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Y CHROMOSOME DISOMY IN A BOY WITH DELAYED PSYCHO-VERBAL DEVELOPMENT, HERMAPHRODITISM AND MICROANOMALIES OF DEVELOPMENT

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XULOSA

Maqolada 2 Y-xromosomali 2 yoshli bolada kechikkan psixo-verbal rivojlanishning kamdan-kam holatlari, tashqi jinsiy a'zolar gipoplaziyasi belgilari haqida gap boradi. Ushbu bemorda qayd etilgan standart (klassik) sitogenetik usul bilan aniqlanmaydigan marker xromosoma primordiyasini aniqlash uchun molekulyar sitogenetik texnologiyalarni, masalan, fluorestsent insitu gibridizatsiya (FISH)ni qo'llash zarurligi ta'kidlangan.

Kalit so'zlar: *Y xromosoma disomiyasi, kechikkan psixo-verbal rivojlanish, FISH.*

РЕЗЮМЕ

В данной статье на примере наблюдения за мальчиком 2-х лет, с задержкой психоречевого развития, признаками гипоплазии наружных половых у которого были выявлены 2Y хромосомы, показана необходимость внедрения молекулярно-цитогенетических технологий для проведения таких исследований, как флюоресцентная in situ гибридизация (FISH) с целью определения природы маркерной хромосомы, тогда как стандартным (классическим) цитогенетическим методом такие отклонения определить невозможно.

Ключевые слова: *дисомия хромосомы Y, задержка психоречевого развития, FISH.*

Various numerical and structural abnormalities of sex chromosomes (gonosomes) occupy a prominent place among the wide range of chromosomal and genomic abnormalities found in children with delayed psycho-verbal and sexual development. The most studied and most frequent syndromes are Sherechevsky-Turner (karyotypes - 45,X; 46,X,i(Xq); 45,X/46,XX and others), Klinefelter (karyotypes - 47,XXY; 48,XXXY and others), trisomies of the X chromosome (karyotype - 47,XXX) and disomies of the Y chromosome (karyotype - 47,XYY) [2; 15]. Both regular and mosaic forms of these syndromes have been observed, and tissue mosaicism is also possible. Patients’ symptoms vary greatly, from almost complete absence, especially in cases of mosaicism with a small fraction of the abnormal clone, to marked mental retardation, developmental malformations and microanomalies, reproductive dysfunction, and other symptoms. The diagnosis of such cases, especially in the case of mosaicism and structural rearrangements, often requires the use of molecular cytogenetic research methods, such as fluorescence in situ hybridisation (FISH) with chromosome-specific and site-specific DNA probes [10], metaphase comparative genomic hybridisation, and serial comparative genomic hybridisation on DNA microarrays (array CGH). These methods make it possible to clarify the genetic diagnosis and provide correct medical and genetic counselling to families [3,4,7,11]. The incidence of Y chromosome disomy syndrome is 1-1.5:1000 newborns [1,2,14], and 0.45-15% of males with psychiatric disorders have Y chromosome disomy. [15]. Basically, Y chromosome disomy results from chromosome misalignment in paternal meiosis II [16]. However, among the optional features, dwarfism, mental retardation of varying severity and disturbances in sexual differentiation (cryptorchidism, hypogonadism, genital dysplasia) are common; Approximately 30% of males with this syndrome have reproductive dysfunction [13], aggressive, sometimes antisocial behaviour, psychopathic traits (impulsivity, lack of attachment, poor self-control of primitive emotions), autistic features; some patients have schizophrenia, depressive psychosis, severe psychopathy and epilepsy. Other abnormalities include macrocephaly, prognathism, protruding eyebrows, high palate, tongue hypertrophy and enlarged limbs. Most published cases of the syndrome were found in psychiatric hospitals for adults and children, in institutions for the treatment of

socially dangerous patients, and in correctional facilities [2,5]. This makes each case very interesting to clinical geneticists and requires thorough study to collect data and correlate phenotype and genotype. We present the results of a study carried out on a male child with a disomy of the Y chromosome and with clinical manifestations that are not typical of this syndrome.

MATERIALS AND METHODS

The results are presented from a 2-year-old boy. Standard methods (GTG and CBG chromosome length staining) were used for peripheral blood lymphocyte culture, preparation of specimens, differential chromosome length staining and karyotype analysis [2]. Besides conventional cytogenetics, molecular cytogenetics - fluorescencein situ hybridisation (FISH) with centromeric DNA probes on X and Y chromosomes was carried out [10; 18; 20]. Standard protocols [17; 19] were used for hybridisation and analysis of the preparations.

RESULTS

In the RSNPMCE of the Institute, a 2-year-old child of the 1st pregnancy, 1st physiological birth, weight 2300 g, length 50 cm, was admitted for examination. The child was referred due to the following clinical signs: hypoplasia of external genitals, delayed psychomotor development. During the examination of the child, the following symptoms were noted: the venous network is visible all over the body, brachycephaly, hypertelorism, short nose with open nostrils, irregular growth of the fingers on the lower limbs, hypoplasia of the testis and micropenis. The child does not walk, does not understand speech, does not speak, is tearful and fearful.

Based on the clinical signs, a decision was made to perform a cytogenetic study. From the analysis of karyotype (Fig. 1) it is seen that the proband's karyotype is 45,X0/47,X+mar+mar. As a result of cytogenetic studies, the karyotype of the proband (GTG- and CBG staining of chromosomes by length) is 45,X0/47,X+mar+mar. To clarify the nature of marker chromosomes FISH study on sex chromosomes was carried out (Fig. 2), at which 1 signal specific to X and 2 signals specific to Y chromosomes were detected in 55 interphase nuclei, and 1 signal specific to X and Y chromosomes was detected in 30 interphase nuclei.

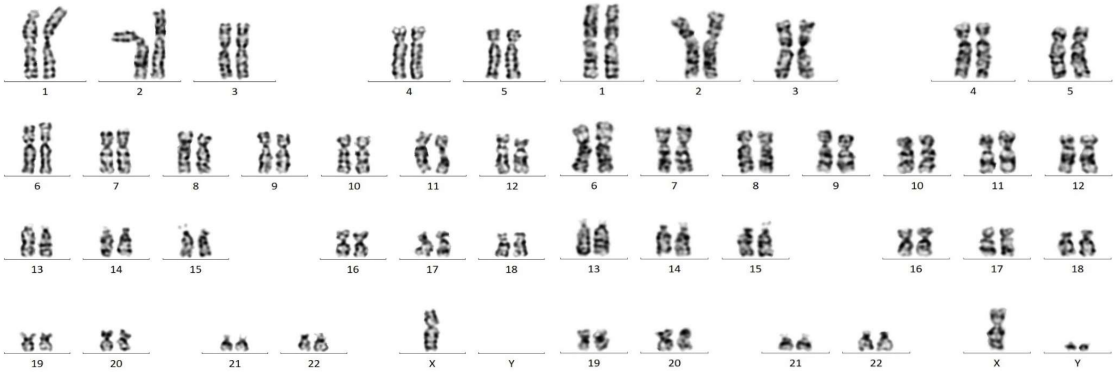

Fig.1 Karyotype 45,X0/ 47,X+mar+mar.

Also, according to the ultrasound of kidneys, the child was diagnosed with anomaly of kidney shape development - Horseshoe kidney. According to the ultrasound of pelvic organs - echographic picture of hermaphroditism.

The child underwent diagnostic laparoscopy: during the revision the uterus with poorly developed appendages opening into the seminal canal was revealed?

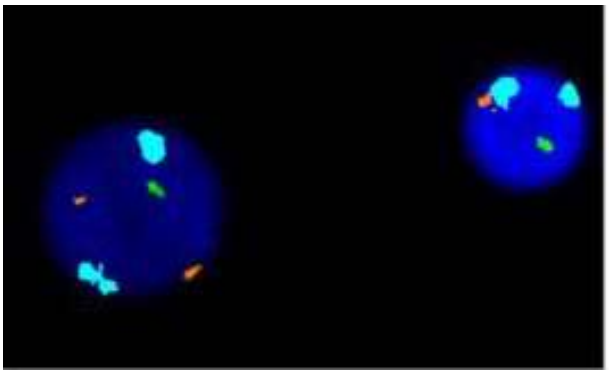

Fig.2 Interphase nuclei of lymphocytes.

Figure (2) shows the interphase nuclei of peripheral blood lymphocytes, each containing two Y chromosomes (red signals).

DISCUSSION

Due to the exceptional variability of the clinical manifestations of this syndrome, ranging from almost

complete absence of any pathological manifestations to severe mental retardation, Y chromosome disomy occupies a special place in the rather wide spectrum of various numerical and structural anomalies of the sex chromosomes (gonosomes); infertility is observed in only 30% of patients and is associated mainly with impaired spermatogenesis. The causes of clinical polymorphism in this syndrome are not always clear and may involve other chromosomal (genomic) microanomalies not detected by classical karyotyping. [4,7]. This case is unusual in that the patient with regular Y chromosome disomy has signs of hermaphroditism as well as renal changes, which is not often observed in this pathology [4]. Considering all the data, karyotyping of the spouses, medical and genetic counselling with possible prenatal diagnosis in case of repeated childbearing was recommended for this family.

CONCLUSION

An unusual case of Y chromosome disomy syndrome in a boy is presented in this article. The influence of the karyotype on the clinical manifestations in the proband is under investigation. The accumulation of data on such cases will make it possible to establish more effectively the phenotype-genotype correlation, the correct description of the phenotypic features in various chromosomal syndromes, and the medical and genetic counselling of families with a child born in a consanguineous marriage.

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