Skin Changes in Suspected Lyme Disease

Dear Editor,

Ticks carry many diseases, bacteria, and viruses and represent a very important healthcare issue both in Croatia and globally. Although most ticks are not infected with pathogens dangerous to humans, some ticks can transmit infectious diseases with significant morbidity and mortality. This is caused by the increasing incidence of many tick-borne diseases over a growing geographical area. Many factors influence which species of ticks are present in a given geographical area, as well as the density of their population and the risk of human exposure to infected ticks. The average morbidity from Lyme borreliosis in the Republic of Croatia is 6.51 infected per 100,000 inhabitants. There can be no Lyme borreliosis without ticks infected by *Borrelia burgdorferi* (1,2).

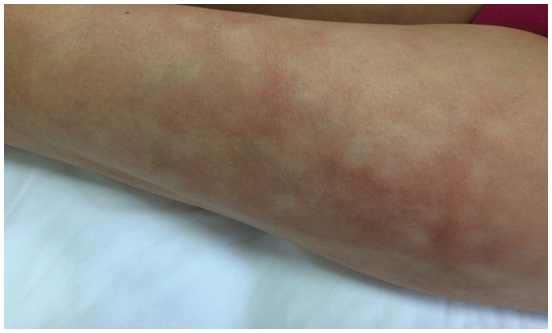

Figure 1a. Figurate erythema on the lower left leg, confluent erythematous foci.

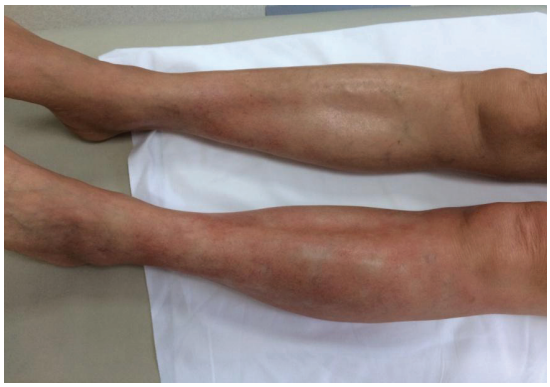

Figure 1b. Figurate erythema significantly more pronounced on the lower left leg.

In Europe, Lyme borreliosis (LB) is caused by the *Borrelia burgdorferi* sensu lato complex genotype. There are three skin manifestations of LB: erythema migrans (EM), borrelial lymphocytoma (BL), and acrodermatitis chronica atrophicans (ACA) (3,4).

Herein we describe a female patient with a diagnosis of Lyme disease based on the non-specific clinical picture and laboratory diagnostics, in whom successful treatment led to complete regression of all skin manifestations.

The patient was a 58-year-old woman with no previous history of severe illness. Notably, the patient history showed that, eight months prior to presenting for the dermatological exam, the patient had

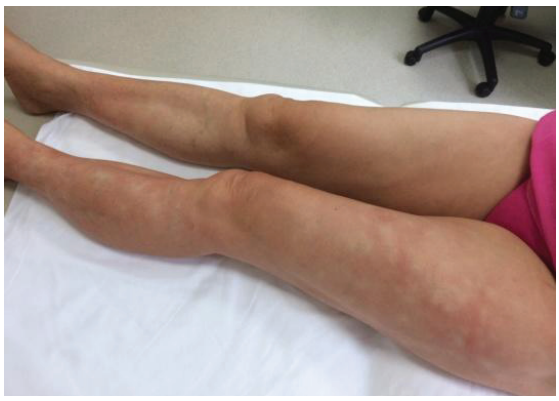

Figure 2a. Before treatment.

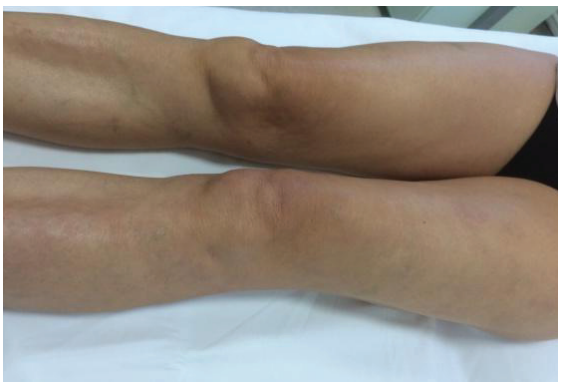

Figure 2b. After treatment.

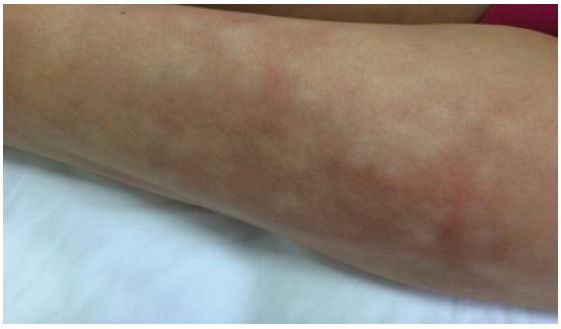

Figure 3a. Before treatment.

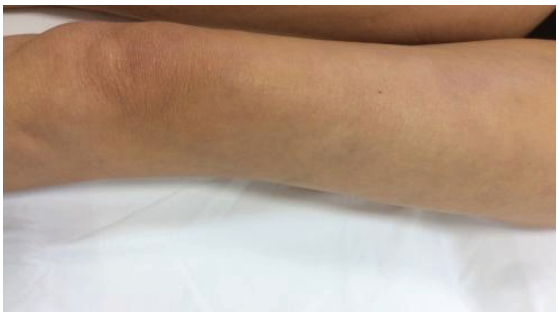

Figure 3b. After treatment.

observed the appearance of edema and demarcated macular exanthema around both ankles and subsequently on the dorsum of the right hand, which spread to the left hand and with gradual spread to both lower legs and the lower extremities, with more pronounced changes on the left leg.

The initial dermatological examination found pronounced skin changes on both legs, especially the left leg, with erythematous changes in the form of figurate erythema forming confluences up to the size of a smaller palm; the skin of the left leg was partially mottled with normal turgor and elasticity (Figure 1a and Figure 1b).

Inguinal lymph nodes were enlarged and painless on palpation. Changes were minimal and discrete on the right leg and were absent on the torso, upper extremities, and skin. Subjectively, there was no itching, burning, or tingling sensation in the affected areas of the skin. The patient subjectively reported feeling well.

Family history showed that the patient's father had died from prostate cancer and that the mother had died from melanoma.

Laboratory findings were as follows: hematological, biochemical, and immunological parameters were normal. Venous and arterial ultrasound of both legs was normal, with the presence of reactively enlarged left inguinal lymph nodes.

Lyme disease was suspected based on the clinical picture, with a differential diagnosis of possible

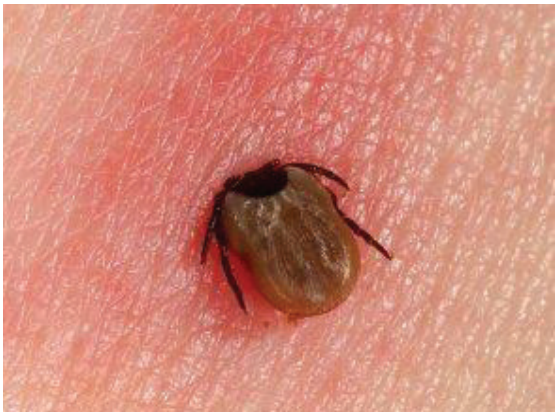

Figure 4. Tick bite on the skin.

livedo reticularis. A biopsy of the skin changes was also performed, with the results showing that the histological picture in the examined material could be compatible with the provisional clinical diagnosis of livedo reticularis.

IgM and IgG specific for *Borrelia burgdorferi* was also performed: IgG was borderline, whereas IgM was positive at 218 U/mL.

Over the next 3 weeks, Amoxil 500 mg thrice daily was introduced to the treatment. After completion of the treatment, there was a gradual regression of all skin changes without the appearance of new lesions (Figure 2a and Figure 2b) (Figure 3a and Figure 3b).

Patient follow-up over the next year did not find any recurrence of similar skin changes.

Herein we have described the case of a patient with atypical skin changes in which the presence of antibodies for *Borrelia burgdorferi* was demonstrated, in which regression of all skin manifestations was achieved after diagnosis and adequate antibiotic treatment.

Lyme disease has a wide spectrum of clinical manifestations that can generally be observed in three stages: the early localized stage, the early disseminated stage, and the late stage of the disease. However, it

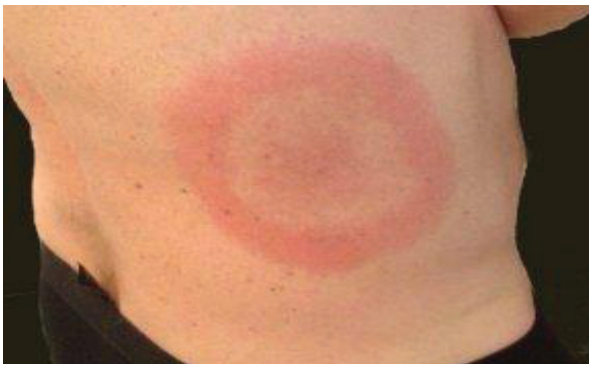

Figure 5. First stage of erythema chronicum migrans.

is also possible for the different stages to overlap and even for the late stage to manifest without any signs and symptoms of the earlier stages.

Early localized stage. Characterized by skin changes – erythema migrans (EM) – usually manifests within a month of the tick bite (usually 7-14 days after the bite) (Figure 4 and Figure 5).

EM manifests in approximately 80% of patients, but only 25% of patients can recall the tick bite. The skin changes are usually localized in the axilla, the groin, the cubital area, or around the waist. The changes are generally not painful, but can itch or be warm to the touch. They gradually spread over days or weeks and can grow to a radius of up to 20 cm. Initially, the coloration can be uniform for several days, after which the redness disappears around a central zone (4-6).

Multiple skin changes are a sign of spirochetemia and not the result of multiple tick bites. Due to timely antimicrobial treatment, multiple skin changes are much rarer today. In the initial days or weeks after infection, patients with early, localized, or disseminated Lyme disease often present with non-specific signs and symptoms resembling a viral infection: fatigue, headache, loss of appetite, joint pain, and regional lymphadenopathy. Fever can be present in approximately 20% of patients.

Laboratory findings in this phase are non-specific. Erythrocyte sedimentation can be slightly increased, leukocyte counts are mostly normal, and anemia and thrombocytopenia are present only rarely (7,8).

Early disseminated stage. This stage is marked by numerous EM lesions (that generally appear days or weeks after the infection) and/or neurological and/or cardiac manifestations (occurring weeks or months after infection). Some of these patients have no data on the presence of early localized Lyme disease.

The most common triad of neurological manifestations are meningitis, neuropathy (usually of the facial nerve) and motor or sensory radiculopathy (Bannwarth syndrome). All these manifestations can appear individually. Cranial nerve neuropathies can often be bilateral.

Late-stage Lyme disease. Characterized by intermittent or permanent arthritis in one joint or several large joints, most commonly the knees, and/or more rarely by neurological symptoms such as discrete encephalopathy or polyneuropathy. Late-stage Lyme disease can develop several years after primary infection, and arthritis can be the first manifestation of the disease, with the early localized and early disseminated stages not manifesting at all. In Europe, patients with late-stage Lyme disease can present with chronic skin changes (acrodermatitis chronica atrophicans), which is not observed in the USA. It is caused by *B. afzelii* and is typically localized to the extensor surfaces of the hands and feet. It is most common in women >40 years of age but can also present in younger populations. However, due to early antimicrobial treatment of the earlier stages of the disease, late-stage manifestations are rare (9). The discovery of the etiology of this disease showed that some well-known clinical entities were also a manifestation of Borrelia infection. The etiology of other dermatologic diseases was thus determined, such as lymphocytoma (or lymphadenosis cutis benigna), which was recognized as an entity as early as 1884, as well as acrodermatitis chronica atrophicans, described in 1888, erythema chronicum migrans (Afzelius-Lipschütz), and the neurological disease called Bannwarth syndrome, the symptoms of which were described as early as 1922 (10,11).

LB and all its dermatological manifestations occur in almost all European countries, predominantly in the central part of the continent. The annual incidence is between 9.4 cases per 100,000 inhabitants in France to 120 cases per 100,000 inhabitants in northeastern Poland, 130 cases per 100,000 inhabitants in Austria, and 155 cases per 100,000 inhabitants in Slovenia (12).

The total prevalence of ACA in all European patients with LB is 1-10%, depending on the region. For example, BL and ACA comprise 0.3% of LB cases in Bulgaria. In Norway, ACA comprises 5% of all clinical LB cases, and in northern Italy that number is 2.5%.

Establishing a diagnosis of ACA is much more difficult than diagnosing EM or benign lymphocytoma (BL) because the clinical manifestations of ACA can vary. Acrodermatitis chronica atrophicans is probably the most common late and chronic manifestation of LB that can be observed in European patients.

The skin changes in our patient were fairly nonspecific, based on descriptions from the literature, but positivity for IgM antibodies was important for establishing the diagnosis, along with the very good response to antibiotics regarding regression of skin changes as well as the histological analysis that, according to the pathohistological diagnosis, indicated livedo reticularis, which is in turn also described in the literature as a possible form of ACA depending on the stage of the disease. Skin changes on the lower extremities are often incorrectly interpreted as vascular insufficiency, e.g. chronic venous insufficiency, superficial thrombophlebitis, hypostatic eczema, obliterative arterial disease, acrocyanosis, livedo reticularis, or lymphoedema, but they can also be the result of ACA, as in our case (13-15).

In cases such as the one we have described, clinical manifestations of Lyme disease can very often vary and differ greatly from the typical clinical picture. This is demonstrated by our case, which also shows that LB and its idiosyncratic manifestations can lead physicians astray in a condition where failing to establish a timely diagnosis can be fatal for the patient. This case report also serves as a reminder that Lyme disease should be considered whenever atypical skin changes are encountered. Given that ACA is a disease in the late stage of Lyme disease and that the changes in our patient were noticed at the very beginning, the disease did not develop to the later stage.

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