Chronic Urticaria Caused by Five Types of Borrelia: Case Study

Sajma Krkic Dautovic¹, Refet Gojak², Nermin Mostarac²

¹Private Practice of Infectious Disease Specialist, Sarajevo, Bosnia and Herzegovina
²Clinic of Infectious Diseases, Clinical Center of University of Sarajevo, Bosnia and Herzegovina.

Corresponding author: Sajma Krkic Dautovic. MD, PhD, Specialist of Infectology, Private Surgery, Sarajevo, Bosnia and Herzegovina. E-mail: sajmadautovic@gmail.com.

**Background:** Lyme disease (Lyme disease-LD) is a disease of humans and animals that is transmitted by hematophagous insects, especially ticks. The causative agent is the spirochete Borrelia burgdorferi, a bacterium with a complex structure and a slow biorhythm, which has the ability to coat the host’s organism with mucus - create a biofilm - or turn into a cyst, and the host does not recognize it and does not create antibodies. This is the reason why, in 10-60% of cases, Borrelia tests are negative, even though it is present. The diagnosis of LD is made clinically, and it is confirmed serologically and microbiologically by isolation and/or detection of the causative agent by the PCR method from tissue samples and body fluids. Lyme disease stage II and III is called “the great imitator” because its symptoms resemble those of other diseases, so diagnostic errors are often made. **Objective:** In this article we presented a case of stubborn urticaria in a 28-year-old saleswoman. **Case presentation:** Mother of two children, who was ruled out by clinical examination for autoimmune diseases and allergies to available allergens. We subsequently confirmed the diagnosis of chronic borreliosis, caused by five types of borrelia, serologically, after advanced intermittent antibiotic therapy, and after acquired food intolerance was discovered. In the available literature, we did not find information that chronic generalized urticaria was caused by Borrelia in combination with food intolerance. **Conclusion:** The presented case of a patient with chronic urticaria indicates that similar cases with urticaria, as well as all skin changes with intermittent walking symptomatology, should: Undergo clinical treatment, rule out immunological diseases and drug allergies, then test for Borrelia (ELISA + immunoblot with Borrelia protein sequences!). Take into account the duration of the disease, the possibility of the disappearance of antibodies created in early childhood or a false-negative finding of antibodies, and in case of a negative finding, do not give up ex-vuvantibus therapy.

**Keywords:** chronic urticaria, chronic borreliosis, food intolerance.

CASE REPORT

August 2017), with burning and itching of the skin. The appearance of an allergic rash is preceded by a frontal headache, then “bumps” of different shapes and sizes break out, sometimes cluster like, which slowly disappear on antihistamines (Figures 1 and 2). The rash appears on all parts of the body, including the soles of the feet, with unbearable itching, swelling of the tongue, dizziness, and difficulty breathing. For the last 15 days, she has had additional pain and stabbing behind the sternum, regardless of the severity of the skin changes, so she cannot take a deep breath, with the feeling that someone is sitting on her chest or that her lungs are in armor. Because of this, sleep is disturbed, in the morning she cannot get out of bed because of the feeling of fatigue. Because of the aforementioned complaints, she often received ampoules of chloropyramine, calcium and dexamethasone in the evening at the Emergency Station. She had no other complaints. Appetite was good, defecation and urination regular. Since the allergy did not go away with prescribed antihistamine therapy for 6 months, in February 2018, it was completely clinically treated at the Dermatovenereology Clinic in Tuzla, but the cause of the urticaria was not found. A triple therapy was applied in the hospital due to a positive test for H. pylori. Upon discharge and recommendation, she takes antihistamines twice a day, despite this, she has a rash and accompanying symptoms almost every day.

Previous medical history: Properly vaccinated in childhood, previously Varicellae. She had occasional sore throats, tolerates penicillin. She thinks she is not allergic to food and pollen, but in the last 3-4 months she became allergic to metamizole sodium hydrate and diclofenac, which she takes for headaches. Menarche at age 13, regular cycle. She gave birth to two healthy children. She lives with her husband and children in the countryside in a private house, with a garden, which she cultivates. Growing up in the countryside, she was often bitten by ticks as a child. Eight months ago (August 2017), and one month before the appearance of the rash, she had a round, continuous redness of the size of her palm, like a red stamp, on her right gluteus, which spread to the left side, and then similar smaller red changes spread to the rest of the skin. At first, there was no itching. Treated as urticaria. Clinical examination by an infectious disease specialist: except for the painful sensitivity of the head to percussion and the sensitivity of the upper Valeoux’s points, the findings on the internal organs are normal. Blood pressure 110/60 mmHg, pulse 84/min. The skin of the trunk and arms is clean, except in the area of the inner sides of both upper legs and the upper quarter of the back of the lower legs, where there are abundantly expressed striped, more longitudinal bluish changes, which he has had for 2-3 years, thought to be stretch marks (Figure no. 3 and 4).

Findings: discharge letter from Dermatology, University Clinical Center Tuzla: dg. Urticaria chr. recidivism. In the findings, apart from the positive serology for H. pylori, all biochemical tests were normal, allergy to metamizole sodium hydrate and diclofenac. Given the chronicity of the disease, a triple therapy was prescribed in the hospital due to a positive test for H. pylori. Upon discharge and recommendation, she takes antihistamines twice a day, despite this, she has a rash and accompanying symptoms almost every day.
tests were negative, as well as the stool test for Candida, parasites and protozoa, total At-IgE=19.1 (N<100). All immunological tests were negative. Borrelia test was not performed.

Conclusion of the infectious disease specialist: based on the anamnestic and epidemiological data, clinical picture, course of the disease, performed examinations and clinical findings of bluish skin changes on the inner side of the upper legs and the back of the lower legs, it is concluded that the patient is dealing with an exacerbation of chronic borreliosis, which had primary dissemination in August last year, with involvement of the skin and respiratory system. It was recommended that a test for vitamin D and serology for Borrelia be performed: ELISA and Immunoblot, that the therapy be started immediately with Clarithromycin 2x500 mg for three weeks, along with Probiotic and vitamins C, B and D, and that the therapy be carried out under the control of an infectious disease specialist. She was warned that from 2-15 days of therapy may have a transient worsening of symptoms (Herksheimer’s reaction).

First control follow-up: May 14, 2018, the patient generally feels better, with the information that since the third day of antibiotic therapy, swelling of the face, rash on the skin of the whole body despite antihistamines, dizziness and severe headache (Herksheimer’s reaction) have appeared. She contacted an infectious disease specialist by phone, and on his recommendation, she additionally took calcium along with antihistamines and continued the antibiotic therapy. From the sixth day of therapy, the rash began to recede from the skin of the arms and trunk, and after 10 days it was expressed only on the face and legs; the dizziness stopped, as did the swelling of the tongue, and a few days before the follow-up, the pressure and pain behind the sternum disappeared. The burning of the skin is occasionally very weak, or absent. The sleep, with antihistamines once a day, was good. Other vegetative functions are normal. Clinical: except for moderately expressed reddish urticarial changes on the skin of the front and inner thighs, and on the skin of both knees, the skin in other parts of the body is clean. The previously described streaky bluish applications on the inner side of the thighs and the upper part of the lower legs are unchanged. Borrelia serology performed was negative: ELISA IgM and IgG-At=negative, as well as Immunoblot with total IgM and IgG-At, and all protein sequences were negative. Vitamin D was significantly reduced to 13 (N=30-50). Due to the favorable effect of Ex-yviantibus therapy, the recommended antibiotic therapy was continued for another two weeks permanently, then intermittently: 10 days at a time, with a pause of 20 days in between. After that, the breaks from antibiotics were extended by 10 days after each intake, with supplements and a diet without sugar and with a minimum of carbohydrates. In the following days, despite the therapy, eruptions of urticaria appear again on the skin of the whole body, especially when she is at work in the store or in the sun. Although less intense than before, along with the urticaria, all other complaints returned. The medical history reveals that she often eats canned tuna and sardines, yellow cheeses and loves chocolate. It was recommended to perform a food intolerance test. The test done (July 23, 2018) showed that she has an intolerance to most of the foods she eats the most (tuna, sardines, chocolate, edible oils, milk and dairy products - except yogurt). She was advised to select the list of foods she is allowed according to the test and to adjust her diet.

Second control follow-up: At the second control, the antibiotic clarithromycin was changed to doxycycline. Four months after the start of the recommended therapy and with the diet, urticaria eruptions are less frequent and less intense, and all complaints are greatly reduced and rare. Urticaria and complaints did not occur if she followed the prescribed diet. Controls were performed every 3 weeks. Due to intolerance to doxycycline, clarithromycin was reintroduced, along with supplements. Since September 2018, it has been checked every 8, later 12 weeks. The complaints of low intensity returned whenever she took food she shouldn’t (chocolate most often) and quickly subsided on antihistamines and calcium. Control serology for Borrelia (June 2019) was resoundingly positive. Immunoblot: total IgM-phase antibodies positive, and positive protein sequences p41, + p39+, OspC+, and p18-limited, , total -AT IgG phase= negative, with positive protein sequences p41+ and OspC+, and borderline p100 +/-. Positive OspC IgM for Borrelia B.sensu stricto, B.Afzelii, B.garinii, B.spielmanii, and p18 IgM was found for Borrelia B.afzeli and B.bavariensis.

At the last follow-up (October 24, 2020), the patient is in a good general condition, without complaints, with clear skin, except for the still visible bluish streaky changes on the skin of the upper legs and the upper part of the lower legs, which are partially white in color. She is satisfied and happy, she does not take antihistamines, calcium or corticosteroids. She avoids direct sunlight and prohibited foods according to the intolerance test. Until the last follow-up, she took antibiotics for 10 days (Clarithromycin for 10 days, with Metronidazole for five days) with breaks of 70 days, with supplements. Since she has not had urticaria eruptions for the last 2 months, only essential oils of wild oregano and tea tree were recommended in the therapy along with a diet according to the food intolerance test.

4. DISCUSSION

Chronic urticaria can be caused by: infectious diseases, autoimmune diseases, and intolerance to certain foods or medicines. In our patient, autoimmune diseases, drug allergy and pollen were excluded. Based on the findings of bluish streaky skin changes (9), we suspected a chronic Borrelia infection, despite negative serological findings, and started ex-yviantibus therapy, in agreement with the patient. Herxheimer’s reaction
to the antibiotic therapy started in the first week was an indication that we are on the right track. Chronic borreliosis was later serologically confirmed under therapy. Under antibiotic therapy, the patient no longer had allergic manifestations to metamizole sodium and diclofenac. We consider the discovered intolerance to a large number of foods to be induced by borreliosis, because in three years we treated eighteen patients with different localization of borreliosis and developed food intolerance (unpublished data).

According to literature data, Borrelia afzelii most often causes skin changes (10). In our patient, B. afzelii was confirmed, as well as an additional four different types of Borrelia. Perhaps this is the reason for the persistence of chronic urticaria and the appearance of bluish streaky changes on the skin of our patient's legs. In 2019, a similar paper was published, in which the case of a patient with multiple episodes of urticaria without data on previous EM rash is presented (11).

5. CONCLUSION

The presented case of a patient with chronic urticaria indicates that similar cases with urticaria, as well as all skin changes with intermittent walking symptomatology, should:
- Undergo clinical treatment, rule out immunological diseases and drug allergies, then test for Borrelia (ELISA+ immunoblot with Borrelia protein sequences!).
- Take into account the duration of the disease, the possibility of the disappearance of antibodies created in early childhood or a false-negative finding of antibodies, and in case of a negative finding, do not give up ex-yuvantibus therapy.

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