

Chronic urticaria and blastocystis hominis infection. A case report

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Abstract. – We report a case of a 45 year old woman which fulfilled the criteria of chronic urticaria (remitting and relapsing bouts of erythematous and pruriginous lesions without angioedema, lasted four months). Cutaneous manifestations were not related to a specific inducing factor, had no benefit from antihistamine and steroid drugs and were associated sometimes with mild gastroenteric disorders. Patient was submitted to extensive clinical, laboratory and instrumental investigations which permit to exclude many conditions: allergy to inhalants, food, insects and drug adverse reactions, autoimmune urticaria, autoimmune diseases, neoplastic and infectious diseases. Finally coproculture disclosed the presence of *Blastocystis hominis* in stool samples thus permitting to associate urticaria to parasitic infection. Both cutaneous manifestations and mild abdomen disorders disappeared after appropriate treatment.

Despite the high diffusion the aetiopathogenesis of chronic urticaria remains often undefined. A large number of parasites have been correlated with urticaria but few data exist as regards *Blastocystis hominis* infection; then our findings may add evidence to the role of this parasite in inducing chronic urticaria. Considering that *Blastocystis hominis* is a modest pathogen for humans, the mechanism is probably the typical one of cutaneous allergic hypersensitivity; antigen parasites induce the activation of specific clones of Th2 lymphocytes, the release of related cytokines and the consequent IgE production.

Key Words:

Chronic urticaria, *Blastocystis hominis*.

Introduction

Chronic urticaria (CU) is defined as an eruption of oedematous and pruriginous papules localized or widespread, lasting for

longer than six weeks. Cutaneous lesions may be accompanied by angioedema which is determined by similar pathological alterations that occur in deep dermis and subcutaneous tissue. Vasoactive mediators released from mast cells and basophils produce the classic wheal and flare reaction. Urticaria affects up to 20% of the general population at least once during their lifetime; diagnosis is easy, but to find an etiology can be challenging and requires a serious methodical investigation in order to uncover diagnostic clues and to exclude serious medical illness¹⁻³.

Even though intestinal parasites are often mentioned as a possible cause, only anecdotal series of cases documented a link between parasites and chronic urticaria⁴.

Case Report

A 45 year old woman presented at our Allergology Unit with a four months history of remitting and relapsing bouts of erythematous and pruriginous lesions extended at trunk and limbs without angioedema. Patient did not refer any past history of allergy to inhalants, food, insects puncture nor of drug adverse reaction. No familial history of allergy was present. Cutaneous manifestations were not related to a specific inducing factor and were associated sometimes with mild abdomen pain and alvus disorders. At the time of our observation, she was assuming a therapy with antihistamine drugs and low doses of steroids without any benefit.

Physical examination confirmed the presence of the typical erythematous wheals accompanied by itching and without angioedema, but it was normal as regards the main organs (chest, heart, abdomen).

To investigate the etiopathogenesis of urticaria, patients was submitted to extensive clinical, laboratory and instrumental investigations, after drug withdrawal. Skin prick tests to a broad range of aero and food allergens, performed with common available kit (Alk-Abello test, Milano, Italy) yielded no reaction; measurements of total serum IgE (PRIST test, Pharmacia, Uppsala, Sweden) and of specific serum IgE (UniCAP-FEIA system, Pharmacia, Uppsala, Sweden) were normal. Intradermal skin test with drugs (antibiotics) executed according criteria established by protocols⁵ and patch test with contact aptens were also negative. The role of food and additives and of natural salicylate was excluded on the basis of negativity of test (elimination diet and double blind placebo-controlled in vivo provocation test-DBPCFC)⁶. We also executed autologous serum skin test through the intradermal injection of indiluted serum and with saline as negative control according protocols⁷; no local erythematous-pomphoid reaction was found.

Laboratory test included specific and aspecific tests and resulted normal, in particular: blood cell count and leukocyte formula, erythrocyte sedimentation rate, C-reactive protein, serum electrophoresis, urinalysis and urine culture, thyroid function test and antithyroid autoantibodies, complement factors C3, C4 and C1 inhibitor, antinuclear autoantibodies (ANA, ENA), rheumatoid factor, serum immunoglobulins, circulating immune complexes, serology for viral, bacterial and parasite antibodies.

To exclude neoplastic and infectious diseases we performed X-ray study of dental series, sinus series and chest and sonography of upper abdomen and lymphonodes; all investigations resulted negative. Gastroscopy with biopsy and specific test for *Helicobacter pylori* was also normal.

Finally coproculture disclosed the presence of *Blastocystis hominis* in three stool samples obtained in three different days. The patient was treated with paromomycin (1000 mg twice a day) and metronidazole (750 mg three times a day) for 10 days. Cutaneous manifestations disappeared one week after starting treatment and the patient remained free of urticaria. The mild abdomen disturbs also stopped in a few

days. Three further stool samples were negative for *Blastocystis hominis* 4 weeks after treatment.

Discussion

Despite the high diffusion, the aetiopathogenesis of chronic urticaria (CU) remains often undefined. Several conditions have been found to be related to urticaria symptoms, whereas the term chronic idiopathic urticaria (CIU) identifies the high percent of conditions in which a pathogenetic factor has not been found. To identify the cause of chronic urticaria requires the exclusion of many other conditions¹⁻³.

Food and drug allergies are the commonest causes including also the more subtle factors as sensibility to food dyes, natural salicylates and benzoic acid derivatives. Identifiable causes of symptoms include occupational exposure, insect bites, physical hypersensitivity (cold, eat, exercise)¹.

A particular form of urticaria is represented by autoimmune urticaria in which autoantibodies directed against IgE-receptor and in a 5% of cases against IgE have been found^{3,8}.

Chronic urticaria may be the presenting symptom of an underlying systemic disease and in particular connective tissue diseases (such as systemic lupus erythematosus, rheumatoid arthritis, Sjögren disease) and systemic vasculitides. An increased incidence in thyroid disease has also been observed^{1,9}.

The association of chronic urticaria with carcinoma of the colon, rectum or lung as well as with lymphoid malignancies has been reported¹.

Undetected infections have long been considered a cause of chronic urticaria even if the incidence seems extremely low. Urticaria has been documented during viral infections such as infectious hepatitis¹⁰ and mononucleosis¹¹. *Helicobacter pylori* infection has been correlated with chronic urticaria in some studies⁴. A large number of helminthic parasites including *Ascaris*, *Strongyloides*, *Filaria*, *Echinococcus*, *Schistosoma*, *Trichinella* have been also associated with allergic cutaneous symptoms¹. Recent studies have suggested a high prevalence of *Toxocara canis*, *Giardia*

lamblia, Fasciola hepatica in patients with urticaria, but antiparasitic treatment had only incostant effect^{12,13}. In our knowledge few data relate Blastocystis hominis infection to chronic urticaria.

Our patient exhibited the clinical pattern of chronic urticaria (remitting and relaxing bouts of cutaneous wheals occurring consistently for a minimum of six weeks); the extensive clinical investigation permit to exclude identifiable causes of symptoms and in particular the hypersensitivity syndromes and systemic diseases. Autologous serum skin test excluded autoimmune urticaria. However, it was possible to reveal a parasitic infection by the presence of Blastocystis hominis in stool sample.

Blastocystis hominis is a frequent intestinal protozoan that seems not merely to be a commensal organism but should be regarded as a potential pathogen. The parasite is transmitted through fecally contaminated water, food or other materials and is localised in epithelial cells of gastro-intestinal tract where it undergoes to asexual reproduction and wide spread. Its presence may induce gastrointestinal symptoms that generally remain mild^{14,15}. The mechanism of chronic urticaria associated with Blastocystis hominis as well as with other intestinal pathogens are not fully identified. The authors hypothesised a pathogenesis similar to that underlying the IgE-mediated allergic response: parasite antigens induce the activation of specific clones of Th2 lymphocytes and the production of specific cytokines (IL3, IL4, IL5, IL13) which determine the antibodies switching and the IgE production. The increase of mast cells and of mononuclear cells in skin biopsy would confirm this mechanism and would be responsible of increased production of hystamine and of the other mediators of early and late inflammatory reaction. The increase of circulating eosinophils which is often found in patients with parasitic infection would be also a factor related to allergic sensibilisation^{1,12,13}.

In our patient cutaneous manifestations had the typical characteristics of chronic urticaria whereas the intestinal colonisation was accompanied by very mild gastrointestinal symptoms and by the absence of the increase of eosinophils. This fact may be explained by the characteristics of Blastocystis hominis that is a modest pathogen for human, where-

as the parasitic antigens have been able to induce the cutaneous allergic hypersensitivity. The specific treatment induced the complete relapse of cutaneous urticaria corresponding to the disappearance of parasite in stools and to the regression also of gastrointestinal disturbs.

In conclusion, our patient had a chronic urticaria with typical clinical characteristics; the casual factor was represented by the intestinal parasitic infection which induced the cutaneous allergic reaction. These findings may add evidence to the role of parasitic infections and in particular of Blastocystis hominis in inducing chronic urticaria.

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