



## **DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF PANDAS SYNDROME**

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**Abstract:** In order to develop a differential diagnostic algorithm, a comparative analysis of clinical manifestations, laboratory and neuroimaging features of PANDAS syndrome, "small" chorea and CNS intoxication was carried out on the example of examination of 89 children aged 6 to 16 years with tickose hypercinesis. Availability of BGSGA against the background of normative parameters of leukocytes, SDS and RF determine the development of neuropsychiatric disorders in the patient group "PANDAS". Morphometric differences of the "PANDAS" group are characterized by the presence of changes in the form of convulsive readiness at EEG.

**Key words:** PANDAS syndrome, "small" chorea, CNS intoxication, children aged 6 to 16, hypercinesis.

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS) is a chronic condition associated with the sudden onset of obsessive-compulsive disorders, ticks and other related diseases in children.

PANDAS syndrome is often mistaken for neuropsychiatric disorders, and many authors view it as a stand-alone condition. However, patients with diagnosed PANDAS often did not respond well to standard tick therapy or obsessive-compulsive syndrome, but showed rapid improvement with penicillin, plasmapheresis, corticosteroids, or immunoglobulin treatment [2, 3].

Currently, scientific research on this problem is devoted to the study of the causal relationship between streptococcal infection and PANDAS. However, the



existence of PANDAS is not yet considered proven, and the sensitivity and specificity of its criteria require special research.

Thus, the contradictory views on the etiology and pathogenesis of the disease, the variability of clinical manifestations, similarity with other neurological manifestations dictate the need for a detailed and comprehensive study of this issue from a neurological standpoint.

**Objective of the study:** to develop a differential diagnostic algorithm for PANDAS syndrome, "small" chorea and CNS intoxication.

**Materials and methods of investigation:** in order to develop a differential diagnostic algorithm, a comparative analysis of clinical manifestations, laboratory and neuroimaging features of PANDAS syndrome, "small" chorea and CNS intoxication was carried out on the example of examination of 89 children aged 6 to 16 years with tick-borne hypercinesis.

The studied clinical groups included 37 children suffering from PANDAS syndrome, 27 children with CNS intoxication and 25 children with small chorea. The control group consisted of 20 healthy children, comparable to patients by sex and age. These children underwent targeted clinical and neurological, laboratory and instrumental examinations.

The diagnosis was based on the results of clinical and neurophysiological (EEG, computerized and magnetic resonance imaging), biochemical and microbiological studies.

The main group included patients with simple and complex motor and vocal tics. Among them there were 61 boys (68,5%) and 28 girls (31,5%), the average age was  $9,9 \pm 0,34$  years.



Based on the current understanding of the nature of hyperkinetic syndromes in childhood and adolescence, as well as the existing and previously voiced syndromes - PANDAS [9], PITANDAS [4] and the recently proposed term PANS [5, 8], we selected the following patients.

In terms of gender participation, the first group consisted of 22 male and 15 female patients (50.5% and 40.5%, respectively), which may indicate that this syndrome prevailed in boys almost 2.5 times more frequently; the average age of the patients was  $10.0 \pm 0.5$  years.

The second group consisted of 19 boys and 6 girls (76% and 24% respectively); the average age of the patients was  $11.0 \pm 0.5$  years. The 1st and 2nd groups did not differ in terms of the mean age indicator. The third group consisted of 27 sick children, 20 boys (75%) and 7 girls (25.9%); the average age of the patients was  $8.8 \pm 0.7$  years.

The control group "relatively healthy faces" was 20 people; 14 boys and 6 girls were in this group; the average age was  $8.1 \pm 0.7$  years.

**Results of the study:** among 37 patients of the "PANDAS" group 15 patients with Tourette-type tickoses (40.5%), 11 patients with chronic simple motor tics (29.7%), 7 patients with chronic simple and complex motor or vocal ticks (18.9%), 3 patients with chronic simple motor and vocal ticks (8.1%) and 1 patient with transient ticks (2.7%) were observed.

Almost all patients of the "PANDAS" group were diagnosed with chronic infection. As a result of questionnaires and information collection, 36 of them (97.3%) were traced to chronic upper respiratory tract and ENT diseases.

Among the patients of the SC group there were 8 patients with chronic simple motor tics (32%), 6 patients with chronic simple motor and vocal tics (24%), 5

patients with chronic simple and complex motor or vocal tics (20%), 4 patients - Tourette type (16%) and 2 patients with transient tics (8%).

In 63% (17 children) of children with CNS intoxication there were chronic simple motor cases and in 37.0% of children there were chronic simple motor and vocal ticks (10 children).

Proceeding from the abovementioned, among the group "PANDAS" patients with hyperkinesis of Tourette's type prevailed (40,5%), in their turn, among children with SC patients, patients with chronic simple motor tics prevailed (32%), whereas during intoxication of CNS chronic simple motor tics (63%) and chronic simple motor and vocal tics (37%).

Obsessive-compulsive disorders (OCD) were found in all PANDAS patients (100%). The severity of obsessive-compulsive disorders ranged from 22 (moderately severe) to 37 (extremely severe obsessive-compulsive disorder); the average Y-BOCS overall severity score was  $32.4 \pm 0.67$ , which corresponds to severe "obsessive-compulsive" disorder (Table 1).

Table 1

**Frequency of "obsessive-compulsive" disorders**

Parameters	«PANDAS» (n=37)	SC (n=25)	Intoxication CNS (n=27)
Average point	$32,4 \pm 0,67$ 22-37 score	$8,4 \pm 2,1^*$ 8-12 score	$0,56 \pm 0,22^{*\wedge}$ 0-3 score
Subclinical state	0 (0,0%)	8 (36,0%)	0 (0,0%)
mild OCD	0 (0,0%)	17 (68%)	0 (0,0%)
Mid-range OCD	12 (32,4)	0 (0,0%)	0 (0,0%)
Heavy OCD	25 (67,9%)	0 (0,0%)	0 (0,0%)



Note: \* - reliability of data to indicators at "PANDAS"; ^ - reliability of data to indicators at SC (P<0.05)

Among the patients of the MCH group, 36% of patients (8 children) had RCDs. The severity of obsessive-compulsive disorders ranged from 4 (subclinical course of development work) to 12 points (obsessive-compulsive disorder of a mild degree of severity); the average points of the overall assessment of the severity of obsessive-compulsive disorders on the Y-BOCS scale were  $8.4 \pm 2.1$  points, which corresponds to "obsessive-compulsive disorder of a mild degree of severity".

In children with CNS intoxication there were no OCDs, the average index for the group was  $0.56 \pm 0.22$ , the variation series was from 0 to 3 points (no symptoms).

Thus, a reliable difference in the relative values of OCD occurrence in the groups "PANDAS" and children with SC, CNS intoxication (confidence coefficient  $t=4.5$ , i.e.  $t>2$ , which corresponds to the probability of error-free prognosis of more than 68.3% and has significant differences;  $P<0.001$ ) was established.

According to the data of the study, the severity of obsessive-compulsive disorders could affect the severity of tickose hypercinesis in the patient group "PANDAS" ( $r=0.578$ ,  $p \leq 0.001$ , which corresponds to a moderate correlation), and, on the contrary, there was no correlation between the severity of ticks and the severity of OKR in patients of the SC group and intoxication of the CNS ( $r=0.201$  and  $r=0.178$ , respectively).

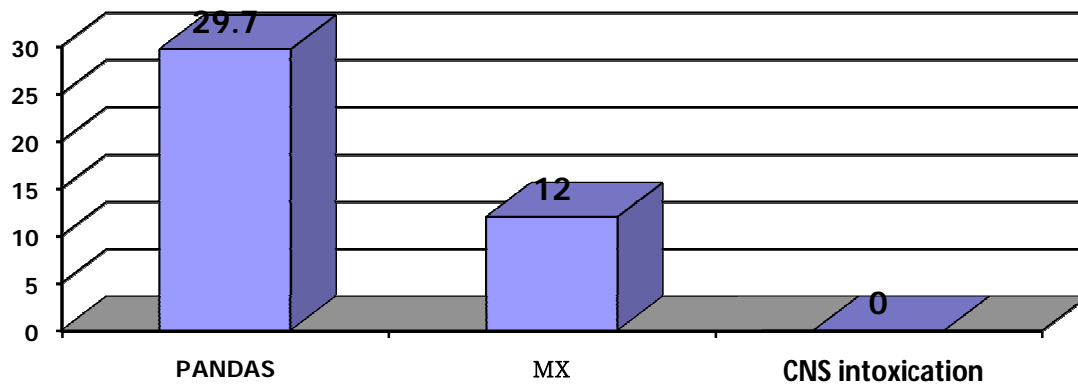
All children with PANDAS and SC showed an increase in the indices of ASL-O from 400 to 800 ME/L, children with CNS intoxication had normal ASL-O indices (up to 200 ME/L) (Table 2).

Table 2

### **ASL-O indicators among the surveyed groups**

	«PANDAS» (n=37)	SC (n=25)	Intoxication CNS (n=27)
ASL-O, ME/l	610±10,8	716,7±20,1	199,3±0,7
	400-800	600-800	180-200

$\beta$ -hemolytic streptococcus was sown in 11 patients (29.7%) with "PANDAS"; in 3 patients (12%) with SC, in patients with CNS intoxication, sowing of  $\beta$ -hemolytic streptococcus was not observed (Fig. 1)



**Fig. 1. Seeding frequency of  $\beta$ -hemolytic streptococcus**

Children with PANDAS showed a 3-fold increase in the indicators of ASL-O against the background of the normative indicators of leukocytes, SDS, DRR and the Russian Federation. In children with SC, along with 3-fold increased SL-ASL-O values, there is a significant increase in SLE, DRR and RF. Children with CNS intoxication are characterized by a two-fold increase in leukocytes, SDS, SDS, however, the indicators of ASL-O and RF are within normal limits.

Morphometric differences of the "PANDAS" group are characterized by the presence of changes in the form of convulsive readiness at EEG.

Thus, on the basis of the received clinical, laboratory and instrumental data the algorithm of differential diagnostics of "PANDAS" syndrome was developed:

**Algorithm of differential diagnostics of "PANDAS" syndrome, "small chorea" syndrome and CNS intoxication**

Expressions	«PANDAS» syndrome	"Little chorea."	Intoxication CNS
Debut of the disease	from 5 to 12 years old	from 3 to 5 years old	Doesn't depend on age.
Anamnesis.	there is a clear connection with the sore throat caused by beta hemolytic streptococcus group A	Possible connection with an angina-induced beta hemolytic streptococcus group A	No connection to an angina-induced beta hemolytic streptococcus group A
Nerve-psychological changes	Presence of mild to moderate obsessive-compulsive disorders ADHD with predominant hyperactivity	Presence of mild to moderate obsessive-compulsive disorders, presence of ADHD with predominance of hyperactivity	No ADHD obsessive-compulsive disorder
Tics	Hypercinesia like Tourette	Chronic simple motor tics	Chronic simple motor and vocal ticks
Clinic	It's going on with a certain periodicity. The time of the so-called attack is from 10 to 15 weeks. There are no rheumatic	No rheumatic nodules, ring erythema, polyarthritis, carditis	

	nodules, ring erythema, polyarthritis or carditis.		
Laboratory data	Increase of ASL-O indicators against the background of standard indicators of leukocytes, JWPs, DRR and the Russian Federation.	Increase of ASL-O, SOE, DRR and RF.	Increase of leukocytes, JWPs, RBCs, ASL-O and RF within normal limits.
EEG	Presence of changes in the form of convulsive readiness at EEG	No changes	Sometimes it is possible to have changes in the form of EEG seizure preparedness in the presence of comorbidity
MRI	Without organic lesions of basal ganglia and cortical structures	Possible organic lesions of basal ganglia and cortical structures	Without organic lesions of basal ganglia and cortical structures
Treatment dynamics	The prescription of antibiotic therapy (penicillin antibiotics) is marked by the leveling of clinical symptoms of the disease, which takes place almost without a trace	Requires long-term treatment and supervision	Etiopathogenic therapy is effective

Proceeding from the laboratory data of the compared groups, it can be assumed that the presence of BGSA carriers against the background of the normative





parameters of leukocytes, SCE, DRR and RF determine the development of psychoneurological disorders in the patient group "PANDAS". Morphometric differences of the "PANDAS" group are characterized by the presence of changes in the form of convulsive readiness in EEG.

**Conclusion:** Based on the results obtained, it was established that the complex of clinical and laboratory and clinical and morphometric studies can serve as objective diagnostic criteria for the characterization of patients with "PANS". The developed differential-diagnostic criteria will make it possible to diagnose and conduct a differentiated approach to the management of patients with tickose hypercinesis of different nature.

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