CLINICAL AND NEUROLOGICAL CHARACTERISTICS OF CHILDREN WITH HEREDITARY SPASTIC PARAPLEGIA OF STRUMPEL IN COMPARATIVE ASPECT WITH CEREBRAL PALSY AND SPASTIC DIPLEGIA

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Abstract*. We compared the clinical and neurological picture of hereditary spastic paraplegia (HSP) and cerebral palsy of spastic diplegia. The results of a neurological examination indicate that in patients in the comparison group, clinical symptoms, especially changes in the cranial innervation and motor sphere, were more pronounced compared to the main group. During a clinical and neurological examination of patients with HSP, we identified both pure spastic paraplegia, characterized only by motor disorders (71.5%), and spastic paraplegia with complications (20%) in the form of dysfunction of the cranial nerves, intellectual impairment of varying degrees (5.4%), pelvic organ dysfunction (4.4%), history of seizures (5.2%), polyneuropathies (3.15%), extraneural symptoms were detected in 3 (3.1%) patients, i.e. congenital skin changes in the form of ichthyosis.*
Keywords*: extraneural symptoms, heterogeneous neurodegenerative diseases, spinal cord, spastic diplegia of cerebral palsy, molecular genetic research methods.*

Relevance: Hereditary spastic paraplegia is a group of clinically and genetically heterogeneous neurodegenerative diseases characterized by progressive spasticity and hyperreflexia of the lower extremities (3,5). In recent years, the frequency of relapses of the disease has been increasing (1.4). According to experts from the World Health Organization (WHO), “the global prevalence of HSP is 1.0-4.0 per 100,000 population; there are different data on the ratio of dominant and recessive forms depending on the inbredness of the population” (1,2). Hereditary spastic paraplegia is most often “masked” under spastic diplegia of cerebral palsy, so it is difficult to differentiate them from cerebral palsy. Comparative clinical and paraclinical characteristics of the course of HSP will improve the tactics of management and treatment of patients with HSP.

Purpose of the study: to evaluate the clinical and neurological characteristics of patients with Strumpel's disease in a comparative aspect with cerebral palsy, spastic diplegia.

Material and methods of research: The study was based on examination data of 153 patients. Of these, the main group (MG) consisted of 95 patients with HSP. The retrospective study included 40 children who applied to the medical and genetic counseling department of the Republican Center “Mother and Child Screening” (Tashkent) for the period 2007-2017. A prospective study was conducted among 55 patients who applied between 2018 and 2023. Patients in the amount of 58 children made up the comparison group (CG) with a diagnosis of cerebral palsy and spastic diplegia, who applied to the clinic of the Republican Psychoneurological Hospital named after. W.K. Kurbanov in the period from 2019-2023. The diagnosis was established on the basis of genealogical, clinical neurological, paraclinical (MRI of the brain, MRI of the spinal cord and ENMG of the nerves of the lower extremities) and molecular genetic research methods. Rating

scales were used (motor activity was assessed using the MRS scale, spasticity was assessed using the Ashworth scale, gross motor function was assessed using the GMFSC).

Results: The MG included 95 children with HSP aged 2-15 years, the CG included 58 children with cerebral palsy and spastic diplegia aged 2-14 years.

Manifestation of pathology (motor disorders) in the MG was detected on average at the age of 3.5±1.1 years, and individually at 4.5±1.2 years. In 36.8% of representatives of the group, the diagnosis of HSP was recorded at 4-7 years of age, in 21% - before 3 years of age; these children were siblings of the proband. We compared the clinical and neurological picture of HSP and cerebral palsy with spastic diplegia. In the CG, symptoms of dysfunction of the cranial nerve and motor sphere were more pronounced, compared to the MG (Table 1).

A differential feature in the clinical picture of HSP was the presence of foot contracture in 65.2% of children (Friedreich's foot): the chance of encountering this symptom in patients with HSP is more than 200 times higher than among children with cerebral palsy (OR = 218.3; 95% CI: 13.1-3644.4; P=0.0002); whereas in children with cerebral palsy, ankle joint contracture was more common, amounting to 36.2% (OR=0.25; 95%CI: 0.11-0.57; P=0.0009). Pelvic dysfunctions occurred in both groups, but more often in children in the CG. Some clinical similarities were revealed in the examined children of both groups: gait disturbances were observed in both groups, i.e. typical spastic gait, motor disorders are often asymmetrical, hyperreflexia, positive foot pathological signs.

Table 1

Frequency of occurrence of individual symptoms in the examined children

Signs of the disease	Frequency of symptoms				Statistical indicators
	MG (n=95)		CG (n=58)		
	Abs.	%	Abs.	%	
Head circumference					
Normal	92	96,8	42	72,4	OR=11.7; 95% CI: 3.2-42.3; P = 0.0002
Hydrocephalus	1	1,05	5	8,6	
Microcephaly	2	2,10	11	18,9	OR=0.1; 95% CI: 0.02-0.43; P = 0.0025
CN					
visual impairment	1	1,05	5	8,6	OR=0.1; 95%CI: 0.01-0.99; P = 0.0490
convergent strabismus	5	5,3	31	53,4	OR=0.05; 95%CI: 0.02-0.14; P < 0.0001
exotropia	3	3,2	14	24,1	OR=0.1; 95%CI: 0.03-0.4; P=0,006
Ptosis	2	2,1	-	-	
chewing disorders	2	2,1	23	39,6	OR=0.03; 95%CI: 0.0073-0.14; P < 0.0001
hearing impairment	-	-	3	5,1	
swallowing disorder	-	-	11	19	OR=0.02; 95%CI: 0.00123-0.4; P=0,0084

speech (dysarthria)	6	6,3	47	81	OR=0.02; 95%CI: 0.0055-0.04; P < 0.0001
Motor sphere					
muscle tone					
increased spastic type	95	100	58	100	
Contracture					
in the elbow joints	-	-	7	12,1	OR=0.04; 95%CI: 0.002-0.64; P=0,024
in the wrist joints	-	-	5	8,6	OR=0.05; 95%CI: 0.003-0.94; P=0,0452
in the knee joints	8	8,4	17	29,3	OR=0.2; 95%CI: 0.09-0.56; P=0,0013
in the ankle joints	12	12,6	21	36,2	OR=0.25;95%CI:0.11-0.57;P=0,0009
Friedreich's foot	62	65,2	-	-	OR=218,3; 95%CI: 13,1-3644,4; P=0,0002
Sensory disorders	10	10,5	5	8,6	
Tendon reflexes					
Increased	95	100	58	100	
with increased reflexogenic zone	95	100	31	53,4	
Positive stop signs					
Babinsky	95	100	58	100	
Gordon	95	100	37	63,8	OR=109.5; 95%CI: 6.5-1854.2; P = 0.0011
Schaeffer	95	100	21	36,2	OR=333,14; 95%CI: 19.7-5640.8; P = 0.0001
Oppenheim	95	100	29	50	OR=191,0; 95%CI: 11,3-3222,3; P = 0.0003
Clonus	68	71,6	14	24,1	OR=7,9; 95%CI: 3,7-16,7; P< 0.0001

During a clinical and neurological examination of patients with HSP, we identified both pure spastic paraplegia, characterized only by motor disorders (71.5%), and spastic paraplegia with complications (20%) in the form of dysfunction of the cranial nerve, intellectual impairment of varying degrees (5, 4%), dysfunction of the pelvic organs (4.4%), history of seizures (5.2%), polyneuropathies (3.15%), extraneural symptoms were detected in 3 (3.1%) patients, i.e. congenital skin changes in the form of ichthyosis.

When assessing gross motor functions on the GMFCS scale, the following indicators were revealed (Table 2): with increasing age of children with HSP, there is a prevalence of levels 4 and 5 of motor dysfunction, in contrast to cerebral palsy.

Thus, among patients with HSP there is a chance of meeting a child with 4 and level 5 at the age of 4-15 years is 55 times higher than before 3 years (OR=55.7; 95%CI: 7.0-441.5; P = 0.0001), and a child with level 5 at the age of 8-15 years is 65 times higher than before 8 years

(OR=65.1; 95%CI: 13.2-21.4; P <0.0001). Within the group with cerebral palsy, such a characteristic tendency towards deterioration of motor functions with age was not identified.

At the same time, when comparing the two groups, there is a 4.3-fold greater prevalence of severe motor impairment (level 5) among patients with HSP of all ages compared to cerebral palsy: OR=4.3; 95%CI: 1.4-13.2; P = 0.0105. In both groups at the age of 4-7 years, levels 2 and 4 prevailed (72.7% and 77.6%). In the main group aged 8-15 years, level 5 prevailed - 21 (22%), while in the comparison group this figure was 4 (6.9%).

table 2

GMFCS by age in the examined groups.

Levels	2	3	4	5	N	5 / (2+3+4) 8-15 years/up to 8 years	(4+5) / (2+3) 4-15 years / up to 3 years	5 / (2+3+4) between groups
Age	Main group							
Up to 3 years	20	1	0	1	22	OR=65.1; 95%CI: 13.2-21.4; P <0.0001	OR=55.7; 95%CI: 7.0-441.5; P = 0.0001	OR=4.3; 95%CI: 1.4-13.2; P = 0.0105
4-7 years	4	1	26	1	42			
8-15 years	4	1	5	21	31			
N	38	3	31	23	95			
	Comparison group							
Up to 3 years	4	3	10	1	18	P>0,05	P>0,05	
4-7 years	8	6	12	2	28			
8-15 years	7	0	4	1	12			
N	19	9	26	4	58			

When assessing spasticity using the Ashworth scale, 2 points were not found in the MG, while in the CG this figure was 8.7% (Table 3.6).

In the group aged 4-7 years, children with 4 points prevailed (92.6%), while in the comparison group children with 3 points prevailed (50%).

The analysis showed that in children with HSP, the course of the disease worsens with age: spasticity in the lower extremities increases, as a result, children with scores of 4 and 5 are found 27 times more often after 3 years than before 3 years (OR = 27.0; 95% CI : 3.0-240.1; P = 0.0031). In the diagnostic aspect, it should also be noted that there is a greater impairment in spasticity in children with HSP compared to cerebral palsy (OR=17.8 95%CI: 7.0-45.2 P < 0.0001).

Muscle strength on the MRS scale in the main group averaged 3-4 points (64.2% and 25.2%), while in the comparison group this figure was 2-3 (51.7% and 36.2%) points (Tables 3,4). There was also a clear trend in the deterioration of muscle strength with age in patients with HSP: at the age of 8-15 years, patients with scores of 4 and 5 are 13 times more common than before 7 years (OR=13.4; 95%CI: 4.4-40.3 ; P < 0.0001).

Significant differences were also found between the two groups: milder impairment of muscle strength of 1 and 2 points is 18 times more common in children with cerebral palsy compared with HSP (OR = 17.8; 95%CI: 7.0-45.2; P < 0.0001).

Table 3

Assessment of spasticity in the lower extremities according to the Ashworth scale in both groups

Points	2	3	4	5	N	Up to 3 years/ 4-15 years	Between groups
Age	Main group					(4+5) / (2+3)	
Up to 3 years	0	6	16	0	22	OR= 27.0 95% CI: 3.0-240.1 P = 0.0031	OR=17.8 95%CI: 7.0-45.2 P < 0.0001
4-7 years	0	0	42	0	42		
8-15 years	0	1	30	0	31		
N	0	7	88	0	95		
	Comparison group						
Up to 3 years	2	9	7	0	18	P>0,05	
4-7 years	3	13	11	1	28		
8-15 years	0	7	4	1	12		
N	5	29	22	2	58		

Thus, the differential diagnostic criterion for HSP is Friedreich's foot (OR=218.3; 95%CI: 13.1-3644.4; P=0.0002); in children with cerebral palsy - contracture of the ankle joint (OR=0.25; 95%CI: 0.11-0.57; P=0.0009). Also, for HSP with age, a significant deterioration in motor functions, deterioration in spasticity, and muscle strength was revealed, which is a diagnostic criterion for making a diagnosis.

Table 4

Assessment of muscle strength using the MRS scale in the examined groups

Points	1	2	3	4	5	(4+5) / (1+3)	(3+5) / (1+2)	(4+5) / (1+2+3)
Age	Main group					Up to 7 /8-15 years	Between groups	
Up to 3 years	0	0	16	6	0	OR=13.4 95%CI: 4.4-40.3 P < 0.0001	OR=17.8 95%CI: 7.0-45.2 P < 0.0001	OR=2.9 95%CI: 1.12-7.68 P = 0.0288
4-7 years	0	1	41	0	0			
8-15 years	0	3	10	18	0			
N		4	67	24	0			
	Comparison group							
Up to 3 years	0	10	7	0	1	P>0,05		
4-7 years	1	12	11	4	0			
8-15 years	0	8	3	1	0			
N	1	30	21	5	1			

The differential diagnostic criterion for HSP is Friedreich's foot (OR=218.3; 95% CI: 13.1-3644.4; P=0.0002); in children with cerebral palsy - contracture of the ankle joint (OR=0.25; 95% CI: 0.11-0.57; P=0.0009). With age, children with HSP showed a significant deterioration in motor

functions (OR=65.1; 95% CI: 13.2-21.4; P <0.0001), spasticity (OR=27.0; 95% CI: 3.0-240.1; P = 0.0031), muscle strength (OR=13.4; 95% CI:4.4-40.3; P < 0.0001).

Conclusions: Thus, in children with hereditary spastic paraplegia, a correlation was found between motor activity, spasticity and muscle strength, and the age of the patients, and in children with cerebral palsy, an inverse correlation was found.

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