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CLINICAL AND KARYOTYPIC CHARACTERISTICS OF SHERESHEVSKI-TERNER SYNDROME IN THE UZBEK POPULATION

Akhmedova K.R., Rakhimova G.N., Alimova N.U., Sadikova A.S., Makhmudova M.M., Yuldasheva F.Z.
Republican specialised scientific and practical medical centre of endocrinology named after Acad. E.H.Turakulov

XULOSA

Kirish. *So'nggi yillarda paydo bo'lgan molekulyar sitogenetik texnologiyalar jinsiy xromosomalarning genetic xaritalarini yaratish orqali ushbu sindromning klinik polimorfizmini tushuntirish imkoniyatlarini kengaytirdi.*

Tadqiqot maqsadi: *O‘zbekiston aholisida turli tipdagi karyotip buzilishlari bo‘lgan guruhlarda klinik belgilarning tarqalishini qiyosiy tahlil qilish.*

Material va usullar: *Shereshevskiy- Tyorner sindromi bo'lgan 79 bemorda 18 fenotipik xususiyat tahlil qilindi.*

Tadqiqot natijalari: *kamida 85% chastota bilan yuzaga keladigan minimal diagnostic belgilar aniqlandi. Ko‘po‘lchovli statistic tahlil o‘tkazildi va O‘zbekiston populyatsiyasida turli xil fenotipik belgilarga ega bo‘lgan bemorlarning 4 ta kariotip guruhi aniqlandi. Natijalar molekulyar sitogenetik tadqiqotlarning nashr etilgan ma'lumotlari bilan taqqoslandi.*

Xulosa. *Mozaik karyotipi bo'lgan bemorlar guruhi (45, X / 40, XX) patologik belgilar bilan eng kam yuklangan. Karyotip 48, X va strukturaviy anomaliyalarga ega bo'lgan guruhlar fenotipik xususiyatlarning taqsimlanishida o'xshashdir.*

Kalit so'zlar: *Shereshevskiy- Tyorner sindromi, karyotip, sitogenetika.*

РЕЗЮМЕ

Введение. *Молекулярно-цитогенетические технологии, возникшие в последние годы, значительно увеличили потенциальные возможности для понимания клинического разнообразия этого синдрома – благодаря разработке генетических карт половых хромосом*

Задача исследования: *сравнительный анализ распределения клинических характеристик в группах с различными вариантами нарушений кариотипа в узбекской популяции.*

Материал и методы: *проанализировано 18 фенотипических характеристик у 79 пациентов с синдромом Шерешевского-Тернера.*

Результаты исследования: *выделены минимальные диагностические признаки, встречающиеся с частотой не менее 85%. Был проведен многомерный статистический анализ и выделены 4 группы кариотипов пациентов с различными фенотипическими признаками в узбекской популяции. Результаты сопоставлены с опубликованными данными молекулярно-цитогенетических исследований.*

Выводы: *Группа пациентов с мозаичным кариотипом (45,X/46,XX) была наименее нагружена патологическими признаками. Группы с кариотипом 45,X и структурными нарушениями сходны по распределению фенотипических признаков.*

Ключевые слова: *синдром Шерешевского-Тернера, кариотип, цитогенетика.*

According to the data of researchers from different countries, the frequency of chromosomal anomalies in humans is quite high and totals approximately 1 case per 170 newborns [2]. More than half of these anomalies are associated with sex chromosome abnormalities. Among these abnormalities, Shereshevsky-Turner syndrome accounts for a significant proportion and is characterised by a marked variability in clinical manifestations and different variants of chromosomal abnormalities [1,3,10]. Such clinical and cytogenetic polymorphism makes accurate and timely diagnosis of Shereshevsky-Turner syndrome difficult. Molecular cytogenetic technologies that have emerged in recent years have expanded the possibilities of explaining the clinical polymorphism of this syndrome by creating genetic maps of the sex chromosomes [4,7,9].

In the present study, we attempted to analyse the spectrum of clinical manifestations of Shereshevsky-Turner syndrome in the Uzbek population and compare it with karyotypic variability.

MATERIALS AND METHODS

Seventy-nine patients with Shereshevsky-Turner syndrome were studied. The patients were enrolled on the basis of referral to the scientific-polyclinical department of the RSNPMCE named after Y.H. Turakulov. Acad. Y.H. Turakulov, as well as in the RSRC ‘Mother and Child’ from 2021-2024. During the examination, a standard phenotype chart was filled out for all patients according to 18 features (Table 1). Mostly phenotypic traits with alternative manifestations were studied. Quantitative traits were divided into alternative groups

for homogeneity of comparisons, e.g. normal and short stature, etc.

This study used clinical and genealogical methods, cytogenetic methods with differential staining (G-staining). Statistical data processing was performed using standard statistical methods (mean and variation statistics).

Table 1

Frequency distribution of phenotypic traits in patients with Shereshevsky-Turner syndrome

Trait	Number of patients	
	#	%
Short stature	56	70,8
Hypoplasia of mammary glands	56	70,8
Scanty secondary hair loss	56	70,8
Short neck	54	68,3
Low hair growth	51	65,5
Thyroid chest	48	60,7
Auricular deformities	45	57,0
Nevus	42	53,1
High palate	27	34
Brachydactyly	24	30,3
Брахидактилия	21	26,5
Cubitus valgus	18	22,7
Decreased intelligence	7	8,8
Hearing loss	7	8,8
Cervical pterygium	6	7,5
Epicanthus	4	5
Renal anomaly	2	2,5

RESULTS AND DISCUSSION

The first stage of the study investigated the occurrence of 17 phenotypic features in all patients with Shereshevsky-Turner syndrome. As shown in Table 1, short stature, low neck hair growth, short neck, thyroid breast, primary amenorrhoea, breast hypoplasia and sparse secondary hair loss and deformed auricles are the most important features (with an incidence of more than 50%).

Table 2

Distribution of the frequency of phenotypic features in different karyotype variants in patients with Shereshevsky-Turner syndrome

Sign	Group of patients							
	1st (n=41)		2nd (n=4)		3d (n=27)		4th (n=7)	
	#	%	#	%	#	%	#	%
Short stature	31	75,6	1	25,01	20	74,12	4	57,11,2,3
Thorax	25	60,9	1	25,01	15	55,61	4	57,1
Short neck	33	80,5	1	25,01	13	48,11,2	4	57,11,2,3
Cervical pterygium	5	12,2	0		1	3,71	0	
Low hair growth	30	73,2	1	25,01	12	44,41,2	5	71,42,3
High palate	12	29,3	1	25,0	10	37,01,2	1	14,31,2,3
Epicanthus	2	4,9	0		1	3,71	1	14,31,3
Brachydactyly	13	31,7	1	25,0	4	14,8	3	42,9
Nevuses	14	34,1	1	25,0	7	25,9	3	42,9
Decreased intelligence	6	14,6	1	25,01	1	3,71,2	1	14,32,3
Cubitus valgus	6	14,6	1	25,01	10	37,01,2	0	
Renal anomaly	2	4,9	0		0		0	
Primary amenorrhoea	28	68,3	1	25,01	20	74,11.2	6	85,71,2,3
Hypoplasia of the mammary glands	29	70,7	2	50,0	20	74,1	5	71,4
Paucity of secondary hair loss	28	68,3	2	50,01	20	74,12	6	85,71,2,3
Deformed auricles	22	53,7	0		15	55,6	5	71,41,2
hearing loss	4	9,8	0		2	7,4	1	14,31,3

Note: 1- P<0.05 reliability of values relative to the indicators of group 1; 2- P<0.05 reliability of values relative to the indicators of group 2; 3- P<0.05 reliability of values relative to the indicators of group 3.

Of the associated somatic abnormalities, high palate, bradydactyly, nevi and cibitus valgus were the most common, with incidence rates ranging from 20 to 45%. In 79 patients with Shereshevsky-Turner syndrome, a total of 4 cytogenetic variants of karyotype abnormalities were identified. X-chromosome monosomy was the most common (80%).

In order to possibly clarify the clinical diagnostic criteria, we performed a comparative analysis of the distribution of features in groups with different variants of karyotype disorders. According to the type of karyotype, patients with Sherechevsky-Turner syndrome were divided into 4 groups: 1 - 41 patients with 45,X monosomy, 2 - 4 patients with mosaic characterised by quantitative rearrangements (45,X/46,XX and 45,X/46,XX/47,XXX), 3 - 27 patients with X structural abnormalities, including mosaic. [46,X, i (Xq); 46,X,del(X), 4th - 7 patients with marker or Y chromosome in karyotype (45,X0/46,XY, 46,X+mar).

As is evident from the data above, 45,X monosomy represents 51.8% of all patients with Turner syndrome.

Table 2 shows the analysis of the distribution of 15 phenotypic characteristics in the group of patients with Shereshevsky-Turner syndrome.

There were statistically significant differences between the groups for 9 of the 15 phenotypic characteristics under investigation.

Shortness of stature was characteristic of most patients in groups 1 (75.6%) and 3 (74.1%) and was less frequent in group 2 (25.0%).

Neck shortening was also less frequently observed in the group of patients with mosaic karyotype accompanied by quantitative rearrangements (25.0%), and was the most frequent (80.5%) in the 'pure' form (45.X). Cervical pterygium was not registered in girls of groups 2 and 4, less frequently in group 3 (3.7%) and significantly more frequently observed in group 1 patients (12.2%). Epicanthus was practically not registered in group 2, with a small frequency in groups 1 and 3 (4.9 and 3.7%, respectively) and was observed in 14.3% of patients in group 4. Nevus was more frequent in group 1 (34.1%) and group 4 (42.9%), slightly less frequent in group 2 (38%). Primary amenorrhoea was also more common in group 4 (85.7%), group 3 (74.1%) and group 1 (68.3%) compared to group 2 (25.0%). Signs such as breast hypoplasia (71.4%, 74.1%, 70.7% and 50%, respectively), scanty secondary hair loss (85.7%, 74.1%,68.3 and 50.0%, respectively) were similarly distributed across the groups. These features were more frequent in groups 3 and 4 compared to group 2.

Thus, the summary analysis of the data for all traits allows us to conclude that group 2 (mosaicism with the presence of a normal clone 46.XX) is the least loaded with pathological traits. Apparently, the presence of a normal cell clone partially compensates for the clinical manifestations of most of the studied features of the syndrome. The 1st (monosomy 45,X) and 3rd (structural anomalies of the X chromosome, including mosaicism) groups have less pronounced clinical differences and in a significant part of cases the distributions of phenotypic features are similar. Similar data are given by a number of authors [3, 6]. The lack of X-chromosome material in the karyotype (in the absence of a normal clone) obviously leads to more pronounced clinical manifestations of the Shereshevsky-Turner syndrome. It can be noted that the 3rd group, according to the general assessment of trait load, occupies a kind of intermediate position between the 1st and 2nd groups, but at the same time is characterised by greater variability in comparison with them.

Karyotype variants with loss of part of the X chromosome material (different division variants) were the most phenotypically similar.

The literature suggests that some loci that determine the Turner phenotype are located in the region of the X chromosome identified as critical for this syndrome [8]. Also on the Y chromosome, a critical region associated with some features of Sherechevsky-Turner syndrome has been identified, located at Yp subinterval 5A-51. [5].

It is hoped that advances in the combination of classical cytogenetics and modern molecular genetics will help to identify the role of specific sex chromosomal regions in the explanation of the wide range of polymorphisms in Sherechevsky-Turner syndrome and the origin of individual clinical manifestations.

CONCLUSIONS:

1. Among all Uzbek patients with Shereshevsky-Turner syndrome, monosomy X was observed in 51.8%, while the rest had various variants of karyotype disorders (structural anomalies of the X chromosome, including mosaicism).

2. The 2nd group of patients is the least loaded with pathological features (mosaicism with the presence of a normal clone 46,XX). The 3rd group of patients (structural anomalies of the X-chromosome) occupies a kind of intermediate position between the 1st (monosomy 45,X) and the 2nd groups according to the general evaluation of the load with traits, but at the same time is characterised by greater variability in comparison with them.

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

Akhmedova K.R., Rakhimova G.N., Alimova N.U., Sadikova A.S., Makhmudova M. M., Yuldasheva F.Z., Yusupova N.T.
Republican specialised scientific and practical medical centre of endocrinology named after Acad. E.H.Turakulov

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