Local Cholinergic Urticaria at Methacholine Test Site

Sir,
Cholinergic urticaria can best be elicited by cycling, treadmill exercise and hot baths (1). After intradermal injections of relatively high concentrations of cholinergic agents, the typical satellite pinpoint weals around the central large weal are seen only in patients with severe cholinergic urticaria (1). Three patients with moderate cholinergic urticaria, exhibiting strong local cholinergic urticaria at the sites of methacholine testing, but only following an exercise test, are presented.

An ergometric exercise test was used for triggering rash of cholinergic urticaria in a normal laboratory room. Before exercise, the local sweating response on healthy upper back skin to intradermally injected (0.1 ml) methacholine chloride (MCh) (Aldrich, Germany), diluted in saline, was routinely measured with the Evaporimeter (Evaporimeter EP1, ServoMed, Sweden). An MCh concentration of 5 × 10⁻⁷ mol/l was used, as it has previously been shown suitable for the measurement of sweating response (2). Apparently such a low MCh concentration has not previously been used to demonstrate a local cholinergic urticarial rash.

During supervised ergometric cycling the subjects wore tight sporting suits to maximize their thermal sweating. The cycling load (range 49–98 W) varied according to the patients' fitness level and the cycling time from 10 to 15 min.

CASE REPORTS

Case 1
A 10-year-old atopic girl in whom rhinitis and conjunctivitis were elicited by birch pollen and oral mucosal symptoms by some fruits, starting about 1 year earlier, exhibited pinpoint itching papules, especially following exercise and sweating. She had, also after exposure to cold weather, flushed lesions rather than frank urticaria on the lower limbs and occasionally swelling around the knees.

Skin prick tests were positive to birch, alder, grasses, cat, dog, mouse, potato, pea, kiwi fruit, hazelnut, peanut, almond and curry. Her total IgE was 460 U/ml. Eosinophils were 13%. Cryoglobulins and nuclear antibodies were negative. Sinus X-ray was normal. In local skin tests to cold and heat flushing but no weals occurred around the test areas.

Case 2
A 27-year-old male with no history of atopy had suffered during the past 10 months from itching pinpoint weals, developing preferentially on the upper trunk and the upper limbs. Lesions were elicited by sweating.

His general health was good. He had only mild perennial rhinitis. Results of routine laboratory tests were normal. The sinus X-ray was normal and skin prick tests were negative.

Case 3
A 56-year-old female, with no history of atopy, had been on antihypertensive medication (atenolol, hydrochlorothiazide + triamteren and enalapril maleate) for 4 years and on peroral medication (metformin, hydrochloride) for diabetes mellitus for 1 year. Acetylsalicylic acid and some other nonsteroidal anti-inflammatory medicines had elicited urticarial skin reactions. For 1 year she had been suffering from small urticarial papules, especially on her upper trunk, elicited by heat and sweating.

Her general health was good. Routine laboratory tests and thyroid function tests were normal; blood sugar was 8.0 mmol/l, alanine aminotransferase 60 U/l, and blood pressure 130/90.

RESULTS

In case 1 small urticarial papules developed densely about 3 cm around the test sites 5 min after cycling (Fig. 1) and then diffusively on the trunk and upper limbs. In cases 2 and 3 a similarly dense cluster of urticarial papules developed within 5–10 min around the test sites in a slightly wider area, i.e. about 4–5 cm from the injection sites. As in case 1 relatively few solitary weals developed a few minutes later diffusely on the trunk.

DISCUSSION

The sweating responses of all 3 patients to MCh were comparable with the levels of other patients with cholinergic urticaria (data not presented) and were also in accordance with the data obtained from young men tested with the same MCh concentration (3).

Commens & Greaves (1) tested 12 patients with cholinergic urticaria by exercise and by intradermal tests with methacholine. Although they used 100–1,000 times higher MCh concentrations, their intradermal testing was positive only in those patients with severe to moderate cholinergic urticaria and it was often not reproducible. The phenomenon of local cholinergic urticaria appearing in our patients after very mild MCh stimulation, but only when the skin was additionally stimulated by exercise, may be regarded perhaps as an accumulative effect after two separate cholinergic stimulations.

Adachi et al. (4) tested 20 patients with cholinergic urticaria with autologous sweat and all showed positive immediate-type reactions. Only a few patients with acute or chronic urticaria and none of 20 controls gave a positive reaction. In view of

Fig. 1. Methacholine-triggered local cholinergic urticarial satellite weals at the test site of the upper back skin in a 10-year-old girl after bicycle ergometry.
these results, it is possible that our 3 patients were particularly sensitive to their own sweat or that their sweat might escape into the tissue more readily than in many other patients with the same disease. On the other hand, visible sweating is not an essential feature, as cholinergic urticaria has been described also in anhidrosis (1).

REFERENCES

Accepted June 25, 1996.
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Atypical Localization of Cutaneous Leishmaniasis

Sir,

Cutaneous leishmaniasis (CL) is a relatively frequent pathology in the Mediterranean basin and in Sardinia (Italy), where it has an incidence of approximately 0.16/1,000 inhabitants (1). In this region the disease is mostly due to Leishmania infantum, and vectors are Phlebotomus perniciosus in 80% of the cases and Phlebotomus perfiliewi perfiliewi in 20% (1). The main CL reservoir is represented by dogs but also rodents have been incriminated. Disease onset occurs after a 2–4 week incubation period and is generally characterised by the appearance of a single nodular lesion, preferentially on the face or forearm (2). We here report a recent case with an unusual morphology and disease location.

CASE REPORT

A 45-year-old man, a building contractor with hunting as a hobby, had a 5-month history of an erythema-infiltrative and intensely pruritic lesion in the perianal region, which had been treated with antihaemorrhoids, antibiotics, antihistamines and corticosteroids, leading progressively to worsening of the objective and subjective symptomaticity. Remote anamnesis indicated chronic hepatitis B virus, well-compensated at clinical and laboratory levels. At the time of referral we observed a large oval-shaped plaque in the perianal region, with a maximum diameter of 8 cm. The lesion was bright red to violaceous in colour, had a hard consistency and was badly demarcated due to perilesional oedema but not painful (Fig. 1). Routine laboratory tests revealed a slight increase of transaminase and gamma GT and moderate thrombocytopenia. Humoral and cell-mediated immunity was normal. Histologic examination showed a dense infiltrate below a mildly hyperkeratotic and acanthotic epidermis involving the skin and part of the hypoderm and consisting of lymphocytes, plasmaocytes, rare neutrophils and histiocytes that were particularly abundant in the papillary derms. In the cytoplasm of the latter numerous Leishmania were present and could also be observed in groups outside the cells. Protozoal typing made it possible to identify Leishmania infantum Zymodeme Montpellier 111. The determination of anti-Leishmania antibodies in serum was negative.

Chest X-rays and abdominal echography were within normal range. Also the search for visceral localization of Leishmania and bone marrow biopsy yielded negative results.

Therapy was started with a single oral dose of itraconazole 200 mg/day for 2 months but with no benefit whatsoever. In fact the clinical pattern was the same and control histology, performed 1 month after the end of therapy, showed no changes in the infiltrate or in the presence of Leishmania. A treatment cycle based on the administration of meglumine antimoniate at an intramuscular dose of 40 mg/kg/day was therefore started. After only 1 week of treatment there was a marked improvement of the clinical pattern, but on the 12th day the patient developed a diffuse and intense urticarial reaction, for which reason treatment had to be stopped. Control histology 30 days after the last dose still showed a considerable number of Leishmania. Consequently rifampicin was given orally at a dose of 600 mg/day for 2 months. At the end of this treatment cycle clinical recovery was almost complete, and histologic control 1 month later revealed a modest and aspecific infiltrate totally lacking Leishmania. After 6 months the clinical symptomaticity was completely resolved and the search for parasites negative.

DISCUSSION

The perianal region is an extremely unusual site for CL, and to our knowledge this is the first case reported. As the protozoa is inoculated into the host by Phlebotomus we decided to look

Fig. 1. Large oval-shaped plaque in perianal region.