Cutaneous Lesions in *Blastocystis hominis* Infection

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Accepted December 16, 2003.

Sir,

The first paper clearly defining the genus *Blastocystis* as a distinct organism was presented by Alexeieff (1) in 1911, who proposed the name *Blastocystis enterocola*. The name *Blastocystis hominis* was proposed by Brumpt (2), and this is the name utilized in the current literature.

B. hominis is now regarded as an intestinal protozoan that seems not merely to be a commensal organism, but should be considered as a potential pathogen (3). Symptoms commonly attributed to infection with *B. hominis* include diarrhoea, abdominal pain, cramps, nausea, discomfort, anorexia, fatigue, flatulence and profuse watery diarrhoea (4–6). During the past few years an association between *B. hominis* infection and some skin disorders such as urticaria (7, 8) and palmoplantar pruritus (9) have been reported. We present here our experience of this association.

CASE REPORTS

Patient 1

A 62-year-old nun presented to our allergy unit in March 2002 with a 1-year history of itching localized initially to the trunk and subsequently anywhere. *Ab initio*, itching recurred at intervals (twice or three times a week), but during the last 2 months it was persistent, predominantly at night. Physical examination revealed no apparent skin lesions except lesions due to scratching, especially on the back. Total blood cell count, serum concentrations of creatinine, bilirubin, electrolytes, alkaline phosphatase, urea, glucose, iron, ferritin, copper, as well as urine status were all within normal values. A search for a possible underlying internal disorder was negative; there were no indications of hepatic or renal diseases, autoimmune diseases or endocrinological diseases.

Total IgE, C3, C4, C1-INH were all within normal limits. Stool examinations on three consecutive samples were performed by microscopy; *B. hominis* was identified in all three faecal samples, obtained on three different days. The patient was treated with oral paromomycin 25 mg/kg body weight for 10 days. Pruritus began to decrease 1 week after the end of paromomycin therapy, and 1 month after treatment it completely subsided. Three further faecal analyses were performed 2 months later; all three stool samples were negative.

Patient 2

A 34-year-old woman was healthy until February 2001 when she began experiencing episodes of generalized urticaria and pruritus. The symptoms recurred initially at intervals (once or twice weekly), but during the last 7–8 months they recurred daily. Her practitioner prescribed oral antihistamines (cetirizine 10 mg daily and loratadine 10 mg daily for 4 and 5 weeks, respectively) and systemic steroids (prednisolone 40 mg daily for 2 weeks and, subsequently, 20 mg daily for 10 days; deflazacort 30 mg daily for 3 weeks), with poor benefits. There was no family or personal history of atopy. She was referred to us in May 2002. Routine haematological and biochemical screening tests, including full blood count, erythrocyte sedimentation rate, antinuclear antibody, rheuma test, Waaler-Rose, cryoglobulins, circulating immune complexes, thyroid antibodies, C3, C4, C1-INH, hepatitis B and C and infectious mononucleosis serology were all negative or within normal range.

Stool examinations on three consecutive samples were positive for *B. hominis* infection. The patient was treated for 10 days by oral administration of paromomycin 25 mg/kg body weight. Four weeks later the patient presented again to us for the persistence of the skin symptoms. Three further stool examinations were performed and *B. hominis* was again identified. The patient was prescribed metronidazole 500 mg three times per day for 10 days; after 2 weeks she experienced an amelioration of her symptoms, and after 2 months she became symptom-free. Subsequent stool examinations were negative for *B. hominis*.

Patient 3

A 69-year-old man was in good health until August 2002 when he began to experience a generalized urticaria and pruritus. His practitioner precribed mizolastine 10 mg daily for 2 months with no benefit; thereafter his dermatologist prescribed cinnarizine 75 mg twice daily for 4 weeks and, subsequently, 75 mg once a day. He was referred to us in February 2003 with acute and generalized urticaria with severe itching. There was evident oedema of the lips, but no hypotension or abdominal pain. Routine laboratory investigation revealed no abnormality. Tests for antinuclear antibodies, anti-DNA, common autoantibodies, rheumatoid factor, serum protein electrophoresis, liver function and thyroid hormones were all unremarkable. Extensive skin testing (prick test) with inhalant, pollen and food allergens failed to reveal any IgE-mediated sensitivity. Phadiatop was negative, and C3, C4, C1-INH were all in normal range. There was no family nor personal history of atopy. Stool examinations were performed, and *B. hominis* was identified in faecal samples on 3 different days. The patient was prescribed paromomycin 25 mg/kg body weight for 10 days. Daily wealing was stopped 2 weeks after the end of treatment; no recurrence was evident on 3 months of follow-up. Three further stool samples were negative for *B. hominis* 6 weeks after treatment.

DISCUSSION

B. hominis infection can usually cause non-specific symptoms such as diarrhoea, cramps, abdominal pain or nausea; however, a number of case reports have suggested that *B. hominis* may be the responsible agent

DOI: 10.1080/00015550410025949

in some diseases including enteritis (10), colitis (11) and arthritis (12). All these associations are based on case reports and detailed epidemiological studies have not been performed to estimate the true prevalence of this intestinal protozoan; large numbers of *B. hominis* cells may be present in stool samples of patients with no symptoms (13). In our patients we have simply observed a complete resolution of skin symptoms after *B. hominis* eradication. In all three cases the stool samples were positive before treatment and negative after therapy. It is of interest to note that skin conditions observed in association with *B. hominis* infection are characterized by pruritus and/or oedema and swellings (7–9). Of interest is the patient suffering from palmoplantar pruritus who experienced the resolution of her symptom after *B. hominis* eradication (9). Certainly, in this patient the presence of *B. hominis* in stool samples and its eradication clarified an essential association between the presence of the protozoan and her skin condition. It is not known whether *B. hominis* is a pathogenic organism or not, so we can only speculate about the association between some skin disorders and *B. hominis*. The protozoan could induce an active inflammation with progressive recruitment of inflammatory cells and accumulation of neutrophils, eosinophils and lymphocytes. This network of inflammatory cells could support the release of a family of histamine-releasing factors with mast cell degranulation (14). We know that mast cell and basophil mediator release can be induced by several triggers other than IgE (anaphylotoxins C3a, C5a, Ils, etc.). This mechanism might explain how some trigger factors other than allergens can induce pseudo-allergic reactions similar, at a clinical level, to typical IgE-mediated reactions, and this evidence could be supported by the modified morphology of gut-associated lymphoid tissue. It is known that the gastrointestinal tract is populated with a large variety of immune cells (B and T lymphocytes, plasma cells, mast cells, macrophages, eosinophils and basophils) capable of initiating and effecting a variety of immunological reactions, so it is possible that *B. hominis* itself, its toxin or its antigens may affect gut-associated lymphoid tissue homeostasis and may activate an immune response (15). Finally, it is possible that *B. hominis* toxin can activate the complement pathway with the generation of the anaphylotoxins C3a and C5a; the interaction of these complement fragments with specific receptors on mast cells and basophils causes histamine release and related skin symptoms.

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