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CLINICAL AND REGIONAL FEATURES OF THE COURSE OF LOWE SYNDROME IN CHILDREN IN UZBEKISTAN

[1]Raxmanova L.K, [2]Madjidova N.M, [1]Karimova U.N, [1]Israilova N.A.

[1]" Tashkent Medical Academy", 2"Andijan State Medical Institute" of the Ministry of Health of the Republic of Uzbekistan, Tashkent

ANNOTATION

In order to study the clinical and regional features of the course of Lowe syndrome in children in the conditions of the Ferghana Valley of Uzbekistan, the data of 250 case histories of children aged 1 to 18 years with a diagnosis of chronic kidney disease (chronic glomerulonephritis-100, chronic pyelonephritis-150) for 2017-2022, who received in patient treatment in the children's multidisciplinary clinic of ASMI, were analyzed. Of these, one patient with a diagnosis of "Lowe syndrome" was in our observation. It was revealed that in the conditions of the Fergana Valley of Uzbekistan, the occurrence and development of Lowe syndrome in children is of a regional nature, which is observed with the early manifestation of malformations, clinical and laboratory changes and progression in stage II-III of chronic kidney disease in patients born from closely related marriages and having pathology at an early stage of pregnancy in the mother. An unfavorable prognosis of Lowe syndrome (oculo-cerebro-renal) with X-linked recessive type of inheritance causes combined damage to the eyes, nervous system and kidneys. Proteinuria in the patient causes proximal tubulopathy at the beginning, and then glomerulopathy and with complete nephrotic syndrome, progressing in chronic kidney disease already in childhood. The basics of early prevention of the development of Lowe syndrome in children in the conditions of the Fergana Valley of Uzbekistan are: inclusion of children born from closely related marriages in the risk group; identification and treatment of pathologies of early pregnancy (7-8 weeks) in the mother; early detection of the stigma of dysembriogenesis in children and consultation of a group of specialists (nephrologist, ophthalmologist, neurologist).

Key words: Lowe syndrome, children, clinic, region, course

INTRODUCTION

It is known that hereditary diseases of the organs of the urinary system often develop gradually, for the first time getting an appointment with a pediatric nephrologist at the stage of developed symptoms of kidney failure. Although the presence of stigmas of connective tissue dysembriogenesis, or small developmental abnormalities, is considered a marker of hereditary and congenital kidney diseases, however, doctors do not always pay serious attention to this.

To date, everyone knows that in 1952 C.U.Lowe, M.Terry and E.A. McLachlan described a congenital syndrome occurring with neurological, renal and ocular abnormalities [1]. The terminology of this syndrome is named by scientists: oculo-cerebro-renal syndrome, Lowe syndrome, Lowe-Terry -McLachlan, Lowe-Bickel syndrome, OSRL, OMIM 309000 [1-4]. The OSRL-1 gene mapped on the long arm of the X chromosome (Xq 24 q 26) contains 24 exons occupying 58 sq. Due to mutation of the OSRL-1 gene encoding 105 kD Golgi protein with

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fofatidinylositol-4,5-biophosphate-5-phosphatase activity, there is a deficiency of fofatidinylositol-4,5-biophosphate-5-phosphatase in the Golgi apparatus [3,4,5].

Clinical symptoms of Lowe syndrome in newborns and infants are caused by renal, neurological, ocular congenital anomalies. Early and older children are characterized by a sharp lag in physical development, strabismus, nystagmus, exophthalmia or microphthalmia, cataracts and / or glaucoma, rickety deformities of the bones of the skeleton, generalized muscular hypotension, hypotrophy or obesity, shortness of breath, attacks of hyperthermia associated with metabolic acidosis [1-5,6,13,14]. Blindness and progression of renal disorders occur early in sick children.

The cause of various neurological disorders, mental retardation, seizures, muscle hypotension in Lowe syndrome is considered to be amino acid deficiency, cystic brain damage, demyelination of nerve fibers, gliosis, violation of the stratification of the cortex and white matter [7,8]. In 90-100% of cases of the disease, bilateral or unilateral congenital cataract or glaucoma is diagnosed [1-5,9]. During external examination, attention is paid to strabismus, blue sclera and pupil constriction, micro or exophthalmos and horizontal nystagmus, which often lead to blindness.

Congenital pathology on the part of the kidneys in Lowe syndrome consists in the fact that as a result of a generalized defect in the proximal tubules of glucose, amino acids, phosphates, bicarbonates transport systems, hyperaminoaciduria, glucosuria with normoglycemia calciuria, phosphaturia, hyperchloremic, metabolic acidosis with hypokalemia type II, which is characteristic of the symptom complex of renal Fanconi syndrome [1-5,9,10,11]. Proteinuria is noted from infancy, initially tubular, in the future, due to the defeat of the glomeruli, proteinuria increases, leading to the development of nephrotic syndrome [3-5, 10-12]. Microscopic examination of the kidneys reveals the development of tubular-interstitial fibrosis, tubulonecrosis, edema of the mitochondria of the tubules, atrophy of the tubules, thickening and splitting of the basement membrane, rupture of cysts and glomerulosclerosis. Renal proximal tubular acidosis of type II in patients proceeds with variable urine PH, therefore, with calciuria, nephrocalcinosis is not formed [2,3].

Treatment of children with Lowe syndrome consists of a restriction in the diet of table salt and galactose without restriction of fluid intake. Metabolic acidosis is corrected according to the bicarbonates / citrates scheme, calcium preparations, phosphate buffer, vitamin D are prescribed under the control of blood and urine analysis [2,3, 9,10, 11].

The prognosis of Lowe syndrome is unfavorable. The risk of death in children who do not receive therapy due to acidemic coma with edema of the brain, lungs, infectious complications and progression to terminal uremia [1-11,13,14].

The purpose of the study: to study the clinical and regional features of the course of Lowe syndrome in children.

Clinical observation

We present a clinical observation of a boy patient with Lowe syndrome. Based on the results of the genealogical method, X-linked recessive inheritance was established (Fig.1).

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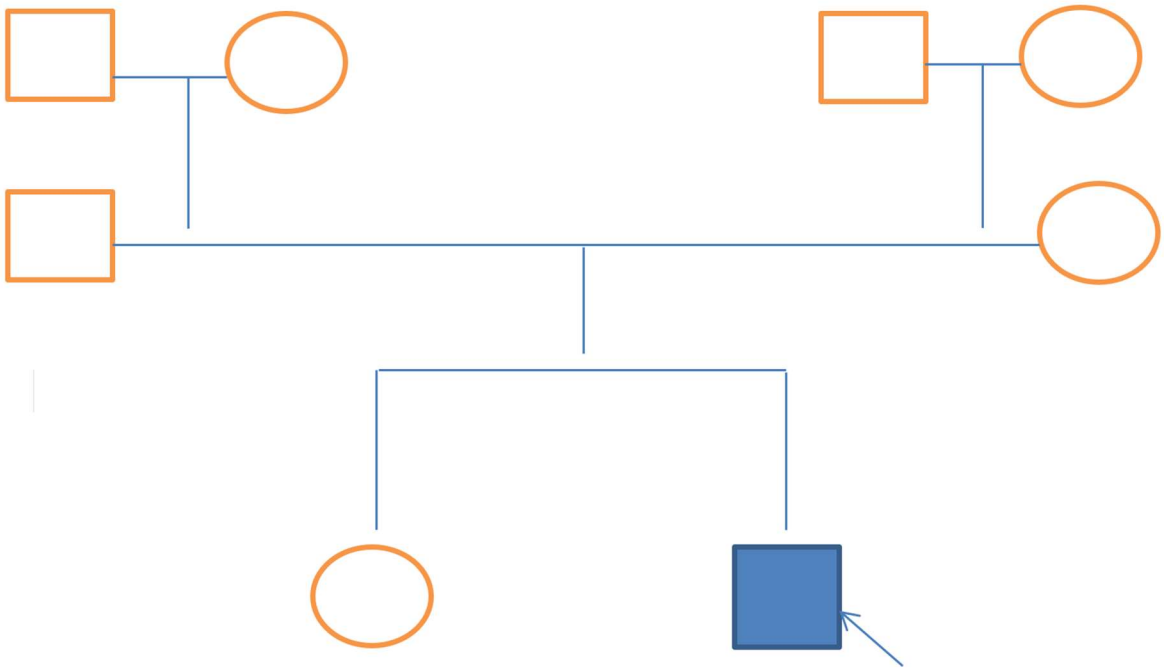

Fig-1. - Lowe syndrome with X-linked recessive inheritance type.

A 2-year-old child was admitted to the nephrology department of the Andijan Regional Children's Multidisciplinary Medical Center.

Complaints from parents about edema throughout the body, oliguria, strabismus, lag in mental and physical development.

Anamnesis morbi. The first symptoms of the disease were observed in the patient at 1 year and were treated with the diagnosis: congenital nephrotic syndrome, kidney function is preserved. Transferred diseases: Congenital heart disease - ventricular septal defect (VSD). Deficiency anemia of the II degree.

Anamnesis vitae: from the anamnesis it turned out that the child was born from parents from a closely related marriage. During pregnancy, there were no special complaints from the mother, there was toxicosis up to 3 months and anemia deficient II degree. The birth proceeded without complications. Paternal relatives have a hereditary pathology – type 2 diabetes mellitus. It was found that the patient's mother suffers from polycystic kidney disease.

Status preseans: the general condition of the child at the time of examination is severe due to the symptoms of general intoxication: lethargy, capriciousness, low appetite. The boy is significantly behind in physical development (does not walk, has only 10 teeth) and in intellectual development (does not speak, does not answer questions). The skin is pale, pronounced swelling throughout the body. Musculoskeletal system – "X" shaped deformity of the legs, muscle tone of the extremities is reduced, hypotension. The stigmas of dysembriogenesis were revealed: protruding and low-lying ears, low forehead, low hair growth on the forehead, short neck, short bridle. Breathing in the lungs is harsh, there is no wheezing. Heart tones are rhythmic, systolic noise at all points. The abdomen is soft, enlarged due to ascites, the liver is + 2 cm enlarged, painless, the spleen is not

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enlarged. Urination is rare, in small portions, urine is yellow. Daily diuresis-350 ml. The chair is regular. There are no meningeal symptoms.

Laboratory tests: general blood test: hemoglobin - 72 g / l, erythrocytes - 2.2 x 10^{12}, leukocytes - 9.9 x 10^{9}, ESR - 20 mm/ h. Total urine analysis: volume - 55 ml, specific gravity - 1008, protein in urine - 2.8 g/ l, squamous epithelium - 7-8, renal epithelium - 5-8, leukocytes - 3-6, altered erythrocytes - 6-8, unchanged erythrocytes -3-4, hyaline cylinders -3-6. Biochemical blood test: hypoproteinemia (total protein - 39 g/l, hypoalbuminemia (14%), urea - 24.2 mmol/l, creatinine - 356 mmol/L. Hypercholesterolemia (14 mmol/l). Acid-base state (ABS): PH-7.23, pO2 (mmHg)-68, pCO2 (mmHg)-34.67, SO2%-88.43, HCO3 (mmol/L)-19.21. Phosphaturia-25.4 mg/kg/day, calciuria-4.5 mg/kg/day. Glomerular filtration rate (GFR) -75.8ml/(min x 1.73 m2) - corresponds to stage II CKD.

Ophthalmologist examination: decreased visual acuity, strabismus and retinopathy.

Examination by a neurologist: organic damage to the central nervous system.

Based on the above information and due to the fact that the child was diagnosed with ocular, cerebral and nephrotic syndrome, the following clinical diagnosis was made: *Lowe syndrome.* Complication: *Stage II CKD*. Concomitant: *Congenital heart defect - ventricular septal defect (LVD). Deficiency anemia of the II degree*.

The patient revealed clinical and biochemical disorders confirming Lowe's syndrome (hypotension, lag in physical and intellectual development, strabismus, retinopathy, phosphaturia, calciuria, changes in ABS, decreased GFR, etc.), which is consistent with literary sources [1-14]. Proteinuria in the patient is caused at the beginning by tubulopathy, and then by glomerulopathy and with complete nephrotic syndrome. It was also noted that the patient had a significant decrease in GFR and early development of stage II CKD, which has a regional character.

Eye changes in Lowe syndrome are represented by bilateral or unilateral congenital cataract, glaucoma is in second place in terms of the frequency of detection [1-5, 15]. On the contrary, our patient had eye pathology in the form of strabismus, decreased visual acuity and retinopathy.

CONCLUSION

1. In the conditions of the Fergana Valley of Uzbekistan, the occurrence and development of Lowe syndrome in children is of a regional nature, which is observed with the early manifestation of malformations, clinical and laboratory changes and progression in stage II-III of chronic kidney disease in patients born from closely related marriages and having pathology at an early stage of pregnancy in the mother.
2. Unfavorable prognosis of Lowe syndrome (oculo-cerebro-renal) with X-linked recessive type of inheritance causes combined damage to the eyes, nervous system and kidneys. Proteinuria in the patient causes proximal tubulopathy at the beginning, and then glomerulopathy and with complete nephrotic syndrome, progressing in chronic kidney disease already in childhood.
3. The basics of early prevention of the development of Lowe syndrome in children in the conditions of the Fergana Valley of Uzbekistan are: inclusion of children born from closely related marriages in the risk group; identification and treatment of pathologies of early pregnancy (7-8

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weeks) in the mother; early detection of the stigma of dysembriogenesis in children and consultation of a group of specialists (nephrologist, ophthalmologist, neurologist).

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