

Otolaryngological symptoms in patients treated for tick-borne diseases

Authors' Contribution:

A—Study Design
 B—Data Collection
 C—Statistical Analysis
 D—Data Interpretation
 E—Manuscript Preparation
 F—Literature Search
 G—Funds Collection

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ABSTRACT:

Introduction: In recent years tick-borne diseases have become a very serious problem. The most common of these infections are borreliosis (Lyme disease) and tick-borne encephalitis (TBE). Lately there is growing incidence of Bartonella, Babesia, Anaplasma and Brucella co-infections. The similarity between the symptoms of tick-borne diseases and other pathologies causes serious diagnostic issues.

Material and methods: 216 patients aged 18–55, who presented to the outpatient clinic for tick-borne diseases in the years 2014–2016, were enrolled in the study. The patients had been diagnosed with Lyme disease and co-infections. The principal diagnostic tests to confirm the infections included ELISA, Western-Blot and circulating immune complexes (CIC).

Results: In the group of 216 patients, 162 presented with otolaryngological symptoms. The most common complaint was tinnitus (76,5%) accompanied by vertigo and dizziness (53,7%), headache (39%), unilateral sensorineural hearing loss (16,7%). The patients also had tick-borne coinfections, among them the most common was Bartonella henselae (33,4%) and Bartonella quintana (13%).

Conclusions: Otolaryngological symptoms are a common manifestation of tick-borne diseases. They are most frequently observed in Lyme disease and Bartonella spp. infections. The symptoms in the head and neck region are usually occur in chronic Lyme disease with predominant IgG antibodies nad VlsE antigen.

KEYWORDS:

borreliosis, Lyme disease, co-infections, bartonellosis, laryngology

INTRODUCTION

In the last few years tick-borne diseases have become a very serious problem. They have started to affect even larger population. The infection is caused by a tick bite. Tick is a vector of numerous pathogens – among others viruses, bacteria and protozoa. In Europe, the most common species of tick is *Ixodes ricinus* [1,2].

The most common tick-borne diseases are borreliosis and tick-borne encephalitis (TBE). In recent years the number of infections caused by pathogens from Bartonella, Babesia, Anaplasma, Brucella and other species has also been increasing. Because of the varied polymorphism of symptoms and imperfection of diagnostic tests these diseases are still difficult to identify and patients still grapple with persistent clinical symptoms and lack of unequivocal and precise diagnosis. Similarity of the symptoms of tick-borne diseases with other diseases poses a serious diagnostic challenge.

AIM OF THE STUDY

The aim of the study was to evaluate the incidence of otolaryngological symptoms in patients with diagnosed borreliosis and other tick-borne diseases and also to evaluate the frequency of presentation of the specific symptoms depending on the stage of the disease.

MATERIAL AND METHODS

A total of 216 patients who presented to the outpatient otolaryngological clinic for a visit in the years 2014–2016, and had diagnosed borreliosis and co-infections, were enrolled to the study. The basic diagnostic tests confirming the above-listed infections included ELISA, Western-Blot and circulating immune complexes (CIC) test. Patients enrolled in the study did not present with any significant abnormalities in imaging (CT of the head,

MRI, Doppler ultrasound of the neck arteries). They denied presence of any traumas or conditions which could contribute to developing symptoms coming from the organs of the head and neck. Patients with chronic metabolic diseases, circulatory and nervous system diseases were excluded from the analysis.

RESULTS

Borreliosis – Lyme disease - is a zoonotic disease caused by spirochetes of *Borrelia burgdorferi* – Gram-negative bacteria from the family of Spirochetaceae and related species.

In Europe, until today, four strains pathogenic for human were described: *Borrelia burgdorferi sensu stricto*, *Borrelia afzelii*, *Borrelia garini*, and *Borrelia spielmanii*.

In the examined group of patients the distribution of spirochete strains described in the study was as follows (Fig. 1)

Among all 216 patients with diagnosed tick-borne diseases 162 patients manifesting otolaryngological symptoms were selected. The main symptom that was reported by the patients was troubling tinnitus (76.5%) – in the overwhelming majority of high frequency. This symptom was most frequently accompanied by vertigo and dizziness (53.7%), headache (39%), unilateral sensorineural hearing loss (16.7%) and others.

Also duration and therefore the advancement stage of the disease influenced the intensity and polymorphism of the symptoms reported by the patients. Antibodies in the IgM and IgG classes present in the blood serum and surface antibody specific antigens were analyzed. In the group of patients with present IgM antibodies OspC antigen and other surface antigens predominated (Fig. 3) whereas in the group of patients with present IgG antibodies V1sE antigen and remaining surface antigens predominated (Fig. 4).

The prevalence of the presence of V1sE and p39 antigens in the case of IgG class antibodies may confirm the thesis that otolaryngological symptoms become noticeable and exacerbated in longer-lasting disease.

Tick-borne diseases are a prominent group of diseases influencing the intensity level of symptoms reported by the patient and reaction to the used treatment. Borreliosis is a dominant disease. However, among the examined patients the presence of other tick-borne diseases was also observed. The largest group included patients infected with bacteria of the *Bartonella henselae* (33.4%) and *Bartonella quintana* (13%) species (Fig. 5). Remaining co-infections, among the patients complaining about otolaryngological symptoms, were observed in single cases.

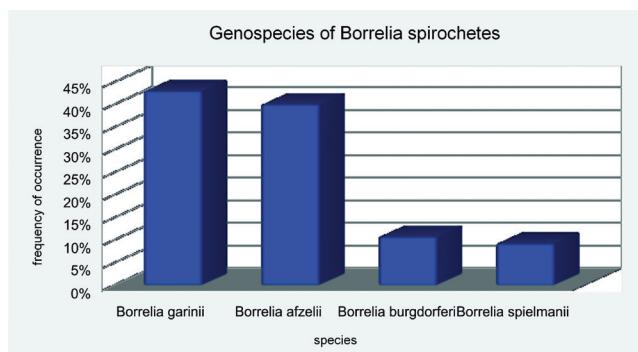


Fig. 1. Genospecies of *Borrelia* spirochetes

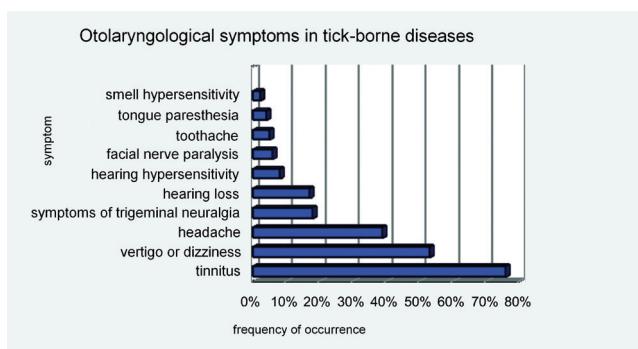


Fig. 2. Otolaryngological symptoms in tick-borne diseases

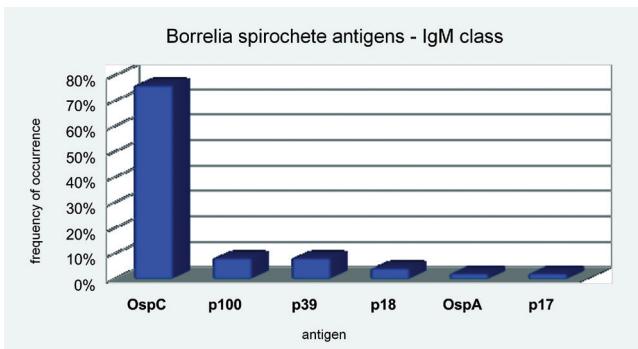


Fig. 3. Borrelia spirochete antigens – IgM class

Taking into account the fact that a major group of patients had positive results of the analyses (as for IgM class, IgG class or both concurrently) not only for borreliosis, but also for other co-infections, during treatment planning, antibiotics having influence on the elimination of abovementioned pathogens were considered. The most effective antibiotic turned out to be Ceftriaxon and the most effective combination treatment – Ceftriaxon with Rifampicin (Fig. 6). The efficacy of this combination treatment mainly suggests the influence of bacteria

from the *Bartonella spp* genus on the severity level of neurological and otolaryngological symptoms and on the incomplete reaction to treatment with the use of a single drug. Administration of medication acting on bacteria from the *Bartonella spp* genus (among others Rifampicin, alternatively Levofloxacin or Moxifloxacin) resulted in a significant improvement and faster withdrawal of symptoms that were troubling for patients (authors' own observation).

DISCUSSION

Borreliosis is a serious chronic multiorgan disease characterized by various clinical symptoms.

The disease has multiannual course and is divided to three disease stages. Two first stages – an early phase – develop within a few days to few months from infection. The third stage is called the late phase of the disease [3,4]. The first period of the disease manifests with skin lesions. A characteristic first sign of the disease is a migrating erythema (*Erythema migrans*) whose presence is an absolute indication for therapy with antibiotics and does not require performing additional immunoserological tests. In the second period it comes to dissemination of the spirochete via blood and lymphatic vessels. And the third stage of the disease may appear after a few months or even years from infection [3,4,5].

Changes within the central and peripheral nervous system, having an undoubtedly association with the occurrence of otolaryngological symptoms, start to show already in the second stage of the disease. In the late phase they increase and become more severe. Neurological disorders in the course of *B. burgdorferi* infection are caused by the direct action of spirochetes or their products on the neurons. A great tropism of these bacteria to the nervous system deserves attention. There is also a suspicion that spirochetes have an ability to find N-acetylglucosamine which is indispensable for their growth and is a component of the connective tissue. Predispositions of *B. burgdorferi* to infect the central nervous system (CNS) result probably from neurotropism of the strain and an immunologically different situation of CNS provided by the blood-brain barrier.

An indirect interaction between the spirochetes and a nerve cell on one hand causes its damage, and on the other hand stimulates immunological response against these bacteria. In neuroborreliosis attention is paid to existing lymphocyte-B- and T-dependent autoreactivity against endogenous neuronal structures (*B. burgdorferi* locates itself in the perineurium and endoneurium within the nerves). Their presence, in association

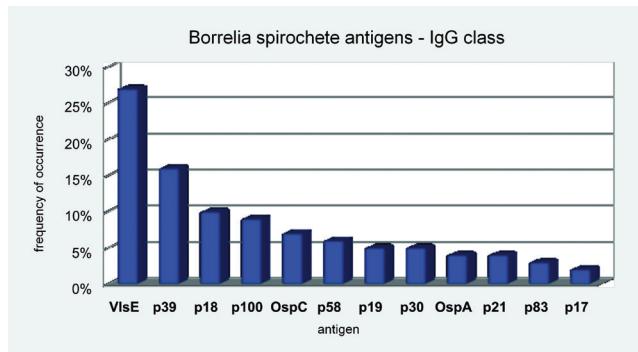


Fig. 4. Borrelia spirochete antigens – IgG class

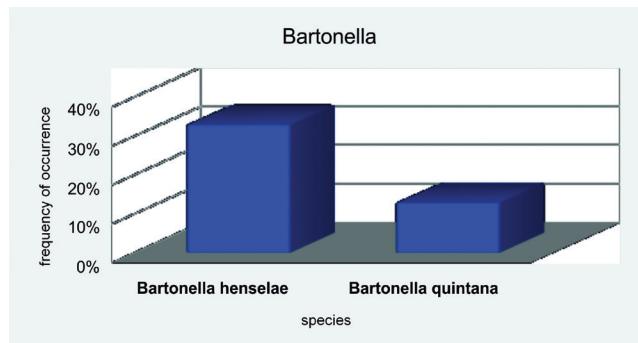


Fig. 5. Frequency of occurrence of species from Bartonella genus

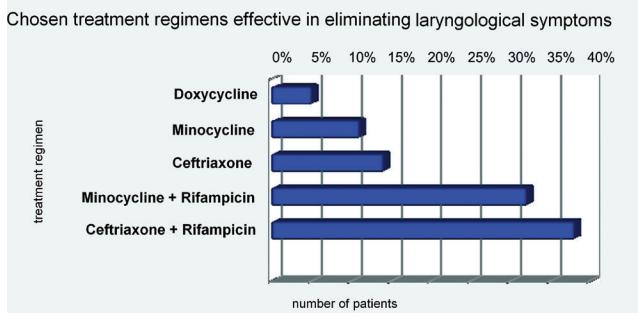


Fig. 6. Chosen treatment regimen effective in eliminating laryngological symptoms

with antigens with enriched 41 kDa fraction of flagellin, may cause triggering of proinflammatory mediators. Inflammatory and angiopathic lesions of peripheral nerves may cause axonal damage, resulting in peripheral neuropathy [11,12]. Therefore the most probable basis of neurological disorders in the course of neuroborreliosis is vascular lesions and in irreversible cases – demyelinating processes. According to Goldfarb, vasculitis may lead to permanent damage of the vessels supplying the nerve and in effect cause axonal neuropathy of various structures of the nervous system [9,10].

The most common symptoms in the course of neuroborreliosis are radicular pain and peripheral nerve paralysis, oculomotor nerve paralysis, paresthesia, face numbness, hearing loss, vertigo or dizziness, ataxia, transverse myelitis, and central nervous system vasculitis [5,6,7,9]. A frequent symptom is uni- or bilateral facial nerve paralysis. In a chronic, untreated borrellosis above-listed symptoms may persist for many weeks or months. It results in irreversible changes in the organism. Undoubtedly the condition of the patient with advanced borrellosis is worse in case of the occurrence of additional co-infections. The most frequent of them is bartonellosis. It is a zoonosis caused by bacteria from the *Bartonella* spp. genus belonging to the order of Rickettsiales. After penetration to a human organism, *Bartonella* genus bacteria undergo adhesion to epithelial cells (especially to the endohelium of blood vessels). During proliferation of the bacteria it comes to secretion of numerous proinflammatory factors and growth factors to the environment. There also follows inhibition of apoptosis of the infected cells. These changes stimulate proliferation of host cells and it comes to formation of tuberous structures in the epithelium of blood vessels which significantly handicaps blood flow in the inflamed vessels [8].

RESULTS:

1. Otolaryngological symptoms are a frequent manifestation of tick-borne diseases.
2. They occur most frequently in the course of borrellosis and infections by *Bartonella* spp. Bacteria.
3. The main symptoms are tinnitus, vertigo, headache and sensorineural hearing loss.
4. Symptoms from the organs of head and neck most often occur in the course of chronic disease (of which a decided prevalence of IgG antibodies and VlsE antigen in the group of examined patients is indicative).
5. Administration of third-generation cephalosporins is an effective method of treatment. It also seems that using combined treatment may be helpful (e.g. third-generation cephalosporin + Rifampicin, alternatively fluoroquinolone).

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