

Blastocystis hominis Associated Acute Urticaria

Rajanshu Verma, MD and Kamiab Delfanian, MD

Abstract: Acute urticaria has many causative factors, which may include infections, medications (nonsteroidal anti-inflammatory drugs, antibiotics, contraceptives and others), insect bites, physical stimuli, allergens or underlying systemic disorders. *Blastocystis* spp, although ubiquitous in developing countries, is rarely implicated in causing disease in the developed world. The authors present a case of acute urticaria caused by *Blastocystis hominis* (protozoan parasite) in an elderly farmer in rural United States. This case vignette emphasizes the importance of checking stool for ova and parasites to look for *Blastocystis* species in patients with urticaria under appropriate clinical settings when other common causative factors of the same have been ruled out.

Key Indexing Terms: *Blastocystis hominis*; Urticaria; Metronidazole; Parasites. [Am J Med Sci 2013;346(1):80–81.]

Acute urticarial lesions appear over minutes to days, rapidly enlarge, coalesce and then quickly disappear. Although underlying etiology may not be found in many patients, viral, bacterial or parasitic infections, immunoglobulin E (IgE)-mediated type I allergic reactions, antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), birth control pills, insect bites, food and food additives, contact with allergens, physical stimuli and systemic disorders are commonly implicated in causing acute urticaria.

Blastocystis, an anaerobic protozoan found in human gastrointestinal tract, is increasingly being recognized as a pathogen and a cause of urticaria. We report a case of 71-year-old farmer who presented with extensive urticaria, which was found to be associated with *Blastocystis hominis* infection.

CASE DESCRIPTION

A 71-year-old white farmer presented with 1-week history of pruritic rash, which started on his forehead and quickly spread to his entire body (forehead, then waistline, underarms, abdomen and then involving back and legs). He tried taking cetirizine, diphenhydramine, prednisone and emollients without much relief. Patient reported no recent insect bites, contact with individuals with similar rash or recent change in medications. He had felt exhausted for last 5 days and had noticed mild diarrhea 3 days ago although did not recall ingestion of any unusual food. There was no accompanying chest or throat tightness, shortness of breath or other symptoms of anaphylaxis. No history of acute onset fever, weight loss or joint pains noted.

Medical history was significant for coronary artery disease, myocardial infarction, glaucoma, sensorineural hearing loss, hypertension, skin cancer (nonmelanoma), actinic keratoses, insomnia and anxiety, type 2 diabetes mellitus and hypothyroidism. There was no history of allergic diseases or asthma.

Prescription medications included aspirin, eszopiclone, levothyroxine, metformin, metoprolol succinate, topical metronidazole, montelukast, nasal fluticasone, ophthalmic latanoprost, multivitamin, timolol eye drops and omega-3 fatty acid. He also took zolpidem and alprazolam as needed as well. Prednisone and ranitidine were started by primary care physician within last few days to help mitigate rash. He denied taking any new supplement or over-the-counter medication.

He worked as a farmer with exposure to cattle, farm animals and admitted to not keeping good hand hygiene. He was a former smoker and quit smoking cigarettes 45 years ago. He drank 3 to 4 beers every other week. He had not noticed any worsening of rash with intake of alcohol.

On examination, he was found to have normal vital signs except elevated blood pressure (140/87 mm Hg). Skin examination showed extensive confluent erythematous maculopapular rash with areas of central clearing all over his abdomen, behind his thighs, on his shins, upper torso and back consistent with urticaria as shown in Figure 1. Rest of the physical examination was unremarkable.

Basic serum chemistries (complete blood count, metabolic panel and liver profile) were all within normal limits except elevated erythrocyte sedimentation rate 33 mm/hr (normal: 0–20 mm/hr), C-reactive protein 6.7 mg/dL (normal: 0–0.9 mg/dL) and blood glucose 432 mg/dL (70–139 mg/dL). Latter was attributed to worsening of his diabetes while being on prednisone for last 1 week. There was no evidence of peripheral eosinophilia.

A diagnosis of NSAID-induced urticaria was initially made and he was continued on emollients, fexofenadine and intravenous methylprednisone. Intravenous insulin for given to control his blood glucose. All medications except those mentioned above were discontinued and search for other causative factors of urticaria was initiated. Results for antinuclear antibody, anticyclic citrullinated peptide, antineutrophil cytoplasmic antibodies (c-ANCA and p-ANCA) were negative. *Clostridium difficile* stool toxin was negative as well. Later, stool sample sent for ova and parasite on admission came back positive for heavy growth of *B hominis* infection. A skin biopsy of the rash was performed, which showed mild perivascular and interstitial inflammation with eosinophils consistent with urticaria. No evidence of vasculitis was present. A diagnosis of *Blastocystis*-associated urticaria was made.

Patient was started on metronidazole (750 mg tablet 3 times a day) for 10 days. Rash had improved within next 3 days and was completely resolved by the end of 7 days.

DISCUSSION

Urticaria or “hives” are pruritic slightly raised plaques or wheals associated with edema, erythema and vascular skin response. Acute urticarial lesions appear over minutes to days, rapidly enlarge and then coalesce and quickly disappear. Although underlying etiology may not be found in many patients, viral, bacterial or parasitic infections, IgE-mediated type I allergic reactions, antibiotics, NSAIDs, birth control pills, insect bites, food and food additives, contact with allergens, physical stimuli and

From the Division of Hospital Medicine, Department of Internal Medicine (rv), Mayo Clinic College of Medicine, Rochester, Minnesota; and Urgent Care (kd), Mayo Clinic Health System in Albert Lea, Albert Lea, Minnesota.

Submitted October 23, 2012; accepted in revised form November 15, 2012.

Correspondence: Rajanshu Verma, MD, Division of Hospital Medicine, Department of Internal Medicine, Mayo Clinic College of Medicine, Rochester, 200 First Street SW, Rochester, MN 55905 (E-mail: verma.rajanshu@mayo.edu).



FIGURE 1. Urticaria associated with *Blastocystis* spp involving thighs and legs.

systemic disorders are commonly implicated in causing acute urticaria.

Blastocystis spp (previously known as *B. hominis*) is increasingly being recognized as a pathogen and a cause of urticaria.^{1–9} It is ubiquitous in developing countries because of poor sanitation and lack of hand washing practices, however, the incidence in developed nations is anywhere between 1.5% and 10%.^{1,9,10} As per our extensive literature search, to date, about 150 cases of *Blastocystis*-induced urticaria have been published worldwide, however, with only one retrospective review from Canada and none from United States.^{1–11} Transmission of *Blastocystis* spp is predominantly fecal-oral and occurs on ingestion of contaminated food or water. It is common in individuals with occupational exposure to animals, indicating a possibility of zoonotic infection.¹

Blastocystis spp is an anaerobic protozoon found in the human gastrointestinal tract. It exists in 4 different forms (cystic, vacuolar, granular and ameboid) with size varying from 5 to 40 μ M (cystic form). Vacuolar and cystic forms are most frequently found in stool samples. Genotypically, 9 different subtypes exist; however, subtype 3 is the most frequently implicated in causing disease.^{1,6,10}

Clinical manifestations of *Blastocystis* infection include watery diarrhea, abdominal cramps, fatigue, nausea, flatulence, angioedema and bloating, with urticaria and arthritis being extraintestinal manifestations.^{1,3,4,8,9,11} Symptoms are more severe in immunocompromised individuals. There seems to be an asymptomatic carrier state, and a large number of individuals (up to 15%) may have stools positive for *Blastocystis* spp without any symptoms.¹

Urticaria from *Blastocystis* is believed to be caused by activation of Th-2 cells, which secrete interleukins (IL; IL-3, IL-4, IL-5 and IL-13), leading to an IgE-mediated response.^{1,3,6,10}

Complement activation with release of C3a and C5a has also been postulated.^{1,7} Subsequent histamine release and mast cell degranulation triggers allergic urticarial reactions.^{1,3,6,10}

Diagnosis of *Blastocystis* spp is made by examining trichrome-stained stool specimen smears or wet mounts under a light microscope. Another commonly used technique is called formol ethyl acetate concentration.¹ Usually, fecal leukocytes

are absent. According to some authors, *Blastocystis* spp are more likely to be pathogenic if >5 organisms are seen per oil immersion field.^{2,9} Enzyme-linked immunosorbent assay, polymerase chain reaction and molecular tests have also been developed; however, they are available for research purposes only. Peripheral eosinophilia, although common with parasitic infections, may not be seen with *Blastocystis* infection as in our case.^{5,6,8,9}

Infection from *Blastocystis* spp is often self-limited and many mild cases resolve within 3 to 5 days without any specific antimicrobial therapy. Supportive measures such as antihistamines, steroids and emollients may be used as adjuncts. Asymptomatic patients with *Blastocystis*-positive stools do not require any treatment. Metronidazole is the most effective and widely studied antibiotic for treating symptomatic infections from *Blastocystis* spp.⁷ Other antimicrobial agents that have been used include paromomycin, tinidazole, trimethoprim-sulfamethoxazole, furazolidone, pentamidine and nitazoxanide.^{7,10} Stool testing may remain positive as prolonged, irregular shedding of the organism after treatment can occur. Follow-up care is essential, as recurrence of symptomatic *Blastocystis* infection has also been reported.¹⁰

CONCLUSIONS

This case vignette emphasizes the importance of checking stool for ova and parasites to look for *Blastocystis* spp in patients with urticaria under appropriate clinical settings when other common causative factors have been ruled out.

REFERENCES

1. Tan KS. New insights on classification, identification, and clinical relevance of *Blastocystis* spp. *Clin Microbiol Rev* 2008;21:639–65.
2. Biedermann T, Hartmann K, Sing A, et al. Hypersensitivity to non-steroidal anti-inflammatory drugs and chronic urticaria cured by treatment of *Blastocystis hominis* infection. *Br J Dermatol* 2002;146:1113–4.
3. Valsecchi R, Leghissa P, Greco V. Cutaneous lesions in *Blastocystis hominis* infection. *Acta Derm Venereol* 2004;84:322–3.
4. Cassano N, Scoppio BM, Loviglio MC, et al. Remission of delayed pressure urticaria after eradication of *Blastocystis hominis*. *Acta Derm Venereol* 2005;85:357–8.
5. Gupta R, Parsi K. Chronic urticaria due to *Blastocystis hominis*. *Australas J Dermatol* 2006;47:117–9.
6. Katsarou-Katsari A, Vassalos CM, Tzanetou K, et al. Acute urticaria associated with amoeboid forms of *Blastocystis* sp. subtype 3. *Acta Derm Venereol* 2008;88:80–1.
7. Pasqui AL, Savini E, Saletti M, et al. Chronic urticaria and *Blastocystis hominis* infection: a case report. *Eur Rev Med Pharmacol Sci* 2004;8:117–20.
8. Kain KC, Noble MA, Freeman HJ, et al. Epidemiology and clinical features associated with *Blastocystis hominis* infection. *Diagn Microbiol Infect Dis* 1987;8:235–44.
9. Vogelberg C, Stensvold CR, Monecke S, et al. *Blastocystis* sp. subtype 2 detection during recurrence of gastrointestinal and urticarial symptoms. *Parasitol Int* 2010;59:469–71.
10. Zuel-Fakkar NM, Abdel Hameed DM, Hassanin OM. Study of *Blastocystis hominis* isolates in urticaria: a case-control study. *Clin Exp Dermatol* 2011;36:908–10.
11. Micheloud D, Jensen J, Fernandez-Cruz E, et al. Chronic angioedema and *Blastocystis hominis* infection. *Rev Gastroenterol Peru* 2007;27:191–3.