHILD WITH SOPH-SYNDROME

A rare case of genetically caused SOPH-syndrome is described in a 5-year old Yakut child. Characteristic features of the follow-up, diagnosis and monitoring over the patient are noted here.

Keywords: SOPH-syndrome, short stature, Pelger-Huet anomaly of leukocytes, atrophy of the optic nerves, children, Yakutia.

Introduction. Rare autosomal recessive, X-linked recessive and autosomal dominant congenital pathology cases are accumulated in indigenous people of the Republic of Sakha (Yakutia), namely in the Yakuts [1,2,5]. N.R. Maksimova, MD, described new cases of genetic disorder in the children population of the Republic of Sakha (Yakutia), namely SOPH-syndrome. The children with such syndrome are born with normal body weight and height, but by the age of 6-7 months optic nerve atrophy and reduced weight and height, as well as the reduction of immunocompetent cells subpopulations, which result in immunodeficiency, are noticed [3,4]. Analysis of catamnesis of the SOPH-syndrome patients and their dynamic follow-up will allow introducing clinical recommendations for monitoring such patients.

A clinical case: A family applied for medical assistance to the Perinatal Center of the Republican hospital #1 (National health center of Yakutsk) in December 2017 complaining of frequent respiratory viral infections, visual impairment, retarded physical and speech developments.

The life history of the patient shows that the girl was born in 2016 in the Yakut family from the second pregnancy. The pregnancy was characterized by isthmic cervical insufficiency with threat of pregnancy loss. There was cephalic presentation in time for labor. The birth weight was 3450g, height 53cm. The Apgar scores were 8/9. There was loud cry, and the neonate was breast fed immediately after delivery and laid on the mother. The girl was breastfed until 1 year and 6 months. Psychomotor development: she holds up her head since 1month, rolls from 4 months, speaks from 13 months and walks from 16 months. She was infected with acute viral respiratory infections, pneumonias, laryngotracheitis, and bronchitis. There were no traumas.

The case history shows reduction of the markers of weight and height, frequent cases of acute viral respiratory infections from the age of 1, the girl was infected with acute pneumonia two times within one year period.

On examination the disease severity was classified as moderate. The physical development is retarded, as well as her speech and psychological development. The girl is malnourished. Cutaneous covering and visible mucous membranes are pale. The skin elasticity is between the normal level. Subcutaneous adipose tissue is mildly expressed. Muscular elasticity is decreased. The pharyngeal tonsils and the soft palate are pink. The chest is of a correct shape, it is not deformed. Respiration is vesicular without wheeze. The heart sounds are rhythmic and clear. The abdomen is soft and painless. The liver and the spleen are within the norm.

According to the test results: The full blood count, taken in 11.01.2018, showed hypochromic anemia. Lymphopenia. Leukopenia. Pelger-Huet anomaly of leukocytes.

Biochemical blood test results, taken in 11.01.2018, showed decrease in the globulin fraction. The immunogram, taken in 22.01.2018, showed IgA 0.1 mg/mL (0.21-2.82g/L), IgM 0.49 mg/mL (0.47-2.40 mg/mL), IgG 1.7 mg/mL (4.83-12.26mg/mL), CD3+81.0% (62-69%), CD4+46.0% (28-76%), CD8+32.0% (4-45%), CD3+CD8+ 1.44% (30-40%), CD19+12,0% (reference ranges 21-28%), CD25+ 7.0% (reference ranges 7-10%), CD3+HLA-DR+ 2.0%, CD16+CD56+ 6.0%. The clinical decision: decrease of contents of A immunoglobulin, G immunoglobulin and cytotoxic lymphocytes CD 3+CD8+.

The electrocardiogram from 12.01.2018 revealed sinus arrhythmia, expressed by bradycardia. Heart rate was 112-91 beats per minute. The electrical axis of the heart was normal. The intraventricular conduction was disturbed. The ventricular repolarization was also disturbed.

The color Doppler ultrasound from 18.02.2020 showed an open oval window of 0.23-0.26 cm. Ectopic tying of the chords of the mitral valve was with minimum regurgitation. A left ventricular trabecula is revealed. The cavities of the heart are not enlarged.

The X-ray exam (18.01.2018) showed the bone age of 2-2.5 years.

The examination by the ophthalmologist (17.01.2018) revealed partial atrophy of the optic nerves.

The consultation with the geneticist (18.02.2018) revealed genealogical anamnesis, which showed no complications caused by the monogenic disorder, the parents are phenotypically healthy.

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Phenotype: a real height is 76cm, (expected height is 86.8cm).

A real weight at the age of 1 year and 10 months is 9 kg instead of 12 kg normally. The BMI is -14.587. The gait is not affected. The constitution is proportional. Nanism. Insufficiency of the body weight is expressed, the skin is clean, pale and elastic. Skin turgor is decreased, the skin is soft and cutis laxa type, and there is a hyperpigmented lesion on the feet. The facial features are small and unexpressed, mild exophthalmos and high pitch voice are noticed. The auricles are not affected and localized typically. The left side of the chest is protruded. The arms and the legs are symmetrically short, and there is micromelia of the hands and feet. The abdomen is slightly enlarged. The liver and the spleen are not affected. The external genitalia are of the female type.

The geneticist administered DNA test to specify diagnosis. A homozygous carrier for the 5741G>A mutation in NBAS gene, causing SOPH syndrome with autosomal recessive type of inheritance, was revealed.

Clinical diagnosis: SOPH-syndrome with nanism, Pelger-Huet anomaly of leukocytes with primary immunodeficiency (Q87.1) is diagnosed. There is a partial congenital atrophy of the optic nerves of the both eyes. Minor anomaly of the heart is noticed with an open oval window of 0.23-0.26cm. There is an ectopic tying of the chords of the mitral valve with minimum regurgitation. Left ventricular trabecula is revealed.

Recommendations: Regular check-ups at the local pediatrician, cardiologist, allergologist and immunologist are recommended to follow up a proband and a family at the medical genetic consultation center. 50 drops of Elkar 30% 3 times a day lasting for a month is administered, the course of treatment is recommended to repeat in 6 months. Likopid 1mg is recommended to be taken once a day lasting for 10 days. Polyvitamins should be taken for a month three times within one year period. Electrocardiogram should be controlled 2 times a year. Echocardiogram should be controlled in 2-3 years. The diet rich in proteins and vitamins is recommended. Sanatorium-and-spa treatment and together with general health improving procedures are recommended.

In 2018 the child was considered as a disabled.

The following two years the child felt well and suffered respiratory and viral infections only two times.

Table 1

Dynamics of the physical development in the SOPH-syndrome child

Date	Age	Weight of the SOPH-syndrome child	Normal weight	Height of the SOPH-syndrome child	Normal height
2018	1year,10 months	9	12	76	86.8
2020	3 years	12	14.85	87.0	97.27
2021	5 years	15.5	18.48	95.6	109.0

Table 2

The immunogram dynamics in the SOPH-syndrome child

Дата	IgA mg/mL	IgA mg/mL	IgA mg/mL	CD3+%	CD4+%	CD8+%	CD4+CD8+%	CD19+%	CD25+%	CD3+HLA-DR+%
11.12.2018	0.1	0.49	1.7	81	46	32	1.43	11.0	7.0	2.0
1.02.2020	0.1	0.52	1.8	86	46	34	1.44	12.0	7.5	2.1
08.02.2021	0.1	0.55	1.85	82	48	36	1.56	13.0	7.7	-

The dynamics of the physical development is represented in the table.

In 2020 the following features were revealed as real weight 12 kg (normally it should be 15 kg); real height 90.7 cm (normally it should be 96.8cm). In 2021 real weight of the patient was 15.5 kg (normally it should be 18.48kg), real height 96.6 cm (normally it should be 109.0).

For the period of 4-year follow-up the patient showed hypochromic anemia, lymphopenia and leukopenia according to the results of the full blood counts, Pelger-Huet anomaly of the leucocytes.

The table 2 shows the dynamics of sharp decrease in immunoglobulin A, immunoglobulin G, decrease in the number of cytotoxic lymphocytes CD3+CD8+.

The patient feels well at the moment. In 2021 she was vaccinated with Grippol, she did not suffer from the acute respiratory infectious diseases during a year.

Conclusion: The clinical manifestations of SOPH-syndrome, a rare congenital disease, are short stature of the child, atrophy of the optic nerves, Pelger-Huet anomaly of leucocytes. Besides these manifestations primary immunodeficiency was revealed. The dynamic follow-up of the children with rare congenital disorders in the Republic of Sakha (Yakutia) allows developing certain clinical recommendations.

Reference

1. Вербицкая Л.И., Григорьева А.Н., Павлова Т.Ю. [и др.] Генетические исследования населения Якутии. Якутск, 2014;336. [Verbitskaya L.I., Grigorieva A.N., Pavlova T.Yu. [et al] Genetic studies of the population of Yakutia. Yakutsk, 2014;336. (In Russ.).]

2.Ноговицына А.Н., Сухомясова А.Л., Максимова Н.Р. [и др.] Генетическое тестирование на наследственные болезни с аутосомно-рецессивным типом наследования в Республике Саха (Якутия). *Якутский медицинский журнал*. 2014:2(46): 40-44. [Nogovitsyna A.N., Sukhomyasova A.L., Maksimova N.R. [et al] Genetic testing for hereditary diseases with an autosomal recessive type of inheritance in the Republic of Sakha (Yakutia). *Yakut medical journal*. 2014: 2(46): 40-44. (In Russ.).]

3. Гуринова Е.Е., Максимова Н.Р., Сухомясова А.Л. Клиническое описание редкого аутосомно-рецессивного синдрома у якутских детей. *Якутский медицинский журнал*. 2014: 2(46): 12-14. [Gurinova E.E., Maksimova N.R., Sukhomyasova A.L. Clinical description of a rare autosomal recessive syndrome in Yakut children. *Yakut Medical Journal*. 2014: 2(46):12-14. (In Russ.).]

4. Максимова Н.Р., Ноговицына А.Н., Куртанов Х.А. [и др.] Популяционная частота и возраст мутации g5741 → a в гене nbas, являющейся причиной SOPH-синдрома в Республике Саха (Якутия). *Генетика*. 2016:52(10): 1194-1201. [Maksimova N.R., Nogovitsyna A.N., Kurtanov H.A. [et al] Population frequency and age of mutation g5741 = a in the gene n bass, which is the cause of SOPH syndrome in the Republic of Sakha (Yakutia). *Genetics*. 2016: 52(10): 1194-1201. (In Russ.).]

5. Пузырев В.П., Максимова Н.Р. Наследственные болезни у якутов. *Генетика*. 2008: 44(10): 1317-1324. [Puzyrev V.P., Maksimova N.R. Hereditary diseases in Yakuts. *Genetics*. 2008: 44(10): 1317-1324. (In Russ.).]