Can allergy affect the course of Lyme disease? A case report

Czy alergia może mieć wpływ na przebieg boreliozy? Opis przypadku

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Abstract

Sometimes other illnesses can complicate the course of allergic rhinitis, making it difficult to recognise or treat. An example of this type of connection is described in our case report of a patient with allergic rhinitis and concomitant Lyme disease. Aim of the study was to present the case of 54-year-old woman with a severe form of chronic allergic rhinitis, given the diagnosis of Lyme disease coexisting with inflammation of multiple joints. A 54-year-old patient with severe chronic allergic rhinitis, given the diagnosis of Lyme disease. Based on our description of the case, it appears that allergic inflammation from immunity in which a number of cytokines have been activated could be a factor favourable for launch by the spirochete *Borrelia burgdorferi* arthritis. Maybe the same immune disorders have led to the development of allergies contributing to such a course of Lyme disease and arthritis development.

Streszczenie

Czasami inne choroby mogą komplikować przebieg alergicznego nieżytu nosa, utrudniając rozpoznanie lub leczenie. Przykład tego rodzaju połączenia opisano w poniższym artykule, który dotyczy pacjentki z alergicznym nieżytem nosa i współistniejącą boreliozą. Celem badania było przedstawienie przypadku 54-letniej kobiety z ciężką postacią przewlekłego alergicznego zapalenia błony śluzowej nosa, u której rozpoznano boreliozę współistniejącą z zapaleniem wielu stawów. Na podstawie tego opisu wydaje się, że zapalenie alergiczne na podłożu immunologicznym, w którym doszło do uaktywnienia szeregu cytokin, mogło być czynnikiem sprzyjającym uruchomieniu przez krętki *Borrelia burgdorferi* zapalenia stawów. Być może te same zaburzenia immunologiczne, które doprowadziły do rozwoju alergii, przyczyniły się do takiego przebiegu boreliozy oraz rozwoju zapalenia stawów.

Introduction

Over 500 million people in the world suffer from allergic rhinitis [1]. It is the most common form of the non-infectious rhinitis occurring in cases when the person is genetically predisposed. Among these predispositions one can mention atopy, caused by Ig-E-dependent reaction for very diversified allergens: inhalants of the outer environment, as well as indoor. The most common outdoor allergens are dust molecules originating from grass, trees, and weed, and indoor are dust mites and animal allergens (cat, dog, cockroach). Nowadays there is a constant rise in morbidity rates for allergic illnesses. This phenomenon is caused, among others, by the air pollution stimulating plants to produce stress proteins. These allergens, simultaneously with dust from contamination, act as a transfer for inhalant allergens. These are

aeroallergens, which are the most frequent cause of allergic rhinitis; not food allergens, which are seldom a reason for this. During the tenor of allergic rhinitis there is infiltration of nose mucosa by various cells: eosinophils, mast cells (in the enlarged number), lymphocytes T CD4, Langerhans cells, and various mediators are then released by them – histamine, cysteinyl leukotrienes, nitrogen oxide, and cytokine (IL-5) [2, 3]. Contrary to allergic rhinitis, Lyme disease is a multi-organ illness caused by *Borrelia burgdorferi* spirochaetes, transmitted by ticks. In the tenor of this issue skin, joints, heart, or neural system overtake can occur [4]. The basic symptom on the basis of which Lyme disease progresses can be surmised is migrating redness [5]. Laboratory diagnostics of this illness is based on positive results of ELISA test, confirmed by Western blot test. However, diagnosis can only be provided combined with clinical symptoms of this [6–8]. Interleukin-33 (IL-33) is a cytokine belonging to the family of interleukin-1; it shows polyvalent activity. Among others, it induces T-helper lymphocytes, mast cells, eosinophils, and basophils to produce cytokines from the Th2 group [9, 10]. It is a vital regulator of allergic afflictions [11]. The main mechanism of action for this cytokine in the case of allergy is mast cell activation to produce various pro-inflammatory cytokines and chemokines [11]. Consequently, IL-33 can play an important role in the pathogenesis of allergic inflammations, such as allergic inflammation of mucosa [12]. This interleukin is believed to have importance in the pathomechanism of autoimmune diseases [13].

The aim of our work was to introduce the case of a 54-year-old woman with chronic allergic rhinitis, who was diagnosed with Lyme disease coexisting with arthritis.

Case report

The 54-year-old woman went to the allergic clinic in 2012 with symptoms of intensified runny nose, nose itchiness, and its blockade. These ailments had been recurring for a few years. She also mentioned the presence of cutaneous changes being some kind of papules on the basis of erythema, placed in the vicinity of haired head skin, cheeks, neck, and lobule of auricle. As a result of the applied diagnostics, allergic rhinitis in the tenor of polyvalent allergy and contact eczema from irritation was recognised. After applied treatment there was an upswing: significantly reduced nose and skin ailments. Half of a year ago the patient, while seeing a doctor, reported the presence of intensified pouring of watery rheum from the nose, nose blockage, and pain of several joints. Based on data from the interview she was directed to the rheumatology clinic. As a result of noticing antibodies against *Borrelia burgdorferi* in her organism, combined with clinical symptoms, she was hospitalised in an isolation ward with the suspicion of joint Lyme disease. In the period of intensified ailments from the side of respiratory tract and joints, she had IL-33 level measured. This was done in the framework of statutory diagnosis. The gauge was done by drawing a sample of blood from the veins (from the ulnar vein) into a tube with a separation gel – consisting of no anticoagulant, which was left for 30 min at room temperature. Then, after the sample curdled, it was centrifuged for 20 min at 2500 rpm (1000 × g), then serum was separated by division into three tubes and stored at 70°C. The concentration of IL-33 was marked with the use of immunoenzymatic method ELISA (Enzyme linked immunosorbent assay), using the ready set of agents SEB 694Hu. The gauge range of the kit was from 15.6 to 1000 ng/ml. After the initial dilution of the 10,000 pg/ml standard, the following standards were acquired: 1000 pg/ml, 500 pg/ml, 250 pg/ml, 125 pg/ml, 62.5 pg/ml, 31.2 pg/ml, and 15.6 pg/ml. Within the set a plate was used with 96 dimples surfaced with antibodies specific for IL-33, conjugated with biotin (in the study, as well as the ill woman, 59 other ill people and 19 volunteers took part). After adding the standards and serum, the plate was incubated for 2 h at 37°C. The content was agitated and then 100 µl of the Reagent A was added. After this, the plate was incubated for 1 h at 37°C. After threefold sluicing of the dimples, 100 µl of Reagent B was added, then everything was incubated for the next 30 min at 37°C. The content was agitated and the plate was sluiced five times. Ninety µl of substract solution (TMB) was added and the plate was incubated again for 20 min at the same temperature (protecting the plate from sunlight). Afterwards, 50 µl of a solution of sulphuric acid was added (Stop Solution) with the aim to end the reaction. The plate was measured using an ELISA reader with the wavelength equal to 450 nm with the capability of automatic concentration calculation. The concentration of IL-33 in the samples was defined comparing the optical density of the studied sample to the standard curve. The statutory measurement was approved by the Bioethical Commission.

In the patient' s case, down to the fact that her rhinitis was surmised to have allergic basis, skin prick tests were conducted with the set of basic inhalation

Table 1. The results of the tests with the set of basic inhalation allergens in the patient's case

Allergen	Derm. pter	Derm. farin	Cl. herb	Alt. ten	Alder	Hazel	Birch	Grass, grain	Rye	Sagebrush	Planatgo	Cat	Dog
Test result	0/0	0/0	1/2	1/2	0/0	3/4	0/0	3/5	3/5	0/0	0/0	0/0	0/0

Table 2. The set of food allergens examined in the patient's case

Allergen	Strawberry	Tomato	Hazel nut	Celery	Citrus fruit	Wheat flour	Cow's milk	Hen's egg	Walnut	Chicken meat
Test result	3/5	0/0	0/0	3/4	0/0	0/0	0/0	0/0	3/6	0/0

Table 3. The results of spirometry

Date	FEV_1 %	FVC %	PEF %	FEV_1/FVC %
06.2012	103	106	128	104
03.2015	104	107	125	105
07.2015	104	105	138	108
09.2016	110	108	134	110
10.2016	110	105	141	113

allergens, according to the Polish Allergological Society, and food allergens (Table 1).

It was stated that the tests were positive in the case of hazel, rye, and grass/grain. As well as the Basic Set, the woman was tested for mould mushrooms, getting a positive result for *Aspergillus fumigatus* – equal to 3/4, *and Penicillium notatutm* receiving the same value. After analysis the connection between the interview and aeroallergen prick test results, the clinical vitality for allergens from every positive test was established (Table 2).

None of the positive tests indicated an allergen clinically significant for the woman. Apart from skin prick tests, bearing in mind the coexistence of eczema in the vicinity of haired head skin, cheeks, neck, and lobules of auricle, a patch test was performed using the European Basic Series. These tests are conducted by laying a few haptens on the skin (especially on the back) [14] for 48 h. It is read after 48 and 72 h. The most commonly used is the European Basic Series, which contains of 28 haptens. Sometimes, for diagnosis a histopathologic test is required [15]. The tests were read according to the procedure after 48 and 72 h. They rendered negative in the case of every tested allergen (hapten). Hence, she was diagnosed with eczema on the basis of irritation. Except from skin tests, the patient underwent spirometry several times with an aim to examine eventual ventilation disorders (Table 3).

The spirometry was, during most of the visits, performed because of allergic rhinitis and its eventual implication on asthma development. It draws attention to the fact that in any of the spirometries obturation or restriction traits were not indicated – all of these rendered correct. The patient also had the level of IL-33 in blood marked using an ELISA test. The ELISA (enzyme-linked immunosorbent assay) test – immunoenzymatic test, is one of the most commonly used screening tests in biomedical research. It is used to indicate several proteins in the examined material using the antibodies coupled with a particular enzyme. Using this test she was diagnosed with elevated level of this cytokine (result: 120.33), comparing to healthy volunteers (100.65). The patient remains under many specialists' care. She still has pains in her joints, but less intensively. She currently takes a second antibiotic, Ceftriaxone, with slight clinical correction.

Discussion

At the beginning, one should ask oneself whether it was the immune disorders, which led to allergy development, contributed to such a tenor of Lyme disease and to development of joint inflammation, or whether in the case of Lyme disease coexisting with allergic afflictions there is a significant rise in the concentration of IL-33. We have not found a similar description in available world literature. However, based on the case of our patient, it seems that allergic inflammation on the immunological basis, when some cytokines were activated, could be an aiding factor for Lyme disease to trigger arthritis. The raised level of IL-33 is connected with various types of inflammation, also among allergic illnesses – having different immunological basis [12–14]. Perhaps in the case of our patient the raised level of this cytokine – associated with allergic inflammation – made it easier for the joint inflammation to develop because there were active immunocompetent cells in the case of allergic affliction. In a similar mechanism, atopic skin inflammation leads to allergic contact eczema [15, 16]. We know also from the Oostig *et al*. studies that *Borrelia burgdorferi* induces a response in the form of production of pro-inflammatory cytokines, primarily IL-1B [17]. As its role in the promotion of allergic inflammation seems to be clear, based on our description of the case, its task in developing the clinical symptoms of Lyme disease have not yet been explained. A great deal of research shows that IL-33 is strongly engaged in the pathogenesis of rheumatoid arthritis [18, 19]. Therefore, it seems that the raised level in the case of our patient could have triggered arthritis in the tenor of Lyme disease. However, it is a description of a solitary issue and thus needs more research.

Conclusions

The issues of Lyme disease occurring in the case of patients suffering from allergic afflictions seems to have heavier tenor than if it touched non-allergic. However, no distinct connections against the background of genetic, immunological, or environmental factors were indicated. Perhaps immunological disorders, which led to allergy development, contributed

to this flow of Lyme disease and arthritis. It should be asked, whether factors genetic in nature do not predispose for this kind of response. Because this interleukin has a role in the pathomechanism of autoimmune illnesses, maybe its raised level in the tenor of the patient's allergic affliction activated the autoimmune process in Lyme disease? Answers to these questions require more research.

Conflict of interest

The authors declare no conflict of interest.

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