



A clinical case of persistent Lyme disease in a child

For citation: *Child's Health*. 2024;19(1):36-39 doi: 10.22141/2224-0551.19.1.2024.1669

Abstract. Background. The relevance of the study is due to the frequent occurrence of Lyme disease (neuroborreliosis) in the spring-autumn period. Official record of Lyme disease in Ukraine has been conducted since 2000, although the first cases were identified in the 1990s. From 2001 to 2023, the incidence of Lyme borreliosis in Ukraine increased almost by 35 times. **Materials and methods.** The authors conducted a retrospective analysis of statistical data on Lyme borreliosis morbidity from 2000 to 2023 and the most common cases of infectious pathology in children during this period. As pediatric infectious disease specialists, the authors present a clinical case recently observed in the pediatric infectious unit in Poltava. **Results.** The diagnosis of Lyme borreliosis is made based on a characteristic clinical picture and a serological confirmation. The latter is crucial in the diagnosis of Lyme borreliosis and includes 2 stages. The first stage is the assessment of immunoglobulin M and G titers by the immunofluorescence assay (IFA). If the result is negative, further investigation is conducted within the first 30 days of symptoms onset by repeated IFA 4–6 weeks after the initial test. If the analysis is conducted ≥ 30 days after the onset of symptoms, further examinations are not carried out, and an alternative diagnosis should be suspected. In case of a doubtful or positive IFA result, the diagnosis is further confirmed by the Western blotting (the second stage). The authors present a case report of a 6-year-old girl M., hospitalized in the pediatric infectious unit of the CE “Municipal Clinical Hospital 1” (Poltava) in March 2023 with a diagnosis of Lyme disease (systemic tick-borne borreliosis), early disseminated stage, myalgia, arthralgia, subacute course, moderate severity. Acetonemic syndrome. Stage 1 deficiency anemia. Metabolic cardiomyopathy. Speech development delay. **Conclusions.** Therefore, it is crucial to recognize Lyme disease with a progressing or remitting disseminated form, as specific therapeutic approaches exist that are effective for this disabling condition.

Keywords: children; Lyme disease; prophylaxis; treatment

Introduction

In the spring and autumn seasons, Lyme disease (neuroborreliosis) is commonly occurred. Official report on Lyme disease in Ukraine has been made since 2000, although the first cases were registered in the 1990s. Starting from 2001, the incidence of Lyme borreliosis in Ukraine has increased almost 35-fold by 2023.

Lyme disease, present in North America, Central and Eastern Europe, including Ukraine, Asia, North Africa and Australia, ranks first among vector-borne diseases in terms of its natural focus. In terms of the rate of spread, it holds the second position after human immunodeficiency virus infection, with up to 50 cases per 100,000 population [1].

The purpose of the study was to analyze contemporary perspectives on the diagnosis and treatment of Lyme disease

in children, as well as to provide a comparative analysis of the incidence rates in Ukraine and Poltava from 2000 to 2023. This analysis was conducted against the backdrop of the increasing infectious pathology in children due to indirect factors contributing to the rise in cases of the specified nosology.

Materials and methods

The authors employed a retrospective analysis of statistical data regarding the incidence of Lyme borreliosis from 2000 to 2023 and studied the most frequent cases of infectious pathology in children during this period. As pediatric infectious disease specialists, the authors present one of the recent cases observed in the pediatric infectious disease unit in Poltava. Scientific literature data have been analyzed using the bibliosemantic study method.

 © 2024. The Authors. This is an open access article under the terms of the Creative Commons Attribution 4.0 International License, CC BY, which allows others to freely distribute the published article, with the obligatory reference to the authors of original works and original publication in this journal.

Для кореспонденції: Пікуль Катерина Вікторівна, кандидат медичних наук, доцент кафедри ендокринології з дитячими інфекційними хворобами, Полтавський державний медичний університет, вул. Шевченка, 23, м. Полтава, 36011, Україна; e-mail: ekateryna.pikul@gmail.com; тел.: +380(99)2697785

For correspondence: Kateryna Pikul, PhD, Associate Professor at the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Shevchenko Street, 23, Poltava, 36011, Ukraine; e-mail: ekateryna.pikul@gmail.com; phone: +380(99)2697785

Full list of authors information is available at the end of the article.

Results and discussion

From historical records it is known that the skin changes characteristic of Lyme disease were first described by the German physician Buchwald in 1883. In 1909, the Swedish dermatologist Afzelius made the first report on migratory erythema at the site of a tick bite. In 1913, the Austrian bacteriologist and dermatologist Lipschütz described migratory erythema, and this pathology was named Afzelius-Lipschütz erythema. Meningitis and radiculoneuropathy were considered mild atypical forms of tick-borne encephalitis. In 1949, the Swedish physician Thyresson first used penicillin for the treatment of migratory erythema. In 1982, the causative agent of the disease was first identified during the study of the contents of the gut of the ixodid tick, and the spirochetal etiology of the disease was detected.

Thus, the causative agent is *Borrelia burgdorferi*, which is transmitted by the ixodid tick. *Borrelia* is an intracellular pathogen with a tendency to chronicity and can provoke autoimmune disease. Rodents and certain domestic animals could be the source of infection. The transmission routes include transcutaneous, transmissive, and sometimes alimentary (raw milk). The source of infection is mammals and birds, which act as hosts for ticks and the main reservoir of the disease [2].

The pathogen persists throughout the lifespan of the tick and can be transmitted transovarially (through eggs) and transstadially (through larvae and nymphs). This means that each developmental stage of the tick can cause infection.

The *Borrelia burgdorferi* species encompasses 12 different species and their genomic strains, belonging to the genus *Borrelia*, family *Spirochaetaceae*. The most clinically significant species within *Borrelia burgdorferi* are *B.afzelii*, *B.garinii* and *B.valaisiana*. They possess three groups of antigens: surface, flagellar and cytoplasmic. In the human body, *Borrelia* can be found in the skin, cerebrospinal fluid, synovial fluid, placenta, and urine. *Borrelia* is relatively resistant to environmental factors, disinfectants, and ultraviolet radiation.

The course of the borreliosis infection process has 3 stages.

Local infection stage. The pathological process develops at the site of the pathogen's penetration. It begins within 2 to 30 days after the attachment of the ixodid tick. The multiplication of the pathogen leads to inflammatory reaction, clinically manifested by erythema and intoxication syndrome (accompanied by migratory erythema).

Dissemination stage. The pathogen spreads from the site of primary penetration. It typically develops approximately 1–3 months after the appearance of migratory erythema. Hematogenous and lymphogenous dissemination occurs to lymph nodes, parenchymal organs, joints, the nervous system, forming metastatic foci of inflammation. Some microorganisms die, intensifying the intoxication syndrome. Generalization of the infection pathological processes creates a groundwork for the progression of organic damage and chronicity (radicular pain with a pain syndrome in the spine, with signs of irritation and loss of sensory and motor functions, facial nerve palsy, infectious encephalitis) [3].

Organ damage stage. This stage, involving organ damage such as myocarditis, hepatitis, arthritis, keratitis, chronic dermatitis, and diffuse atherosclerosis, may occur several

months or years later. Diagnosis is performed using the immunofluorescence assay (IFA), polymerase chain reaction (PCR) and the material for the study includes cerebrospinal fluid, blood, and synovial fluid.

The diagnosis of Lyme borreliosis is made based on a characteristic clinical picture and a two-step serological confirmation. A two-step nature of serological verification is crucial in Lyme borreliosis diagnosis. The first stage (IFA) is evaluation of immunoglobulins (Ig M and G using the IFA. If its result is negative, further investigation is carried out within the first 30 days from the onset of symptoms and the IFA should be repeated 4–6 weeks after the initial test.

If the study was conducted after ≥ 30 days from the onset of symptoms and the IFA result is negative, no further examinations are conducted, and an alternative diagnosis should be suspected. In case of a doubtful or positive IFA result, further confirmation of the diagnosis is carried out using the Western blotting method.

The second stage (Western blotting) is conducted only in case of confirmed or doubtful results from the IFA. It is not advisable to perform the Western blotting without the preliminary diagnostic stage using the IFA. In this context, if symptoms of the disease are present for < 30 days, the Western blotting is used to assess IgG and IgM; if symptoms of the disease are present for > 30 days, the Western blotting is used to evaluate only IgG [4].

Lyme borreliosis post-exposure prophylaxis is mandatory.

According to the recommendations of the Centers for Disease Control and Prevention, post-exposure prophylaxis for Lyme borreliosis (a single-dose oral administration of 200 mg doxycycline) should be considered if all of the following conditions are met:

- The engorged *Ixodes scapularis* tick has been removed ≥ 36 hours after attachment.
- No more than 72 hours have passed since tick removal.
- The prevalence of *B.burgdorferi* in local ticks is $> 20\%$.
- There are no contraindications to the use of doxycycline. It is important to monitor the tick bite site for one month and initiate treatment if clinical symptoms of Lyme borreliosis appear.

Generally, patients suspected of having multiple sclerosis and Parkinson's disease in the United States are screened for the presence of Lyme borreliosis [5].

Thus, when it comes to the prevalence of Lyme disease in Poltava region, we can note that more than 1,000 cases were reported from 2010 to 2020, while in Poltava there were 235 cases over the last 7 years. In particular, in the pediatric infectious disease unit at the CE "Municipal Clinical Hospital 1", we observed an upward trend in the number of cases among the pediatric population. In 2020, three children underwent treatment for Lyme borreliosis, whereas and in 2023, there were already 7 patients.

We report a case of the 6-year-old girl M. (medical record No. 200) who was admitted to the pediatric infectious disease unit at the CE "Municipal Clinical Hospital 1" in March 2023 with the diagnosis of Lyme disease (systemic tick-borne borreliosis), early disseminated stage, myalgia, arthralgia, subacute course, moderate severity. Ace-

tonemic syndrome. Stage 1 deficiency anemia. Metabolic cardiomyopathy. Speech development delay.

Upon referral of a pediatric infectious disease specialist, the patient was hospitalized to the unit with complaints of pain in the calf muscles, the area of the thighs and knee joints, general weakness and fatigue. From the medical history it is known that in September 2022, a tick bite was recorded, and migratory erythema appeared. Laboratory tests showed positive antibodies to IgM and negative antibodies to IgG *Borrelia burgdorferi* were obtained. The child received outpatient treatment (cefodox for 14 days at the age-appropriate dose). A progressive decrease in IgM antibodies and an increase in IgG *Borrelia burgdorferi* were observed. According to the mother, since November 2022, the child has been experiencing pain in the knee joints, calf muscles and the thigh area. The girl was examined by a pediatric infectious disease specialist, and laboratory testing (Western blotting) revealed an increase in IgM antibodies and a moderate increase in IgG *Borrelia burgdorferi*. **Neurological status:** moderate severity, lethargic, low mood. Pupils and palpebral fissure were normal, with equal pupils. No motor impairments were noted, muscle tone was satisfactory. Reflexes from the upper extremities were equal (D = S) on the hands, and tendon-periosteal reflexes from the lower extremities were brisk and equal, D = S. Abdominal reflexes were equal, D = S. Statics and coordination during the Romberg test were without impairments. Meningeal signs were negative. No seizures. Delay in speech development. The objective status was unremarkable, joint movements were in a full range, though painful in the knee joints and calf muscles. **Laboratory tests:** complete blood count showed red blood cells: $3.8 \cdot 10^{12}/L$, white blood cells: $6.1 \cdot 10^9/L$, hemoglobin: 102 g/L, erythrocyte sedimentation rate: 10 mm/h, platelets: $289 \cdot 10^3/L$, eosinophils: 10 %, band neutrophils: 4 %, segmented neutrophils: 45 %, lymphocytes: 39 %, monocytes: 8 %. Blood glucose: 4.9 mmol/L. IgG antibodies to the causative agent of Lyme disease (*Borrelia burgdorferi*) by PCR — positive. Western blotting for *Borrelia burgdorferi* in the blood serum showed IgM antibodies of 3.51 (elevated) and IgG antibodies of 6.45 (elevated); p41 — borderline result, OspC (*B. burgdorferi*, *B. afzelii*, *B. garinii* — antibodies to IgM). Venous blood test for toxoplasmosis and chlamydia showed negative result. Urinalysis revealed no pathology, except for the presence of acetone in urine. No helminth eggs were found. ECG revealed sinus rhythm, tachycardia, heart

rate 111 beats per minute, vertical position of the electrical axis of the heart. Repolarization process disturbances in the left ventricular posterior wall. Abdominal cavity ultrasound without pathology. The following treatment was prescribed: a 21-day course of antibiotic therapy (ceftriaxone), lactiale germina forte, activated charcoal, suprastin, 0.9% sodium chloride solution, dexamethasone, phenistil.

After the treatment, the patient's condition improved. Continued observation and further treatment by a pediatric cardiologist have been recommended. Outpatient supervision by a pediatrician, infection disease specialist, neurologist, and cardiologist in the place of residence has been advised.

Conclusions

In summary, it is crucial to recognize a patient with progressing or remitting disseminated Lyme disease, as the specific therapeutic approaches, effective for this debilitating condition, exist.

Further research should provide more insights into its underlying mechanisms, facilitating the development of more effective treatment approaches. The results obtained from the studies will enable pediatricians to adjust their actions in addressing the timely diagnosis and treatment of children with a preliminary diagnosis of Lyme disease.

References

1. Kramarov SO, Hrechukha, YeO. Topical issues of Lyme disease. An overview of current international guidelines. *Aktual'naâ Infektsiologiâ*. 2019;7(5):284-289. Ukrainian. doi: 10.22141/2312-413x.7.5.2019.183709.
2. Nykytyuk SO, Klymniuk SI. Lyme borreliosis in children. *Achievements of clinical and experimental medicine*. 2020;(1):14-25. Ukrainian. doi: 10.11603/1811-2471.2020.v.i.11064.
3. Picul EV. Infectious encephalitis in children. *World of medicine and biology*. 2016;(58):52-59. Ukrainian.
4. Smiyan SI, Shkilna MI, Regalyuk VV, et al. Modern aspects of etiology, pathogenesis, clinical course and treatment of Lyme-arthritis (review, own observations). *Ukrainian journal of rheumatology*. 2018;(2):40-45. Ukrainian.
5. Tarianyk KA, Lytvynenko NV, Shkodina AD, Kaidashev IP. The role of circadian regulation of ghrelin levels in Parkinson's disease (literature review). *Wiad Lek*. 2021;74(7):1750-1753.

Received 05.01.2024

Revised 15.01.2024

Accepted 24.01.2024 ■

Information about authors

Kateryna Pikul, PhD, Associate Professor at the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Poltava, Ukraine; e-mail: ekateryna.pikul@gmail.com; phone: +380(99)2697785; <https://orcid.org/0000-0002-5724-4343>

Valentyna Ilchenko, PhD, Associate Professor at the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Poltava, Ukraine; e-mail: v.ilchenko@pdmu.edu.ua; phone: +380(66)52544335; <https://orcid.org/0000-0002-1945-0250>

Konstantin Prylutskiy, PhD, Assistant at the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Poltava, Ukraine; e-mail: konstantinpryluckij7@gmail.com; phone: +380(93)24823841; <https://orcid.org/0000-0002-2016-9810>

Oksana Muravlova, PhD, Associate Professor, Head of the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Poltava, Ukraine; e-mail: o.muravlova@pdmu.edu.ua, mur_ov_pdmu@ukr.net; phone: +380(50)7619084; <https://orcid.org/0000-0002-5319-7092>

Zlatozlava Shaienko, PhD, Associate Professor at the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Poltava, Ukraine; e-mail: z.shaienko@pdmu.edu.ua, zlataligonenko@gmail.com; phone: +380(50)0333392; <https://orcid.org/0000-0002-8718-7589>

Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Information about funding. The paper is a fragment of the scientific research conducted by the Department of Endocrinology with Pediatric Infectious Diseases and the Department of Therapeutic Dentistry at Poltava State Medical University on the topic "Development of pathogenetic prevention of oral lesions in individuals with internal diseases" (state registration number 0121U108263, execution period 2020–2026), in which the authors are co-executors.

Authors' contribution. Kateryna V. Pikul — research concept and design, data collection, data analysis and interpretation, writing the article; Valentina I. Ilchenko — data analysis and interpretation, writing the article; Konstantyn Y. Prylutskiy, Zlatozlava O. Shaienko — editing the text, final approval of the article; Oksana V. Muravlova — research concept and design, editing the article.

Пікуль К.В., Ільченко В.І., Прилуцький К.Ю., Муравльова О.В., Шаєнко З.О.
Полтавський державний медичний університет, м. Полтава, Україна

Клінічний випадок хвороби Лайма з хронічним перебігом у дитини

Резюме. Актуальність дослідження обумовлена тим, що у весняно-осінній період нерідко зустрічається хвороба Лайма (нейробореліоз). Офіційна реєстрація хвороби Лайма в Україні ведеться з 2000 року, хоча перші випадки були виявлені в 1990-х. У 2001–2023 рр. рівень захворюваності на Лайм-бореліоз в Україні зріс майже в 35 разів. **Матеріали та методи.** Автори провели ретроспективний аналіз статистичних даних щодо захворюваності на Лайм-бореліоз у 2000–2023 рр. та найбільш частих випадків інфекційної патології в дітей за цей період. Як дитячі інфекціоністи, автори наводять клінічний випадок, який нещодавно спостерігали в педіатричному інфекційному відділенні в Полтаві. **Результати та обговорення.** Діагноз Лайм-бореліозу встановлюється на основі характерної клінічної картини та серологічного підтвердження. Серологічна верифікація має вирішальне значення в діагностиці Лайм-бореліозу та включає 2 етапи. На першому визначають титри імуноглобулінів класу М та G методом імунофлуоресцентного аналізу (ІФА). Якщо результат негативний, дослідження проводиться протягом перших 30 днів від початку

симптомів, ІФА треба повторити через 4–6 тижнів після першого тесту. Якщо дослідження виконане через ≥ 30 днів з моменту появи симптомів, подальші обстеження не проводяться, необхідно розглянути альтернативний діагноз. У випадку, коли результат ІФА сумнівний або позитивний, діагноз підтверджують методом вестерн-блотинга (другий етап). Наведено клінічний випадок у дівчинки М., 6 років, яка перебувала на стаціонарному лікуванні в дитячому інфекційному відділенні КП «Перша міська клінічна лікарня» (Полтава) у березні 2023 р. з діагнозом: хвороба Лайма (системний кліщовий бореліоз), рання дисемінована стадія, міалгія, атралгія, підгострий перебіг, середньої тяжкості. Ацетонемічний синдром. Дефіцитна анемія 1-го ступеня. Метаболічна кардіоміопатія. Затримка мовленнєвого розвитку. **Висновки.** Отже, дуже важливо розпізнати прогресуючу чи ремітуючу дисеміновану форму хвороби Лайма, оскільки існують певні терапевтичні підходи, які ефективні при цьому інвалідизуючому стані.

Ключові слова: діти; хвороба Лайма; профілактика; лікування