Urticaria Associated with Amoeboid Forms of *Blastocystis* spp

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**Authors’ contributions**

This work was carried out in collaboration among all authors. Author VK made the clinical observations and wrote the first draft. Author AG made the specific microbiologic studies and verification. Author VB summarized the results, performed the statistical analysis and finalized the study. All authors read and approved the final manuscript.

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**ABSTRACT**

*Blastocystis* spp pathogenic potential remains controversial. Recently, many researchers have suggested the possible etiological relationship between symptomatic skin rashes and Blastocystic morphological forms, genetic diversity and microbiota interaction. A small observation series of acute and chronic urticaria caused by *Blastocystis hominis* in elderly patients has been herein presented. These cases emphasize the importance of adequate parasite verification under appropriate clinical settings and upon elimination of other more common causative factors as well as the significance of proper etiological treatment in urticaria patients.
Keywords: Blastocystis hominis; amoeboid forms; urticaria.

1. INTRODUCTION

Blastocystis spp are unicellular enteric protozoan parasites evenly presented in humans worldwide [1]. The prevalence reported ranges from 30-50% in developing to 1.5-10% in industrialized countries [2]. Most of the affected individuals are asymptomatic, which led to the suggestion that the organism is a mere commensal in the human intestine [3]. Advanced epidemiologic data proved the association of the parasite with a wide range of symptoms and pathological conditions including abdominal pain, fatigue, diarrhea, irritable bowel syndrome, and some skin rashes such as urticaria [4,5]. A series of six patients with generalized erythematous wheals and minor gastrointestinal symptoms, who proved to be infested with amoeboid Blastocystis spp and completely cured upon etiological therapy, is herein presented.

2. CLINICAL OBSERVATION

Six adult patients (mean age 31.64 years, varying from 18 years to 64 years) with equal sex distribution, presented with widespread pruritic rash, started on the forehead and quickly involving the entire body. The onset of the disease in five of the patients was within 6 weeks, while only one patient claimed to suffer episodic crops since 3 months. All patients reported no previous insect bites, recent medication change or ingestion of any unusual food prior to the appearance of the dermatological symptoms. No history of acute fever, weight loss or arthralgia was noted. Shortness of breath or throat tightness was also missing. The patients had insignificant medical history with no asthma or allergic conditions present. They denied taking any supplement or over-the-counter medications. An eliminated diet and antihistamine regimen was started by primary care physicians within at least 2 weeks for all of them with no significant improvement. On physical examination intermittent well-circumscribed, erythematous and oedematous papules (Fig. 1) and circinate plaques (Fig. 2) on the face, neck, upper and lower extremities that came and went over a period of less than 24 hours were noted. Dermographism was negative in all patients. Mild abdominal pain was proven on palpation in all six patients. A decrease of stool consistency was observed visually in four patients. Basic serum chemistries (complete blood count, metabolic panel and liver function tests) were all within normal ranges. None showed peripheral eosinophilia and elevated total IgE. There were no indications of hepatic, renal, autoimmune or endocrinological diseases. Histological examination showed mild perivascular and interstitial inflammation with scattered eosinophils consistent with urticaria. No evidence of vasculitis was found. Stool examination disclosed Blastocystis spp (Fig. 3), and ruled out any other pathogen intestinal parasite. All patients had more than 5 organisms per high power field. The parasite was isolated upon cultivation on Robinson's medium and proved to be present in amoeboid forms. Oral antiprotozoal regimen of 2 g tinidazole (four doses of 500 mg, every 12 hours in two consecutive days) was performed for all patients. The patients experienced complete clearance of skin lesions up to 3 days after receiving the total cumulative dose (mean 2.84 days). The minor gastrointestinal symptoms had also disappeared. The one month-follow-up stool analysis was negative for Blastocystis sp. No relapse of urticaria was seen in any of the patients after the parasite eradication.

Fig. 1. Multiple erythematous papules with hypopigmented halo

3. DISCUSSION

Blastocystis spp. is an anaerobic protozoan found in poor-oxygen environment of human gastrointestinal tract [6]. Four different major morphologic forms have been demonstrated: The vacuolar, granular, amoeboid, and cystic [7]. Irregular polymorphic amoeboid forms are observed predominantly in the infected individuals. They are highly implicated in some specific intestinal syndromes, including enteritis and colitis, as well as non-specific symptoms
such as diarrhea, abdominal cramps and nausea [8]. Urticaria is a monosymptomatic, polyetiological syndrome, associated with a variety of underlying conditions. Parasitic infestations have long been considered a strong pathogenic factor, depending on host immunity-parasite life cycle interaction. Recently, it was shown that almost 60% of patients with acute and chronic urticaria showed Blastocystis infestations in comparison to only 8% of healthy controls [9]. Most of these patients experienced some intestinal symptoms, which completely resolve together with the skin rash after successful protozoa eradication.

Despite the well-proven higher incidence of Blastocystis infestation in patients with urticaria, the causal pathogenetic association remains to be determined. Some authors suggested that Blastocystis always need a cofactor such as anti-inflammatory drug to trigger mast cell degradation and profound anaphylactic reaction [10]. Others hypothesized that parasite antigens activate Th2 cells to secrete inflammatory interleukins (II-3, II-4, II-5, and IL-13), leading to an IgE-mediated response [11,12]. Our observation does not contribute to any of these presumptions, since no drug induction or elevation of total IgE was detected. We rather confirm the speculation of Yan et al. [13], who believed that only the amoeboid form of Blastocystis spp might have pathogenic potential by adhering to the gut epithelial cells and affecting immune homeostasis with consequent recruitment of inflammatory cells. Moreover, by invading the gut wall, they facilitate the absorption of other antigens [14].

The amoeboid forms were found in more than 95% of urticaria patients, which undoubtedly confirm their greater virulence [5]. The variation of host intestinal microbiota and the symbiotic role of other pathogenic microorganisms, e.g. viruses or bacteria, may also contribute to the modification of Blastocystis spp biological behavior [15,16]. Thus, the alternative way of complement activation with the release of C3a and C5a leads to accumulation of higher histamine levels and subsequent greater mast cell degranulation, which triggers exuberant allergic urticarial reaction.

Diagnosis of Blastocystis spp is made by examining trichrome-stained stool specimen under a light microscope [8]. Usually fecal leukocytes are absent. More than five organisms per field are considered pathogenic [17]. Usually no peripheral eosinophilia is detected, as in our cases. The self-limited nature of the disease, together with the controversial potential pathogenicity evokes an equivocal treatment. Metronidazol is the most effective and wide used drug for treating symptomatic cases. Paromomycin, tinidazole, trimethoprim-sulfamethoxazole, furazolidone, pentamidine and nitazoxanide complete the therapeutic range [7]. Stool testing is necessary to follow-up as prolong shedding and re-infestation may occur [9].

4. CONCLUSIONS

Blastocystis infection has been controversially discussed in the urticaria pathogenic pathway over many decades [18]. The etiological role of amoeboid Blastocystis spp in acute and chronic urticaria, depending on the geographical region, pathogenetic subtypes, concomitant viral and bacterial infections, drug intake or nutrition influence has long been suspected. Our observation provides further evidence of the pathogenicity of amoeboid Blastocystis spp and proved that a successful eradication resulted in complete clearance of all dermatological and gastro-intestinal symptoms. We therefore
suggest that precise etiological verification of parasite infestation should be performed to all unresponsive patients with urticaria of unknown aetiology and minor gastrointestinal symptoms in order to administer appropriate anti-parasite treatment.

CONSENT

As per university standard guideline participant consent have been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


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