

Seronegative Borreliosis?

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Dear editor,

We report a 14-year-old female patient who was presented at the Dermatologic polyclinic with complains of a severe redness on the lateral part of the left lower leg, without any subjective complains, including itching. Within the dermatological examination, an oval annular lesion with a diameter of 5 to 6 cm and active erythematous peripheral edge with central punctual erythema was established, slightly resembling clinically purpura policosa or tinea cutis glabra (Fig 1a, 1b). The duration of the complains was approximately 2,5-3 months, with increasing of the size and slightly fuzzing of the peripheral contours in comparison with the initial clinical picture during this period. No history for tick or other insect bite in recent months was reported. A lack of improvement after initial treatment with topical clotrimazole and corticosteroids containing creams, accompanied by oral antihistamines with duration of 15 days, was reported.

A lack of improvement with oral administration of terbinafine 250 mg/daily for 2 weeks was also presented. Topical application of Pimecrolimus 1% Cream 2 times per day for a period of 4 weeks was initiated as a following therapeutic choice, also without evidence of improvement after it. The conducted laboratory tests and serological screening, as well as the performed imaging diagnostic procedures were within the normal range. Serological and immunological screening for ANA antibodies, Anti-Borrelia burgdorferi antibodies (ELISA), ACE enzyme C3 and C4 fractions of the complement were also without deviations. Microscopic examination and mycological culture on Sabouraud Dextrose Agar were negative for fungal pathogens. The patient refused categorically the performance of a skin biopsy.

The diagnosis of erythema chronicum migrans was made clinically and therapy with doxycycline 100 mg- 2 times daily was initiated for a period of three weeks. Complete remission of the clinical symptoms was observed on day 12, without application of any additional local therapy (Fig. 1 c).

Regarding some collectives and recently described studies the serologic confirmation is fast always required for the diagnosis of Lyme borreliosis in all of the patients except those with well confirmed and typical erythema chronicum migrans lesion (ECM), [1]. However, it should be assumed that all serology

markers should be positive in patients with duration of the complaints more than two months [2].

The kinetics of antibodies to Borrelia burgdorferi following successful treatment of early and late cutaneous borreliosis could be analysed in consecutive serum samples by an enzyme-linked immunosorbent assay (ELISA) technique [2]. Reading the observation of other colleagues twenty-three patients with culture positive erythema migrans were followed for 23+/-14 months: 41% stayed seronegative, 35% showed an isolated immunoglobulin M (IgM) response, 8% an isolated IgG response and 16% a combined IgM and IgG responses [2]. In general, antibody levels peaked within the first 3 months of symptom onset, whereafter a gradual decline was observed within 1 year [2]. Twenty-two patients with chronic cutaneous borreliosis were followed for 23+/-11 months and all patients stayed IgG positive [2]. Nearly three-quarters showed a clear decline in IgG levels over the years, while the rest did not [2]. After 9+/-1 years 88% of 16 patients examined were still IgG positive [2]. Twenty percent of the patients remained seronegative throughout other study, within which antibodies for borreliosis are examined by immunoblot methods [3].

Interesting is the fact that seronegative children with arthritis showed positive DNA samples for Borrelia DNA in the synovial fluid of joints, affected by the infection [4]. Similarly in patients with chronic lymphatic leukemia, the negative serologic reactions should be due to the inadequate immune response, as a result from the immune cells damage within the framework of the underlying disease, or the performed combined chemotherapy [5]. In those serological negative cases, the conduction of a PCR in the cerebrospinal fluid seems to be from a paramount importance, as it will provide a positive result, however [5].

In conclusion, specific treatment should be initiated in all patients with typical clinical picture of erythema chronicum migrans, namely the ring-shaped skin lesion, centred on the bite: purpura pulicosa, which expands outwards, appearing within 2 weeks after an insect bite [6]. The therapy could be and should be initiated even the serology is negative. The initiating of an effective antibiotic therapy is essential and beneficial for patients with typical clinical picture of ECM, regarding the fact that substantial number of patients stayed seronegative, as in the case presented by us [2, 3].



Figure 1a,b: Clinical manifestation of erythema chronicum migrans in a 14-year-old female patient: typical clinical picture of a ring-shaped skin lesion, located on the left leg, with no evidence of central insect bite. **1c:** Clinical manifestation of the lesion which was significantly improved with complete remission of the symptoms after therapy with doxycycline 100 mg- 2 times daily for three weeks.

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