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TABLE OF CONTENTS

AGRICULTURAL SCIENCES

BIOLOGICAL SCIENCES

MEDICAL SCIENCES

ETIOPATHOGENESIS AND PHENOTYPIC SIGNS OF ISOLATED DUPLICATION OF THE SHORT ARM OF THE SECOND CHROMOSOME (LITERATURE REVIEW)

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Introductions. The first child with the isolated duplication of a short arm of chromosome 2 (2p) was described in 1973. In 1978 the first description of a syndrome appeared, and in 1995 the information on a syndrome was supplemented. At the end of the twentieth century, about 25 cases were registered in the literature. In most of the cases described, these are duplications of 2p in combination with other chromosomal abnormalities. Isolated duplications are much less common than 2p duplications in combination with deletion of the other arm of the chromosome. This may be due to the sensitivity of the methods used to analyze chromosomes until the mid-1990s. Modern methods, such as FISH and microchips, provide a greater opportunity to detect structural changes in chromosomes. As early as 2000, Aviram-Goldring published data on the peculiarities of the phenotype with isolated 2p duplication based on 17 clinical cases in children from birth to 7 years. The most common signs were low birth weight, developmental delay, unusual facial features.

In some cases, visual disturbances, lung defects, abnormalities in the development of the genitals in boys are described. In small duplications, which were located closer to the end of the short amr in the area of the 2p25 locus, only such signs as developmental delay and long thin fingers were noted. In general, information on the etiopathogenesis and phenotypic characteristics of people with 2p duplication is not generalized.

Aim. To summarize the available scientific information on the etiopathogenesis and phenotypic manifestations of duplication of the short arm of chromosome 2 in humans.

Materials and methods. Review of scientific literature for the last 25 years.

Results and discussion. According to the literature, a 2p duplication occurs during the formation of a sperm or ovum, or in an embryo immediately after conception. Sometimes during the formation of the ovums or sperm cells or during the process of transcription and replication, parts of the chromosomes may break or be arranged differently than usual. Also, many cases of 2p duplications are the result of reciprocal translocations.

Etiopathogenesis. In people with 2p duplication, one chromosome has a normal structure, with the excess of homologous chromosome 2. If this occurs on chromosome 2, the chromosome often breaks and the extra part is inserted into the space between the broken ends before they connect. Sometimes there is only one break, and an extra piece of chromosome 2 joins the end of chromosome. If the additional part of the genetic material is located closer to the centromere, duplication is called proximal, if closer to the end of the short arm of the chromosome – distal. Sometimes duplication is present only in some cells, such duplication is called mosaic. Sensitive molecular methods, such as in situ fluorescence hybridization (FISH) or comparative genomic hybridization (array-CGH or microchips), are needed to detect duplication.

Gene disorders. The presence of additional chromosome material means that some genes are present in three copies instead of two. It has been suggested that genes at the 2p24 locus are important for neural tube development. It is believed that

the SOX11 genes in 2p25.2 and MYT1L (myelin transcription factor1) in 2p25.3 play an important role in the development of the central nervous system, so in 2p duplications they may be associated with developmental delays and learning difficulties. A gene known as the MYCN oncogene (synonymous with N-MYC), found in the 2p24.3 locus, may be involved in the development of certain forms of cancer from immature nerve cells (neuroblastoma). However, this assumption needs further research.

Signs of 2p duplication at different stages of ontogenesis.

The course of pregnancy by a fetus with a 2p duplication may be accompanied by the threat of termination of pregnancy, polyhydramnios, preeclampsia. The first signs of duplication are high AFP levels at 15-20 weeks of gestation. Sometimes ultrasound in early pregnancy reveals a thickening of the cervical region, fetal growth retardation, insufficient fetal activity, days; congenital malformations of the central nervous system. The average weight of such children at birth was 2727 g. From birth, it is possible to identify a cleft palate, hernia, congenital heart defects. Newborns have feeding or breathing problems: with heart disease during feeding, shortness of breath and cyanosis may occur. The features of the phenotype include: high or convex forehead, hypertelorism of the eyes, saddle nose, low-set rotated ears; small triangular mouth with a thin upper lip. Limb changes include: short and wide big toes, syndactyly.

The distal location of the duplication (closer to the end of the short arm) is characterized by long, thin and flexible fingers and toes. Children with proximal duplications usually grow slowly. Their growth corresponds to low growth rates for children of the appropriate age. Some children with distal duplications have a thin and fragile physique. No relationship was found between length at birth and growth in adulthood. Sucking and swallowing may often be difficult. At the same time, children with distal duplication felt well during breastfeeding. In case of serious feeding disorders, tube feeding should be performed. In case of reflux, you should follow the correct position of the body during feeding and during sleep, use thickeners and drugs to neutralize stomach acid, in severe cases, perform surgery -

fundoplication.

Regardless of which part of the chromosome is duplicated, half of children have heart problems, the most common of which are atrial septal defect and ventricular septal defect, which can lead to pulmonary hypertension. Other possible heart problems are coarctation of the aorta, hypoplasia of the left heart, and vascular transposition. Frequent infections can cause an increase in adenoids, which can lead to sleep apnea. Duplication of 2p increases the risk of diaphragmatic hernia. Umbilical and inguinal hernias are also noted. In children with 2p duplication, congenital intestinal pathology, intestinal shortening, Meckel's diverticulum, incomplete intestinal rotation are described.

Renal abnormalities were detected in only 4 of the 34 cases described in the medical literature. This is a reduction in the size of the kidneys, a horseshoe-shaped kidney. Bladder-ureteral reflux is described. In some children with duplication of 2p there are such anomalies of lung development as hypoplasia or aplasia of the lungs, violation of their division. Respiratory complications are common in children with 2p duplication. They are at risk for frequent respiratory illnesses, often suffer from stridor, and are prone to gastroesophageal reflux, which can lead to aspiration pneumonia. The most common pathological conditions of the ocular apparatus were strabismus, dacryocystitis, farsightedness and myopia, defects of the anterior part of the eye, cataracts. Stricture and ectopia of anus were observed in four children with a 2p duplication.

Some children with 2p duplication may have macrocephaly or dyscranium. They may be given a brain scan. In rare cases, hydrocephalus, spinal cord abnormalities. At duplication of 2p hearing usually does not suffer, however exudative otitis quite often meets. Problems with teeth can include enamel hypoplasia, small teeth, delayed eruption of permanent teeth, occlusion.

To date, a special rearrangement of chromosome 2 has been described in a small number of children and adults: inverted duplication and deletion 2p (inv dup del 2p). In this case, the additional part 2p is located in the opposite direction to the normal part of the chromosome. The literature describes 8 children and one adult

with inverted duplication 2p and deletion of the end of the short arm. In all cases inv dup del 2p there was a delay in language, motor and mental development, but its degree is different, even within one family. Cases of hyperactivity, autistic disorder, passive behavior are described. Most of the children had vision problems. Spinal curvature was observed in three out of five children. The growth of such children is low. Two children had serious heart defects that required surgical treatment. Three children had kidney problems, one of which had impaired single kidney function. The cleft palate, congenital malformation of the brain are described.

Risk for offspring. The risk for the next sib to have a 2p duplication depends on the chromosome structure of the parents. If the parents have normal karyotypes, the risk to the offspring is minimal. If one of the parents has chromosomal changes that affect 2p, the probability of recurrence of chromosomal pathology increases. In this case, parents may be offered options for prenatal diagnosis (chorionic villus sampling, amniocentesis) and preimplantation genetic testing with IVF and embryo biopsy. Adults with small 2p duplications can start families and plan to have children. Only one family is described, where a father from inv dup del 2p passed this violation on to his two children.

Conclusions. A 2p duplication means that the body's cells have additional genetic material on the short arm of chromosome 2. The frequency of 2p duplication is unknown. Like most other chromosomal aberrations, having extra material on chromosome 2 is associated with a risk of birth defects, developmental delays, and learning difficulties. The nature and degree of manifestation of violations varies depending on what additional material is present and in what quantity. For the purpose of primary prevention, families who are planning a pregnancy should be recommended medical genetic counseling in combination with modern methods of diagnosing chromosomal aberrations.