

Case Reports

Eradication of *Blastocystis hominis* prevents the development of symptomatic Hashimoto's thyroiditis: a case report

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Abstract

In this case report we describe a 49 year-old man who presented with chronic urticaria, angioedema and soft stool consistency. During diagnostic examinations Hashimoto's thyroiditis was found even though the patient never had clear symptoms of this disease. *Blastocystis hominis* was isolated through a stool microbiologic examination, implicating that this parasite can cause the development of Hashimoto's thyroiditis and chronic urticaria. After two-weeks treatment with metronidazole the *Blastocystis hominis* was eradicated, then urticaria and angioedema disappeared. During the four years of follow-up, the patient presented without any symptoms, whereas thyroid hormones were normalized and anti-thyroid antibodies declined. For the first time in the literature we show that eradication of *Blastocystis hominis* can prevent the development of both symptomatic Hashimoto's thyroiditis and chronic urticaria.

Key words: *Blastocystis hominis*; urticarial, angioedema; Hashimoto thyroiditis; metronidazole.

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Introduction

Blastocystis hominis is the most common protozoan parasite in humans with incidence between 5-75% depending on the country's level of development [1-3]. Previously, it was considered as a non-pathogenic parasite [4]. However, a number of case reports recently showed that *Blastocystis hominis* infection is associated with chronic urticaria [5-7]. The study of Zuel-Fakkar *et al.* reported that *Blastocystis hominis* was found in 60.6% of patients with urticaria, whereas no parasite was isolated in healthy controls [8]. In general, urticaria is a very common skin disorder that can have immune, non-immune or idiopathic causes [9]. The idiopathic urticaria is accounted for in 75% of all urticaria cases [10]. Skin lesions appearing within a six-week period characterize acute urticaria, whereas chronic urticaria is defined as the presence of urticaria over a longer period of time. The prevalence of chronic urticaria is around one percent in the general population. Around 40% of patients with chronic urticaria have accompanying angioedema, typically affecting face, lips and periorbital region [11]. Chronic urticaria has also been associated with the presence of anti-thyroid

antibodies, or autoimmune thyroid disease, such as Hashimoto's thyroiditis with reported prevalence from 12-29% [11-14]. Urticaria is usually treated with oral antihistamines, but in some cases more aggressive treatment with corticosteroids, or cyclosporine is required [15].

It has been demonstrated that *Blastocystis hominis* can cause cutaneous allergies by activation of specific Th2 immune cells producing interleukins IL-3, IL-4, IL-5 and IL-13, which mediate IgE allergic response [2,16]. However, it has not been reported so far that *Blastocystis hominis* is a pathogen that could directly promote the development of autoimmune disease. In this case report we present how the treatment of *Blastocystis hominis* can prevent the development of urticaria and symptomatic Hashimoto's thyroiditis.

Case Report

A previously healthy 49 year-old man presented with urticaria, starting in his forearms and his back that lasted for a few hours and disappeared without treatment. After a few days the same symptoms appeared again, but then he had angioedema of upper lip. This urged him to seek medical help. During the

visit to his General Practitioner (GP), the patient reported that in the previous month had less consistent and “mushy” stools. He had no other symptoms, underlying conditions, and did not take any therapy. To treat urticaria a second generation of selective antagonist of histamine receptor H1 (loratadin) 10 mg daily was administered. Alongside with loratadin he underwent a restrictive diet, which did not contain any well-known allergens (fish, sea fruits, cheese, dairy products, nuts, wild animal meat, vine, artificially colored products, etc.). The aforementioned symptoms presented regardless of therapy every few days for more than two months. Meanwhile, a search had been started to find the possible cause of the disease. Firstly, blood analyses were performed: blood count, differential blood count, glucose, urea, kreatinine, minerals, C-reactive protein, alkaline phosphatase, lactate dehydrogenase, creatine kinase, aspartate aminotransferase, alanine aminotransferase, gamma glutamyltransferase, total proteins, electrophoresis of proteins, IgA, IgG, IgM, C3, C4, eosine cationic protein, anti-streptolysine O titer, reuma factor, Waaler-Rose test, latex agglutination test, anti-nuclear antibodies, hemoculture, urinoculture, stool culture for viruses and bacteria, hepatitis A, B, C and HIV markers and tumor markers. The results of those tests were in reference values. A total IgE was slightly elevated, 74.4 kU/L, (reference for age <50 kU/L). TSH was elevated, 8.48 mIU/L (reference 0.456-4.68 mIU/L), FT3 were in normal range, 4.97 pmol/L (reference interval 4.26-8.10 pmol/L) and FT4 was slightly decreased, 8.48 pmol/L (reference interval 10.0-28.2 pmol/L). Anti-thyreoglobulin (anti-TG) antibodies were elevated, 31.96 IU/mL (reference interval 0.00-4.20 IU/mL), and anti-thyroid peroxidase (anti-TPO) was dramatically increased, 707.61 IU/mL (reference interval 0.00-5.60). Thyroid gland ultrasonography showed diffuse hypodense areas. The ultrasound of the abdomen was normal. In addition, the prick skin test was performed for 13 standard inhalatory and 15 nutritive antigens, which were in reference range. At the same time, following stool

cultures for the presence of parasites *Blastocystis hominis* were isolated on three separate occasions. Thus, the attention was focused on positive stools and thyroid hormone findings. The disorder of thyroid hormones, elevated anti-thyroid antibodies and thyroid ultrasonography suggested that patient had symptomatic Hashimoto’s thyroiditis. A nuclear medicine specialist recommended the treatment of hypothyreosis by levothyroxine in dose of 50 µg daily for five days, and then 100 µg twice a week, whereas metronidazole was given orally at a dose of 400 mg three times daily for 14 days for eradication of *Blastocystis hominis*. Within one week of therapy symptoms of chronic urticaria disappeared, and after 14 days metronidazole therapy eradication of *Blastocystis hominis* was achieved and the consistency of stool was normalized. The therapy for hypothyreosis was continued but after two weeks of levothyroxine treatment specific symptoms like sweating, tremor, and heat intolerance. These symptoms urged us to reconsider levothyroxine treatment. At that time, patient’s control thyroid hormones were: TSH 0.002 mIU/L, FT3 12.4 pmol/L and FT4 28.0 pmol/L, and consequently, levothyroxine treatment was terminated after only two weeks of therapy. Six months later, TSH, FT4 and FT3 levels were normalized, and anti-TG and anti-TPO levels were decreasing (Table 1). In the last four years of follow-up both parasitological and bacteriological stool cultures were negative, and the patient was symptom-free with normal physical activity, while anti-TG and anti-TPO levels were declining (Table 1).

Discussion

In this case report we proposed a connection between *Blastocystis hominis*, chronic urticaria and symptomatic Hashimoto’s thyroiditis. Recently a few reports associating *Blastocystis hominis* and chronic urticaria [5,6,17] were published. Furthermore, the chronic urticaria was reported to be associated with Hashimoto’s thyroiditis, although normalization of

Table1. Thyroid hormones and antibodies levels during four-year follow-up

Date: (After therapy)	April 2009	1 month	6 months	1 year	2 years	3 years	4 years	Reference interval
TSH	8.48	0.002	3.11	3.23	2.71	1.64	2.88	0.465-4.68 mIU/L
FT3	4.97	12.4	5.83	6.48	6.57	5.06	6.39	4.26-8.10 pmol/L
FT4	8.32	28.0	13.6	11.8	12.4	12.1	13.4	10.0-28.2 pmol/L
Anti-TPO	707.61	-	483.63	293.05	218.25	-	-	0.0-5.60 IU/mL
Anti-TG	31.96	-	12.8	5.14	5.99	-	-	0.0-4.20 IU/mL
<i>Blastocystis hominis</i>	3× pos.	3× neg.	3× neg.	3× neg.	3× neg.	-	-	-

thyroid hormones does not improve chronic urticaria [10,12,14,18]. Although the patient was under levothyroxine therapy, it was not a sufficient dosage or duration for developing the described symptoms of thyreotoxicosis. Interestingly in this case report we observed that the eradication of *Blastocystis hominis* prevented all symptoms and finally stopped the development of symptomatic Hashimoto's thyroiditis. It has been demonstrated that *Blastocystis hominis* has the ability to modulate autoimmune response towards Th2 immune response [16]. A study by Hussein and colleagues reported that patients with *Blastocystis hominis* had elevated levels of serum specific IgG antibodies [19]. Some *in vitro* studies have shown that *Blastocystis hominis* can produce cysteine protease and can induce IL-8 production using NF-κB pathway, as well as the induction of apoptosis [2]. Thus, there is an evident possibility that *Blastocystis hominis* can affect human immune system pushing it towards Th2 response [16].

Chronic urticaria is associated with Hashimoto's thyroiditis, but this connection has not yet been clearly explained. It has been suggested that all patients with chronic urticaria must be tested for anti-thyroid antibodies [20]. Our clinical observation that eradication of *Blastocystis hominis* resolved chronic urticaria and Hashimoto's thyroiditis raises a possibility that there is a connection between these three clinical entities. Based on our observation we propose that in susceptible host *Blastocystis hominis* inadequate immune response can be triggered and the organism pushed towards autoimmune diseases. Altogether, this places the *Blastocystis hominis* from the original point of a nonpathogenic organism to an area of clinical interest. We hope that our clinical observation will contribute to further understanding of Hashimoto's thyroiditis pathogenesis.

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