



Problems of Diagnostics and Treatment of Tick-Borne Borreliosis in Children

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Abstract: This article provides information about the study included 74 children with Lyme borreliosis aged 1 to 18 years (1-5 years - 24 (32.4%) patients, 6-10 years - 29 (39.2%) patients, 11-17 years old - 21 (28.4%) patients), of which 34 (46%) were boys and 40 (54%) were girls. also to evaluate the effectiveness of prevention and antibiotic therapy of CB in children.

Key words: diagnosis, treatment, tick-borne borreliosis.

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Relevance. The problem of tick-borne borreliosis (TB, Lyme borreliosis) is currently devoted to a large number of scientific studies, and, nevertheless, many questions remain in the study of this pathology. Both early diagnosis of the disease in the absence of a pathognomonic symptom in the form of annular erythema, and clinical diagnosis in stages II and III of the disease are difficult due to the polymorphism of the clinic. Late etiotropic treatment or lack of prevention leads in the future to a long course of the infectious process and disability not only for adults, but also for children (according to some authors, at least 10% of cases among children). Currently, there is a global spread of this disease and its steady increase. Since the official registration of Lyme borreliosis in 1991, the number of infected people has increased annually by 3-4% worldwide. The overall incidence of tick-borne borreliosis in the Republic of Belarus in 2014 was 1,220 cases per year (1,030 cases in 2013), among children - 90 cases (84 cases in 2013) or 4.71 cases per 100,000 child population.

Objective: To characterize the features of the course and specific immune response in children with CF, as well as to evaluate the effectiveness of prevention and antibiotic therapy of CF in children. To study clinical and laboratory parameters and specific immune response in children with different stages of CB. To evaluate the effectiveness of prevention and antibiotic therapy of CB in children.

Materials and methods. The study included 74 children with Lyme borreliosis aged 1 to 18 years (1-5 years - 24 (32.4%) patients, 6-10 years - 29 (39.2%) patients, 11-17 years - 21 (28.4%) patients), of which 34 (46%) were boys and 40 (54%) were girls. The diagnosis of Lyme disease was made on the basis of epidemiological history (tick bite), clinical picture and serological diagnostic data: NRIF with an antigen from *Borrelia* and detection of antibodies (AT) in the IgM and IgG classes to *Borrelia* by ELISA in blood serum. A set of reagents for the detection of IgG and IgM to the causative agents of ixodid tick-borne borreliosis - VIDAS Lyme IgM (LYM) - VIDAS Lyme IgG (LYG) was used in the laboratory of the UZ "GDIKB" when conducting ELISA. PCR diagnostics and immunoblot were not

performed in patients. Therapy of patients with Lyme borreliosis was carried out according to the clinical protocol for the diagnosis and treatment of children with infectious diseases in the Republic of Belarus. The epidemiological, clinical, laboratory and instrumental data obtained during the study were processed by statistical analysis methods (Statsoft Statistika 6.0).

Results and its discussion. A tick bite was found in 47 (63.5%) patients, and the most common places of its localization were the parotid region and earlobe - 8 (17%) children, the anterior lateral surface of the thigh and lower leg - 13 (28%) patients, the lateral surface trunk, as well as the axillary and shoulder regions - 7 (15%) children, respectively. Children suffered from tick bites from May to September, with the highest frequency in June and July (31.9% and 34%, respectively). In 61 (82.4%) children, CF was diagnosed at stage I of the disease, among them 52 (85.2%) patients were identified with the erythematous form, and 9 (14.8%) patients with the non-erythematous form. The main clinical symptom in the form of annular erythema was recorded 10 days after the tick bite in 15 (31.9%) patients, after 14-28 days - in 20 (42.6%) patients, after 29 or more days - in 12 (25.5%) of children. General infectious syndrome in the form of weakness, malaise was noted in 15 (24.6%) patients, headache in 20 (32.8%) patients, drowsiness in 10 (16.4%) patients. For patients with the erythematous form at the onset of the disease, the following were most characteristic: subfebrile fever - 82% of children, respiratory syndrome - 60% of children, and regional lymphadenitis - 60% of patients. At the same time, for patients with an erythema-free form, arthralgia was more characteristic in all children, headache in 75% of children, weakness and malaise in 54% of patients. Serodiagnosis by NRIF was performed in 24 patients with stage I CB. Half of the children had a negative result - less than 21 days had passed since the tick bite. A doubtful result - the titer of anti-borreliosis antibodies - 1:32, was recorded in 9 (28%) patients (20-28 days have passed since the tick bite). A positive result, an AT titer of 1:64, was obtained in 3 (22%) patients (more than 28 days after the tick bite). Forty-four patients underwent ELISA, and in 18 (41%) patients anti-borreliosis antibodies of the IgM class were detected (28 or more days after the tick bite), in 26 (59%) children IgM was negative (less than 21 days after the tick bite). In 10 (13.5%) patients aged 5-10 years, the disease was diagnosed at the stage of early dissemination (stage II of the disease). In 5 (50%) children, a history of a tick bite was established 6-12 months before clinical manifestations. All patients at this stage were observed: subfebrile fever, intoxication, lymphadenopathy within 14-30 days prior to the main diagnosis. 6 (60%) patients were diagnosed with neuroborreliosis in the form of encephalitis, serous meningitis and meningoencephalitis (2 patients, respectively). The leading clinical symptoms in these patients were: cerebroasthenic syndrome - in all children, convulsive syndrome - in 4 children, focal symptoms in the form of photophobia, speech prolongation - in 3 patients, damage to the facial nerve in the form of Bell's palsy - in 1 child. Meningeal syndrome was detected in 4 children. In the cerebrospinal fluid of these patients, cytosis was 56-312 cells•10⁹/l, lymphocytes in the leukocytogram were 89-92%, protein - 0.5-1.5 g/l, glucose and chlorides were within the normal range. CSF serodiagnosis was not performed in patients with neuroborreliosis. In 3 patients in stage II, only monoarthritis of the knee joint was detected, in 1 patient with arthritis, damage to the cardiovascular system was diagnosed in the form of myocardial dystrophy with rhythm disturbance in the form of AV blockade of I-II degrees. Erythema migrans was detected only in 1 child with neuroborreliosis. Serodiagnosis was performed in all patients. NRIF was performed in 6 patients, the titer of anti-borreliosis antibodies in all was higher than the diagnostic value and amounted to 1:128-1:256. In 4 patients, ELISA revealed antibodies of the IgG class in the diagnostic titer. In 3 patients (4.1%), CB was diagnosed at the stage of late dissemination (Stage III) also on the basis of clinical and serodiagnosis: in 1 patient, antibodies of the IgG class to *Borrelia* were detected in a diagnostic amount, in 2 patients, the titers of anti-borreliosis antibodies in NRIF were 1:256. Clinically, neuroborreliosis in the form of serous meningitis was diagnosed in all patients, and Bannwart's syndrome was diagnosed in 1 patient. None of the patients had a history of tick bites. 2 patients with a diagnosis of vegetative dysfunction with cephalic

syndrome were referred to the GDIKB by cardiorheumatologists, 1 patient was referred by a neurologist with a diagnosis of cerebroasthenic syndrome for further examination. All these patients complained of prolonged weakness, headaches, poorly relieved by analgesics, decreased concentration and attention, and prolonged non-permanent subfebrile condition for 4-6 months. Only 6 (8%) patients after a tick bite were prescribed prophylactic ABT with amoxicillin: 2 children received the drug for 3 days, 4 patients - for 5 days. In all children, stage I of mild severity developed as a consequence. Treatment of patients with stage I Lyme borreliosis was carried out with amoxicillin or doxycycline, as well as azithromycin (if allergic to beta-lactam antibiotics for 10 days) for 14 days. After ABT in ELISA (47 children), 57% of patients did not detect anti-borreliosis antibodies of the IgM class, the previous values of IgM were detected in 21% of children, in 22% of children there was a decrease in the amount of IgM to zero. In NRIF (30 patients), in 5 (17%) children, the titer of anti-borreliosis antibodies remained the same, in 10 (33%) patients there was an increase in titer to 1:64, in 10 (30%) children - a decrease in titer from 1:32 to negative values, in 6 (20%) children - the titer was negative. Patients with stage II CB were treated with ceftriaxone at a dose of 70-100 mg/kg/day for 21 days. Using the NRIF method (6 children), 1.5-2 months after the therapy, the patients showed the same titers of anti-borreliosis antibodies (in 32% of patients), in 68% of the children there was a decrease in the titer of antibodies (from 1:256 to 1:128 and from 1:128 to 1:64). ELISA method (4 patients) in 7 children, the number of IgG antibodies remained the same, in 25% of patients it decreased to zero. Children with stage III Lyme borreliosis were prescribed ceftriaxone at a dose of 100 mg/kg/day for 28 days intravenously. When determining the titer of anti-borreliosis antibodies in them after 2-3 months in the NRIF (2 patients), in half of the children the titer of anti-borreliosis antibodies remained the same, or decreased from 1:128 to 1:256. ELISA was performed in 1 patient - the number of IgG antibodies was the same.

Conclusions: CB prophylaxis is not always effective if the duration of ABT is not observed. In a third of patients in stage I and in all patients in stage II and III of CB, the general infectious syndrome, subfebrile fever, and lymphadenopathy prevail in the clinic, which is not a specific sign of this pathology and requires a mandatory examination of patients with these symptoms for Lyme borreliosis. The diagnostic value of the titer of anti-borreliosis antibodies significantly depends on the stage of the disease: diagnostic titers of antibodies in stage I of the disease are found only in half of patients after 28 or more days from a tick bite, which can make it difficult to diagnose CB in the early stages of the disease and worsen the prognosis of the course of the disease. The most sensitive method of serodiagnosis of CB, especially in stage I, is the ELISA method. Appointment of adequate ABT in children with Lyme borreliosis at various stages of the disease leads to clinical recovery. After ABT of stage I CB, 57% of patients did not detect anti-borreliosis antibodies of the IgM class, in 43% of patients the amount of IgM remained the same or decreased. In patients with stage II and III Lyme borreliosis within 3 months after treatment, the titer of antiborreliosis antibodies remains the same or decreases.

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