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Urticaria developing into mastocytosis

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Key words: child; chronic urticaria; cutaneous mastocytosis.

● CHRONIC urticaria (CU) is a disorder characterized by widespread hives that appear almost daily for at least 6 weeks. Children are affected less frequently than adults. Since, in most cases, the cause of CU cannot be determined, the disorder is considered idiopathic. Mastocytosis is an uncommon disease characterized by overproliferation and accumulation of mast cells in various organs. The skin is the most commonly involved organ, and urticaria pigmentosa (UP) is the most common form of cutaneous mastocytosis. This disease is characterized by reddish-brown maculopapular lesions that may show a wheal and flare reaction after stroking (Darier's sign). The diagnosis should be confirmed by skin biopsy to detect increased dermal mast-cell accumulation (1). The infantile form bears a more favorable

prognosis, and the regression of most skin lesions occurs in 80% of pediatric patients by puberty (2).

A 5-year-old child, with a personal history of seasonal rhinitis and asthma, had been seen in our outpatient clinic for urticarial reactions for 1 year. On the first visit, an evanescent pruritic and erythematous maculopapular lesion appeared suddenly on his lower back. He later experienced generalized evanescent hives every day, requiring treatment with an H₁-receptor antagonist. No physical factors, foods, or drugs were involved.

The biochemistry, blood count, rheumatoid factor, complement (C3 and C4), C-reactive protein, serum immunoglobulins, serum protein electrophoresis, and erythrocyte sedimentation rate were within normal limits. The antinuclear antibody test; stool analysis for parasites; and serologic analysis for HBV, HCV, hydatidosis, brucellosis, and salmonellosis were all negative. Skin prick tests with common aeroallergens and foods showed a selective reaction to *Olea europaea* (olive) pollen. Total serum IgE was 223 kU/l.

Four months later, the physical examination revealed urticarial lesions and scattered maculopapular red-brown lesions on the trunk with a wheal and erythema reaction after mechanical stroking (Darier's sign). Skin biopsy revealed perivascular accumulations of mast cell and a diffuse mast-cell infiltration of the papillary dermis, establishing the diagnosis of cutaneous mastocytosis.

Two months later, the red-brown macules scattered over the whole body and the urticarial episodes disappeared. The abdominal sonography and skeletal scintigraphy were normal. Plasma histamine and tryptase levels were within the normal range. In the cytogenetic analysis, 75 metaphases were studied on peripheral blood mononuclear cells without findings.

Trisomies 8 or 9 were not found in our patient. Finally, although increased numbers of the brown macules persisted on the trunk, the patient remained asymptomatic without therapy.

We present a child with CU that evolved to UP. This is the only case reported. The inflammatory nature of both disorders was indirectly supported by the fact that both responded to treatment with topical corticosteroids (3). Histopathologic studies of CU have reported an increase in the number of mast cells, lymphocytes, and monocytes. Natbony et al. propose that a released lymphokine or monokine may cause mast-cell proliferation (4); however, the specific factor has not been found. UP is a disease with a papillary dermis infiltration by mast cells, which cluster mostly around blood vessels. One theory holds that mastocytosis is a hyperplastic response to an abnormal stimulus. Mast cells are derived from CD34+ hematopoietic progenitor cells, and their maturation typically occurs in peripheral tissues. Stem cell factor (SCF) is essential for normal mast-cell development and survival. Subcutaneous administration of recombinant human SCF can induce mast-cell hyperplasia *in vivo* in man (5). It has been discovered that an inflammatory cytokine called mast-cell growth factor (MCGF), which is produced by keratinocytes and fibroblasts, causes mast-cell proliferation in experimental animals (6). Allison & Schmidt observed and treated a case of asymptomatic UP on the trunk that was reactivated by an episode of contact dermatitis on the hand. It is postulated that eczematous inflammatory mediators play a role in the overall pathogenesis (7). MCGF and other inflammatory mediators may play an early role in the development of skin lesions. It is likely that local levels of SCF regulate mast-cell numbers in normal tissues and also contribute to the striking alterations in mast-cell numbers discovered in association

with various immunologic reactions, reparative responses, and disease processes. It is possible that in our patient the development of human mast-cell populations could have been influenced by a complex interplay of cytokines and growth factors. This complex interplay could have been the cause, first, of the patient's CU, and then of his UP.

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Food allergy to frog

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Key words: anaphylaxis; food allergy; frog.

• THE frog is known to be potentially allergenic, and has been the object of some case reports of occupational allergy. The cases described were, briefly, as follows:

- a laboratory technician who complained of asthma when handling frogs (*Rana esculenta*) in experiments (1)
- a laboratory technician with respiratory and contact allergic reactions to the brain and secretions of the bullfrog (*R. catesbiana*) (2)
- a professional frog catcher complaining of conjunctivitis and rhinitis that progressed to asthma, after inhalation of a fluid excreted by the frogs when caught (3)
- a female frog-skinner (*R. esculenta*) who developed respiratory symptoms to skin antigens (4)
- a cook who complained, after occupational handling of frog's legs, of itching of the hands, dyshidrotic changes in his fingers, red skin eruptions, and an initial anaphylactic reaction while tasting (5).

In Italy, frogs were once a popular food, and were caught by the consumers themselves in ponds and canals. Today, they are considered a delicacy, are served (usually fried) especially in country restaurants, and are available frozen in many shops and supermarkets.

We here present the first nonoccupational case of allergic sensitization to frog as food. A 6-year-old girl was admitted to our hospital for an episode of severe anaphylactic reaction after the ingestion of boiled frogs (*R. esculenta*). When 7 months old, she had had atopic dermatitis, diagnosed as allergy to milk

and eggs. Successively, she developed allergy to fish, chronic rhinitis, recurrent bronchospasm, and an episode of severe urticaria-angioedema after ingestion of goat's milk. She underwent *in vivo* and *in vitro* allergologic screening with the following results:

- skin prick test (glycerinated extracts from Lofarma SpA, Milan, Italy): *Dermatophagoides* mix 3+, *Parietaria* pollen 3+, grass-pollen mix 3+, cow's milk 4+, milk albumin 4+, milk casein 4+, milk globulin 4+, hen's egg yolk 3+, hen's egg white 3+, codfish 4+, sole 4+.
- RAST (reagents Sferikit[®], Lofarma SpA, Milan, Italy): milk class 3, egg white class 3, egg yolk class 3, codfish class 4, peach class 2, soy negative.

The RAST to frog used solid phases (polystyrene beads) coated with an extract (5% w/v in PBS) obtained from the meat (all body) of frogs, with ¹²⁵I-labelled-anti-IgE and reference curve from a commercial source (Sferikit[®], Lofarma SpA, Milan, Italy). The RAST for frog was positive with 13.9 RAST units, corresponding to class 3. Six sera from patients with allergy to pollens, mites, and foods and three sera from healthy subjects were tested as controls and proved to be negative.

The mother of the patient stated that she had introduced frogs in her daughter's diet not as a delicacy, but as a protein source to make up for the many foods the child had to avoid because of her multiple sensitizations. The double-blind, placebo-controlled challenge test and prick-prick test were excluded for safety reasons, in view of the severity of the anaphylactic reaction reported.

In conclusion, we described a case of IgE-mediated anaphylaxis due to the ingestion of frog's meat (*R. esculenta*) in a child with multiple sensitizations to inhalant and food allergens.

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