Urticaria associated with amoeboid forms of Blastocystis spp

Type of article

13. Case reports / Case studies (Mainly for bio-medical journals)

No Methods and results section appears in this kind of article.

Urticaria associated with amoeboid forms of Blastocystis spp

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 Blastocystic 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.

Key words: Blastocystis hominis, amoeboid forms, urticaria

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.

Clinical observation

Six adult patients (mean age 31.64 years, varying from 18 years to 64 years) with equal sex distribution, presented with wide-spread 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 and circinate plaques 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, 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 anti-protozoal 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 gastro-intestinal 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.

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 (Il-3, Il-4, Il-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 accummulation of higher histamine levels and subsequent greater mast cell degranulation, which triggers exuberant allergic urticarial reaction.

Diagnosis of Blastocystis spp is made by examining trichome-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].

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.

References

1. Wawrzyniak I, Poirier P, Viscogliosi E. Blastocystis, an unrecognized parasite: an overview of pathogenesis and diagnosis. Ther Adv Infect Dis 2013; 1: 167-178.
2. Balint A, Doczi I, Bereczki I. Do not forget the stool examination! Cutaneous and gastrointestinal manifestation of Blastocystis sp. Infection. Parasitol Res 2014; 113: 1585-1590.
3. Verma R, Delfaniana K. Blastocystis hominis associated acute urticaria. Am J Med Sci 2013; 346: 80-81.
4. Tan K, Mirza H, Teo J. Current views on clinical relevance of Blastocystis spp. Curr Infect Dis Rep 2010; 12: 28-35.
5. Hameed D, Hussanin O, Zuel-Fakar N. Association of Blastocystis hominis genetic subtypes with urticaria. Parasitol Res 2011; 108: 553-560.
6. Gupta R, Parsi K. Chronic urticaria due to Blastocystis hominis. Australas J dermatol 2006; 47: 117-119.
7. Pasqui A, Savini E, Saletti M, Guzzo C, Pucetti L, Auteri A. Chronic urticaria and Blastocystis hominis infection: a case report. Eur Rev Med Pharmacol 2004; 8: 117-120.
8. Tan K. New insights on classification, identification, and clinical relevance of Blastocystis spp. Clin Microbiol Rev 2008; 21: 639-665.
9. Zuel -Fakkar N, Hameed A, Hassanin O. Study of Blastocystis hominis isolates in urticaria: a case-control study. Clin Exp Dermatol 2011; 36: 908-910.
10. Biedermann T, Hartmann K, Sing A. Hypersensititvity to non-steroidal anti-inflammatory drugs and chronic urticaria cured by treatment of Blastocystis hominis infection. Br J Dermatol 2002; 146: 1113-1114.
11. Valsecchi R, Leghissa P, Greco V. Cutaneous lesions in Blastocystis hominis infection. Acta Derm Venereol 2004; 84: 322-323.
12. Katsarou-Katsari A, Vassalos C, Tzanetou K. Acute urticaria associated with amoeboid forms of Blastocystis spp. subtype 3. Acta derm Venereol 2008; 88: 80-81.
13. Yan Y, Su S, Lai R, Liao H, Ye J, Li X. Genetic variability of Blastocystis hominis isolates in China. Parasitol res 2006; 99: 597-601.
14. Tan K, Singh M, Yap E. Recent advances in Blastocystis hominis research: hot spots in terra incognita. Int J Parasitol 2002; 32: 789-804.
15. Parija S, Jeremiah S. Blastocystis: taxonomy, biology and virulence. Trop Parasitol 2013; 3: 17-25.
16. Tan T, Suresh K. Predominance of amoeboid forms of Blatocystis hominis in isolates from symptomatic patients. Parasitol Res 2006; 98: 189-193.

17. Vogelberg C, Stensvold C, Monecke S. Blastocystis sp. Subtype 2 detection during recurrence of gastrointestinal and urticarial symptoms. Parasitol Int 2010; 59: 469-471.
18. Lepczynska M, Chen WC, Dzika E. Mysterious chronic urticaria caused by Blastocystis spp.? Int J Dermatol 2016; 55: 259-266.