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THE ATYPIC COURSE OF INFECTIOUS PATHOLOGY EVOKED BY INTRACELLULAR AGENTS

The investigationv of several citokines (interleukines 1-β, 6, TNF) in children who suffer from asymptomic course of respiratory pathology was provided in order of revealing the early features of intracellular pathology – chlamydial and mycoplasmic. There were investigated 70 children in the age from 7 to 15 years. The results of carried investigations testified about pathogenetic role of citokines in prolonged respiratory diseases caused by intracellular infections.

The positive marker and particularly molecular-genetic diagnostics based the necessity of ethio- and pathogenetic therapy. The prolonged infection (chlamydial and mycoplasmic) may be the cause of fevers and the background for the development of diseases with autoimmune mechanism. The differential ethiopathogenetic therapy decreased the manifestation of infectious process and normalized the temperature, preventing the formation of system diseases of connective tissue.

Keywords*: children, persistent infection, cytokines, causal therapy.*

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Torpid, oligosymptomatic respiratory diseases in children, poorly responding to conventional therapy, is one of the most pressing problems of child infectology and pediatrics as a whole. Such diseases may be accompanied by prolonged fever related to the phenomenon of altered reactivity with hypersensitivity and allergic component, in which case cytokines

have pathogenetic significance [1, 7, 8]. Most authors recognize that by its etiological, clinical and pathogenic nature of fevers of unknown origin (PUO) we can determine the background to the development of persistent intracellular infections, which gives reason to treat these children as a group threatened by these diseases often caused by atypical pathogens - chlamydiae and mycoplasma [2, 3, 5, 9].

The leading role in PUO pathogenesis is performed by a "key" mediator interleukin-1-Я (IL-1 Я) which participates in the processes of inflammation and immune regulation with the properties of endogenous pyrogen, and is synthesized by cells of monocyte-phagocyte series.

This study was aimed at defining the role of Chl. pneumoniae et Myc. pneumoniae in the manifestation of a torpid, oligosymptomatic respiratory disease, as well as assessing the dynamics of cytokines (IL-1 Я,-6, TNF) on the background of a causal treatment [4, 6].

Materials and methods. The study included 70 children with respiratory diseases at the age of 7 - 15 years from diagnostic department Kharkov Regional Clinic of Infectious Diseases. 30 (43%) children were diagnosed with persistent intracellular infection caused by chlamydiae and mycoplasma, while 10 (33%) patients suffered from active infection (detection of Chl. pneumoniae or Myc. pneumoniae DNA in a bunch of blood by positive polymerase chain reaction) - these children were included into the 1st supervision group. 15 (50%) children had latent infection (only specific Ig G to chlamydiae and mycoplasma) - they were included into the 2nd group. The 3rd group consisted of 5 (17%) children with PUO not infected with the above-mentioned pathogenic agents.

To verify the etiologic factors we studied DNA of intracellular agents by PCR in a blood clot; the enzyme-linked immunosorbent assay (ELISA) was used to detect specific antibodies in blood serum. Definition of IL-1 Я, -6, TNF in the serum was performed using enzyme immunoassay systems manufactured by JSC "Vector-Best" (RF) according to the instruction.

Discussion of Results. Study of infection etiology manifested with prolonged fever and respiratory syndrome showed that 17 (57%) of 30 children with persistent infection had serological and molecular-genetic features of chlamydial infection, 9 (30%) children had signs of mycoplasma infection and 4 (13%) children had mixed (chlamydial - mycoplasma) infection.

The clinical picture of group I children showed minimal signs of intoxication, pale skin, Banti syndrome, lymphadenopathy in the absence of catarrhal and dyspeptic signs. Percussion - auscultation and radiography showed no changes, except for an increase of thymus gland.

Intoxication in children of group II was endogenous and manifested predominantly with violation of health; the reaction of lymphohysteocytic system showed a moderate lymphadenopathy. Radiological analysis also showed an increase of thymus gland.

Children of group III negative for chlamydiae and mycoplasma standards had thymus gland consistent with age parameters.

Taking into account the sensitivity of chlamydiae and mycoplasma to macrolides, in the treatment of six patients of group I we used clarithromycin (klacid, klamed). It is a natural antibiotic that violates the synthesis of microbial protein in the cell. The drug is active against atypical intracellular pathogens. Depositing in macrophages and neutrophils, clarithromycin enters the inflammation and defeats phagocytic activity. Second course of treatment, given the persistent course of chlamydiosis and mycoplasmosis, was performed in a month.

Monitoring was carried out in 2 and 6 months after treatment.

Treatment efficacy was assessed by reduction of intoxication symptoms, normalization of body temperature, dynamics of peripheral blood interleukin status indicators and long-term results of treatment based on the follow-up for 6 months.

When evaluating haemogram (Table 1) in children with active atypical infection the number of leukocytes and segmented neutrophils was lower, while the number of eosinophil and ESR was higher in children of group I, that is, with active infection course. In other groups there were no deviations from clinical blood ratios.

Table 1

Haemogram indicators in children with PUO before and after treatment

Group		Leukocytes	Segmented neutrophils	Eosinophils	ESR
I (n=30)	before	4,5±1,92	41,12±11,81	8,9±3,14	25,14±8,97
	after	8,7±1,54	48,12±8,34	4,3±1,97	11,34±5,86
II (n=10)	before	8,10±1,33	54,34±7,56	3,0±1,8	7,0±2,43
	after	8,20±1,35	54,30±7,52	2,8±1,6	7,2±2,45
III (n=15)	before	8,35±1,43	53,24±7,16	3,4±2,2	6,8±2,33
	after	8,25±1,38	52,34±7,26	3,0±1,8	7,5±2,48

Repeated examination of peripheral blood carried out after 2 months of treatment showed a significant tendency towards normalization of indicators.

The results of interleukins study are shown in Table 2.

Table 2

Indicators of interleukins in children before and after treatment

Group		IL-1Я (ng/ml)	IL-6(ng/ml)	TNF(ng/ml)
I (n=30)	before	0,234±0,013	0,435±0,027	0,156±0,010
	after	0,430±0,020	0,578±0,032	0,097±0,009
II (n=10)	before	0,345±0,018	0,657±0,038	0,096±0,008
	after	0,435±0,023	0,796±0,042	0,082±0,007
III (n=15)	before	0,442±0,027	0,884±0,055	0,075±0,004
	after	0,442±0,027	0,884±0,055	0,075±0,004

Low levels of pro-inflammatory IL-6 at both active and latent course of discussed intracellular pathogens contributed to the current and long-term chronic infection.

Treatment with the use of causal and pathogenetic therapy during the second study (in 2 months) showed an increase in levels of IL-1 and 6 of the infected children, in group III the results remained almost at the same level as before therapy.

2 months after the targeted treatment of children infected with various intracellular pathogens, on the background of the clinical well-being, there was a significant reduction in cases with active disease – in 40% of children chlamydiae and mycoplasma DNA was not detected, while in 30% of children with latent infections there was a decrease in the level of specific antibodies.

Follow-up during 6 months showed complete absence of episodes of fever and respiratory events in 50% of children from group I with active infection and in two thirds of patients from group II with latent infection.

Conclusions. Therefore, persistent infection, particularly chlamydiae and mycoplasma, may cause long-term respiratory problems and be the background to the development of autoimmune diseases. Directed differentiated etiopathogenetic therapy allows, on the one hand, to stop the infection process, on the other hand - to normalize body temperature and to prevent the formation of systemic diseases of connective tissue with autoimmune development mechanism.

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АТИПИЧНО ПРОТЕКАЮЩАЯ ИНФЕКЦИОННАЯ ПАТОЛОГИЯ У ДЕТЕЙ, ВЫЗВАННАЯ ВНУТРИКЛЕТОЧНЫМИ ВОЗБУДИТЕЛЯМИ

Было проведено исследование детей с торпидным, малосимптомным течением респираторной патологии, обследованных на ряд цитокинов (интерлейкинов 1-β, 6, ФНО) с целью усовершенствования ранней диагностики внутриклеточных инфекций – хламидийной и микоплазменной. Обследовано 70 детей в возрасте от 7 до 15 лет. Результаты проведенных исследований указывают на патогенетическую роль цитокинов при вялотекущей респираторной патологии, вызванной персистирующими внутриклеточными инфекциями.

Положительная маркерная и особенно молекулярно-генетическая диагностика является показанием для проведения направленной этиотропной и патогенетической терапии. Персистирующая инфекция, в частности хламидийная и микоплазменная, может быть причиной длительных респираторных заболеваний, и являться фоном к развитию заболеваний с аутоиммунным механизмом развития. Направленная дифференцированная этиопатогенетическая терапия позволяет, с одной стороны, купировать инфекционный процесс, с другой – нормализовать температуру тела и предупредить формирование системных заболеваний соединительной ткани.

Ключевые слова: *дети, персистирующая инфекция, цитокины, этиотропная терапия.*

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АТИПОВИЙ ПЕРЕБІГ ІНФЕКЦІЙНОЇ ПАТОЛОГІЇ У ДІТЕЙ, ВИКЛИКАНОЇ ВНУТРІШНЬОКЛІТИННИМИ ЗБУДНИКАМИ

Було проведено дослідження дітей із торпідним, малосимптомним перебігом респіраторної патології, обстежених на ряд цитокінів (інтерлейкінів - 1-β, 6, ФНП) з метою удосконалення ранньої діагностики внутрішньоклітинної патології – хламідійної, мікоплазменної. Було обстежено 70 дітей у віці від 7 до 15 років. Результати проведених досліджень свідчать про патогенетичну роль цитокінів при тривалій респіраторній патології, викликаній персистуючими внутрішньоклітинними інфекціями.

Позитивна маркерна й особливо молекулярно-генетична діагностика є показанням для проведення спрямованої етіотропної та патогенетичної терапії. Персистуюча інфекція, зокрема

хламідійна та мікоплазменна, може бути чинником тривалих лихоманок, і є фоном для розвитку захворювань з аутоімунним механізмом розвитку. Спрямована диференційована етіопатогенетична терапія дозволяє, з одного боку, купувати інфекційний процес, з іншого – нормалізувати температуру тіла та попереджати формування системних захворювань сполучної тканини.

Ключові слова: *діти, персистуюча інфекція, цитокіни, етіотропна терапія.*

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