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Review Article

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The Problem Of Diagnosis Of Lyme Arthritis In Children

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Abstract

The aspects of the clinical presentation, diagnostic approaches and treatment of the disease are discussed.
We present two cases of Lyme arthritis and non-rheumatic arthritis. Particular focus is given to borrelial joint disease.
We suggest that informing health professionals about such Lyme disease treatment outcome should help practical physicians to distinguish it from allergic reactions or other conditions and improve treatment outcomes.

Keywords: : Lyme disease, Lyme arthritis, child, ELISA, Western –blot, IgM, IgG.

Topicality. In endemic areas, Lyme arthritis (LA) is the main cause of joint swelling. Because of the shared inflammatory nature and common clinical features, acute LA is often misdiagnosed as septic arthritis (SA), while the recurrent disease is sometimes difficult to distinguish from other causes of chronic arthritis. In Ukraine, there is a constant increase in cases of Lyme disease. This does not follow clear guidelines, and there is no consensus on the treatment of childhood arthritis. In this context, we sought to characterize the epidemiology and clinical picture of a large local cohort.

Lyme disease (HL) - systemic tick-borne borreliosis, Lyme borreliosis, chronic migratory erythema, tick-borne erythema) is a natural focal transmissible disease caused by borrelia (Borrelia burgdorferi) and is manifested by migratory ring-shaped erythema, fever, central and peripheral lesions nervous system, heart, and large joints [1,2.3]. Borrelia burgdorferi infection manifests itself in the form of dermatological, neurological, ophthalmological diseases, and diseases of internal organs. Clinically, there are three stages of borrezia: Stage I. The typical primary manifestation of Borrelia burgdorferi infection is chronic migratory erythema: reddening of the skin that appears around the tick bite area and spreads in the form of a ring. Redness is accompanied by flu-like general symptoms with fever, chills, headache, and vomiting. In some cases, lymphadenopathy is observed. The result of this stage can be spontaneous recovery or its development into a generalized form of borreliosis. The transition phase is usually asymptomatic: in stage, I, immunoglobulins and antibodies to Borrelia burgdorfery can be detected by serological methods in 50-90% of patients. II stage. Several symptoms can develop within several weeks to several months after a tick bite.

Arthritis, especially of the knee joints, and general non-localized bone, joint, and muscle pain. In stage II, antibodies to Borrelia burgdorferi are detected in 50-90% of patients. In the early phase of this stage, mainly immunoglobulins are detected, but at the end of the phase, only IgG-class antibodies are often detected. A common late-stage complication of this disease is oligoarticular arthritis, often affecting the knee joint.

Methods

This is a retrospective review of medical records of 100 children who were examined at the children's regional hospital in the period from January 2017 to May 2022. Demographic, clinical, and laboratory data were collected and analyzed.

Markers of inflammation were determined, namely the level of leukocytes, rheumatoid factor, CRP, ANA, ASO, ELISA, and Blot, joint ultrasound was performed. In 2022 in the city of Ternopil and the region there were 112 appeals about tick bites.

Research results. As a result, Lyme arthritis was confirmed in 16 children, rheumatoid arthritis in 30 children, in the remaining cases - infectious-allergic coxitis and arthritis of other etiology. In patients with Lyme arthritis, there were 9 girls and 7 boys. Clinical symptoms such as headache, fever, muscle pain, joint inflammation, joint pain, fever, enlarged lymph nodes, erythema migrans, damage to the ankle-foot and knee joints, combined with coxitis, on ultrasound, bursitis, joint synovium in all studied patients.

In 3 cases, in the case of the chronic course of arthritis with JRA, tick bites were noted and preventive treatment with antibacterial therapy was carried out. Acute manifestations were less common (62%), while the remainder (48%) had either persistence or recurrence of symptoms (Figure 1). Fever was observed in 10% of patients.

Elevated inflammatory markers and elevated CRP levels were common in arthritis.
Seasonal distribution and clinical characteristics at initial presentation and admission are summarized in Figure 2.

Pediatricians in endemic areas, especially those providing primary, hospital, or emergency care, should be familiar with the clinical presentation and have a high index of suspicion for LA to prevent inappropriate treatment [4].

Research results

As a result, Lyme arthritis was confirmed in 16 children, rheumatoid arthritis in 30 children, and the remaining cases - infectious-allergic coxitis and arthritis of other etiology. In patients with Lyme arthritis, there were 9 girls and 7 boys. Clinical symptoms such as headache, fever, muscle pain, joint inflammation, joint pain, fever, enlarged lymph nodes, erythema migrans, there is damage to the ankle-foot and knee joints, combined with coxitis, on ultrasound, bursitis, joint synovitis is diagnosed in all studied patients. The duration of the pain syndrome ranged from 1 to 6 months.

Clinical Case 1

A 5-year-old boy was admitted to the regional hospital with complaints of swelling of the right knee; pain, increase in body temperature to subfebrile numbers. It is known from the anamnesis that the first signs of arthritis of the right knee joint appeared 1 month before hospitalization. Erythema migrans and other early signs of infection were not reported. A few days before the onset of symptoms, the patient had diarrheal syndrome for 3 days, as a manifestation of an enterovirus infection. During the objective examination, the range of motion in all joints has not changed, the movements are painful in the hip joints, and no local changes have been detected. Hepatomegaly attracted attention. Other physical examinations were normal. On examination, he was subfebrile. In connection with the maintenance of hyperthermic and pain syndrome, he was hospitalized in a specialized department of the hospital. A laboratory study showed an erythrocyte sedimentation rate of 45 mm/h, in a general blood test, leukocytes were normal, rods 15%, segments 16%, procalcitonin 0.24; there was a high level of C-reactive protein (CRP) CRP 7.6-11 mg/dL, the patient was treated by a pediatrician with nonsteroidal anti-inflammatory drugs (NSAIDs), received antibacterial therapy (cefix), but the effect was slightly positive. An ultrasound examination performed 1 month after the start of treatment revealed no structural changes. An ultrasound of the right hip joint, the capsular-cervical space is 5.7 mm, the joint capsule is thickened by 2.2 mm, and the joint space is widened by 7.2 mm. Ultrasound signs of arthritis of the right hip joint.
Computed tomography of the hip joints and pelvic bones revealed small synovitis of the right hip joint. There is no CT evidence of bone pathology at the study level. Against the background of treatment, the pain syndrome was contained and further examinations were directed to the exclusion of the autoinflammatory process. ANA, IFT methods were negative, the procalcitonin level corresponded to a low probability of sepsis (0.24 ng/ml); calprotectin 1520.4 ng/ml.

Taking into account the clinic of the disease (prolonged fever, myalgias, and laboratory confirmation of an elevated IgM level (44.85 units/ml) and immunoblot of OspCBg IgM and OspCBb IgM, it should be assumed that the child has: Lyme disease, early disseminated form, Lyme arthritis. The child is prescribed amoxicillin 50 mg/kg/day, 250 mgx33 times a day for 21 days, Nurofen 150 mg 2 times a day continued. On the 5th day of antibacterial therapy for Lyme Arthritis, a rash appeared, which may indicate Jarisch-Herxheimer reaction in this patient.

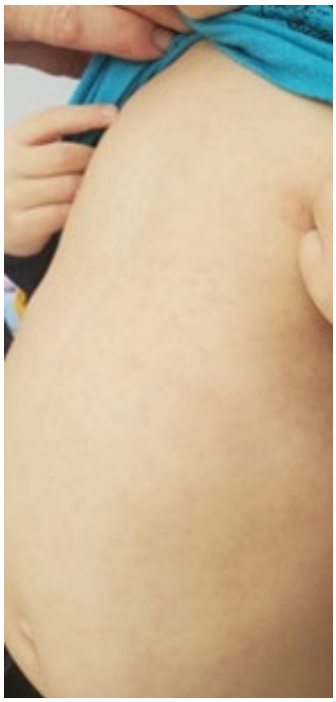

Figure 1: Rash on the skin

It should be kept in mind appearence of rash on the basic of antibacterial therapy may indicate Jarisch-Herxheimer reaction

In endemic areas, Lyme borreliosis exposure should be questioned in patients with arthritis.

Clinical case 2

Complaints of a girl upon admission of pain in the knee joints, morning stiffness up to 7 minutes. Medical history: the pain started 1.5 years ago, she did not consult a doctor. 2 years ago, there was a tick bite. the tick was infected with Borrelia. At the same time, preventive treatment with amoxacillin was carried out. Objective data: pain in the knee joints, free movements, circumference of the right joint 36.0 cm, left 36.5 cm.

Laboratory examination

ANA, antinuclear antibodies 1:100, immunoblot-p41, p39 detected, Ig M detected, IgG - not detected. Ultrasound of the joints, MRI is normal. There are no convincing data for JURA and Lyme arthritis. Treatment with Diclober Retard (Olofen 100, Nolpase 20 mg 1 tablet 30 minutes before meals. Antibacterial therapy is prescribed for preventive purposes.

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Discussion

Lyme arthritis is the most common manifestation of the late stage of Lyme borreliosis: it is reported in a third of cases [5,6]. Lyme arthritis was first described by Steer et al. in 1977 in children and adults with oligoarticular arthritis living in the Old Lyme area of Connecticut [7]. endemic areas of Lyme borreliosis are North America and Central Europe. Transient arthralgia manifests as early Lyme disease and develops several weeks after infection [8]. However, the early stages of Lyme borreliosis can be asymptomatic, and in these cases, arthritis can be the first clinical manifestation of the disease [9]. Lyme arthritis usually develops over months and is associated with innate and adaptive immune responses [10]. Lyme arthritis is treated with antibiotics for 2–4 weeks, and most patients recover [8, 11]. However, in a small number of patients, synovitis may persist for months to several years, even after 1–2 months of antibiotic treatment, and is antibiotic-resistant (or slowly resolving) Lyme arthritis [12]. Lyme disease is an intermittent or chronic mono- or oligoarthritis affecting the knee. Lyme arthritis (LA) can usually be prevented by early treatment of acute LB [13].

Virtually all untreated LA patients have high levels of serum immunoglobulin G antibodies and sometimes low levels of immunoglobulin M antibodies to Borrelia burgdorferi (Bb) by ELISA and Western blot. These immune responses can persist for years after antibiotic treatment, and therefore serological results do not accurately distinguish between active and past infection [14]. Most patients with LA respond well to standard courses of antibiotic treatment, but a small percentage have persistent synovitis of the knee, in some cases possibly related to the triggering of an autoimmune process.

Other patients develop a syndrome of diffuse arthralgia, myalgia, fatigue, and subjective cognitive difficulties during or shortly after LB that persists despite antibiotic treatment. However, with Lyme arthritis, even without specific therapy, the initial number of patients prone to arthritic attacks decreases annually by 10–20%, and after 5 years, only a few people experience arthritic attacks. Therefore, it is believed that ultimately immune mechanisms eliminate B. burgdorferi s.s. from the joint However, in the skin, B. afzelii, for example, can persist for decades, and at the same time, chronic atrophic acrodermatitis develops, which indicates the inefficiency of the local intradermal immune response. In the case of IBD, a dependence was found between the nature of the damage to the nervous system, as well as the probability of developing arthritis, which is difficult to treat with antibiotics, and the hlA status of a person [2,7]. The clinical characteristics of children with Lyme arthritis vary with age. 10% of adults with Lyme arthritis develop chronic arthritis. Chronic arthritis occurs less often in children with Lyme arthritis [8]. There is controversy in the literature as to whether Borrelia infection can cause nonspecific symptoms [10]. These nonspecific symptoms may consist of fatigue, pain in the extremities, and neurocognitive problems. The pain syndrome in the joints is sometimes unbearable and does not respond to the action of non-steroidal anti-inflammatory drugs. The patient looks for a cold place, sometimes immerses in water and holds the limb there. sometimes such persons turn to a neurologist with radicular pain. The late spread stage lasts months or years after the tick bite and occurs in 60% of untreated patients. Such patients may have periodic attacks of arthritis [10,15,16].

Elevated inflammatory markers and synovial pleocytosis were common, in contrast to fever, which was less common [17].

The evidence base for biological markers for A-RLA is limited. However, a number of promising biomarkers were identified. Cytokines and chemokines related to the Th17 pathway, together with a number of miRNA species (miR-146a, miR-155, and let-7a), may be promising candidates for predicting A-RLA.

A panel of several biomarkers can provide a clinically meaningful prediction of possible resistance at first diagnosis [18].

The development of arthritis depends in part on spirochetal factors, including the type of ribosomal spacer and the sequence of outer surface protein C. The immunological background includes a Th1-related response, but IL-17 provides an additional pathway for the development of arthritis. Autoimmune mechanisms can lead to antibiotic-resistant arthritis. [19].
Lyme arthritis usually presents as acute inflammatory monoarticular arthritis, which is often difficult to distinguish from septic arthritis.

While treatment for Lyme arthritis focuses on antibiotic therapy, septic arthritis requires surgery plus antibiotic therapy. Delay in Lyme serology results may complicate surgical decisions in Lyme-endemic areas [20]. On the other hand, antibiotic treatment in patients with spirochetal infections can cause Jarisch–Herxheimer reaction (JHR) [21]. This complication develops up to 10 days, usually within 24 hours after antibiotic treatment of the Lyme disease and is manifested by fever, chills, severe pain and skin rash. It was examined in our patient.

Rheumatoid arthritis (RA) and Lyme arthritis can be difficult to distinguish because the symptoms are similar. This represents a significant clinical challenge, as treatments are quite different in both diseases.

It is now known that LA is caused by a tick-borne spirochete that spreads to the joints, where it induces a marked proinflammatory response. In the majority of examined patients, arthritis resolves with antibiotic treatment. However, in the United States, about 10% of arthralgia patients develop persistent synovitis that persists for months or even years after apparent elimination of the spirochete from the joint by antibacterial therapy. Differential diagnosis of acute infection to chronic synovitis can help in diagnosis, but also other forms of chronic inflammatory arthritis, including RA [22].
We received confirmation of the diagnosis of Lyme arthritis after a two-stage serological diagnosis and determination of OspCBg IgM and OspCBb IgM diagnostics.

According to Nimmrich, S. Becker, (2014) Antibodies against OspA, as an indicator of the later stage of infection, were observed more often in the refractory group, without reaching a significant level. No clinical marker has been identified as an indicator for severe or prolonged courses of Lyme arthritis.

Practical significance

Pediatricians in endemic areas, especially those providing primary, hospital or emergency care, should be familiar with the clinical presentation and have a high index of suspicion for LA to prevent inappropriate treatment.

Conclusions.

1. Acute monoarthritis of the knee is the most common presentation (54% in our cohort) and is often misdiagnosed as septic arthritis, leading to unnecessary hospitalizations and aggressive interventions.
2. Lyme arthritis occurs more often in children with significant synovial pleocytosis. When evaluating a child with arthritis, laboratory results are not specific and should be used with caution.
3. There are unusual cases that require careful differential diagnosis.

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