

Successful Treatment of Recurrent Cholinergic Urticaria with Updosing Regimen of Loratadine

(Keberhasilan Penatalaksanaan Urtikaria Kolinergik Rekuren dengan Peningkatan Dosis Loratadin)

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ABSTRACT

Background: Cholinergic urticaria is a form of urticaria induced by active or passive heating up of the body core temperature. Inability to avoid trigger factors of cholinergic urticaria may lead to difficulties in disease management. **Purpose:** To know the diagnostic and treatment approach of a patient with cholinergic urticaria whom unable to avoid trigger factors. **Case:** A 24-year-old male presented with a 2-month history of urticaria induced by exercise. He is a professional running athlete. Examination revealed numerous small wheals, 2 to 5 mm in size, surrounded by large flares and some were coalesced to form large areas of erythema, which first appeared on the thighs then spread to involve trunk and limbs, return to normal skin within 30 minutes to 2 hours. The lesions also occurred after hot showers provocation but not to cold showers. Provocation tests for other types of urticaria were negative. Diagnosis of cholinergic urticaria was made. **Case management:** Loratadine, in an updosing regimen until of 30 mg/d, suppressed the urticarial eruption. However, recurrences occurred immediately during vigorous exercise when lowering the dose into 10 mg/d of loratadine. **Conclusion:** Patient's inability to eliminate trigger factors can be challenging in the management of cholinergic urticaria. Therapeutic approach of updosing regimen of antihistamine gains good result and safe.

Key words: cholinergic urticaria, exercise-induced, loratadine

ABSTRAK

Latar belakang: Urtikaria kolinergik adalah urtikaria yang diinduksi oleh pemanasan suhu tubuh secara aktif maupun pasif. Ketidakmampuan untuk menghindari faktor pencetus dapat berakibat pada sulitnya penatalaksanaan. **Tujuan:** Mengetahui pendekatan diagnosis dan penatalaksanaan pasien dengan urtikaria kolinergik yang tidak dapat menghindari faktor pencetus. **Kasus:** Seorang laki-laki 24 tahun dengan keluhan urtikaria selama 2 bulan yang diinduksi oleh olahraga. Profesi pasien adalah atlet lari profesional. Pemeriksaan menunjukkan urtika kecil multipel, berukuran 2 sampai 5 mm, dikelilingi oleh makula eritematus dan beberapa lesi menjadi area kemerahan yang luas, yang awalnya timbul pada paha lalu menyebar pada badan dan lengan, kembali menjadi kulit normal dalam waktu 30 menit sampai 2 jam. Lesi juga timbul setelah mandi air panas tetapi tidak dicetuskan oleh mandi air dingin. Tes provokasi untuk tipe urtikaria yang lain menunjukkan hasil negatif. Diagnosis urtikaria kolinergik ditegakkan. **Penatalaksanaan:** Loratadin, dengan dosis yang ditingkatkan sampai 30 mg/hari, dapat menekan timbulnya urtikaria. Terjadi rekurensi saat berolahraga ketika dosis diturunkan sampai 10 mg/hari. **Kesimpulan:** Ketidakmampuan pasien untuk mengeliminasi faktor pencetus menjadi tantangan dalam penatalaksanaan urtikaria kolinergik. Pendekatan terapi dengan meningkatkan dosis antihistamin memberi hasil yang baik dan aman.

Kata kunci: urtikaria kolinergik, diinduksi olahraga, loratadin

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BACKGROUND

Cholinergic urticaria is defined by itching and whealing after active heating up of the body core temperature (e.g. exercise) or passive heating (e.g. hot bath). A typical description is one of tiny short lived wheals with a pronounced flare reaction that is frequently localized to the trunk and limbs.¹ Other

morphological patterns, including angioedema, can occur. Cholinergic urticaria occurs most frequently in young adults and equally in both sexes. Prevalence can be as high as 20% in the 26–28-year age group.²

Cholinergic urticaria must be differentiated from exercise induced urticaria/anaphylaxis, which is induced by exercise but not passive warming and is

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more often associated with systemic symptoms than cholinergic urticaria.³

Avoidance of trigger factors for the treatment of cholinergic urticaria is desirable, but not always simple. We present here a patient with cholinergic urticaria after exertion to sweating or passive heating with hot water. This case was particularly intriguing because the patient is a running athlete who exercise vigorously on a daily basis. Recurrent episodes brought the need of updosing regimen of antihistamine.

CASE

A 24-year-old male running athlete presented with a 2-month history of developing numerous itching erythematous skin lesions immediately after vigorous exercise. Cutaneous examination during his first visit to the clinic revealed numerous small wheals, 2 to 5 mm in size, surrounded by large flares and

some were coalesced to form large areas of erythema (figure 1), which disappeared within 30 minutes. The wheals usually developed every workdays after he exercised vigorously to the point of sweating, first appeared on the thighs, then spread to involve trunk and limbs, return to normal skin within 30 minutes to 2 hours. This condition has been appeared and recurred for 2 months although the patient has taken cetirizine 10 mg daily when he experienced the symptoms. Drowsiness was also reported by the patient when he took cetirizine. No systemic symptoms such as hypotension, angioedema, and bronchospasm. There was no history of drug, food, or emotional stress as the triggers. The patient denied of any prior dermatologic or systemic diseases, especially of atopy. The family history was also free of any skin diseases including urticaria.

Provocation testing using various physical triggers were performed. Exercise using stationary

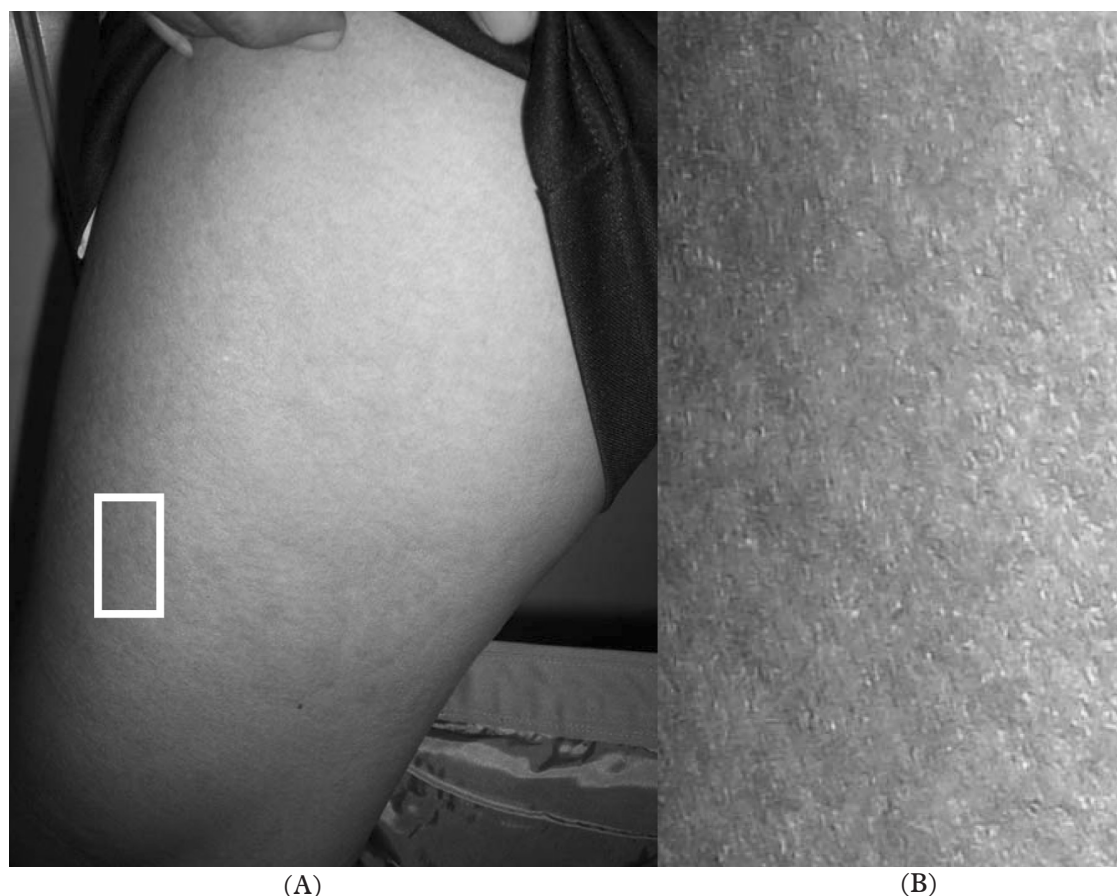


Figure 1. (A) numerous small wheals, 2 to 5 mm in size, surrounded by large flares and some were coalesced to form large areas of erythema on the thigh of the 24-year-old running athlete, which presented immediately after vigorous exercise. (B) Larger magnification of the area marked in (A) better demonstrates the morphology of the wheals.

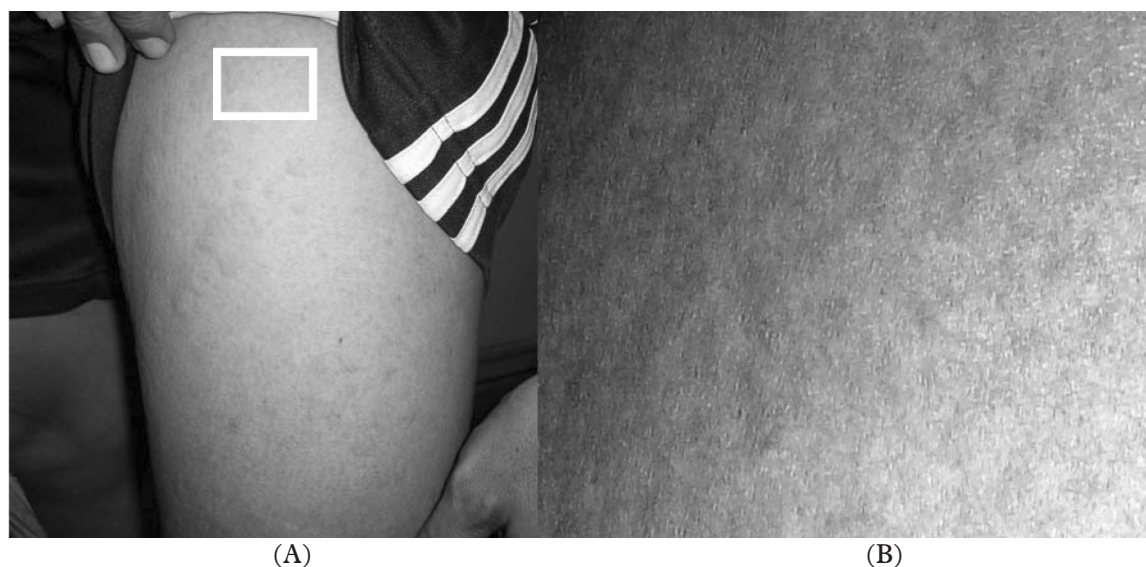


Figure 2. (A) Exercise using stationary bicycle to the point of sweating then continue for 15 minutes reproduced the same wheals as in figure 1. (B) Larger magnification of the area marked in (A) numerous small wheals characteristic for cholinergic urticaria.

bicycle to the point of sweating then continue for 15 minutes reproduced the same wheals (figure 2). Hot bath of approximately 42° C for 15 minutes also triggered the urticarial lesions. Diagnosis of cholinergic urticaria was made. No lesions occurred after a cold shower and provocation tests for cold contact urticaria, heat contact urticaria, solar urticaria,

and vibratory urticaria. Dermographism were normal. Methods and results of the tests are described in table 1. Education and suggestion had been given to the patient regarding the eliciting factors especially exercise, but elimination could not be made by the reason of professional career.

Table 1. Methods and results of the provocation tests performed⁶

Cholinergic urticaria

Test 1: Exercise using stationary bicycle to the point of sweating then continue for 15 minutes

Result: wheal presence (+)

Test 2: Hot bath of approximately 42° C for 15 minutes

Result: wheal presence (+)

Cold contact urticaria

Test : Melting ice cube in thin plastic bag (approximately 4° C) for 5 minutes

Result: wheal presence (–)

Heat contact urticaria

Test : Heat source (warm water of approximately 45° C in pyrex glass) for 5 minutes

Result: wheal presence (–)

Solar urticaria

Test : Exposure of visible light using slide projector, 10 cm distance

Result: wheal presence (–)

Vibratory urticaria

Test : Vortex vibrator for 10 minutes, 1000 rpm

Result: wheal presence (–)

Aquagenic urticaria

Test : Wet cloths at body temperature applied for 20 minutes

Result: wheal presence (–)

Symptomatic dermographism (urticaria factitia)

Test : Moderate stroking of the skin with a blunt smooth object (closed ballpoint pen tip)

Result: wheal presence (–)

The following laboratory investigations were within the normal range: complete blood count and WBC differential count including eosinophils, hemoglobin, erythrocyte sedimentation rate (ESR), blood glucose, liver enzymes, renal function tests, total albumin, total serum IgE, urinalysis and stool examination. Prick allergy tests for inhalants and food agents were performed and showing negative results.

Oral treatment with the non sedating H₁-antihistamine (nsAH) loratadine 10 mg/d in a single morning dose was conducted. Loratadine was taken 1–2 hours before exercising and only in weekdays of exercise. Symptoms still persists under the treatment of loratadine 10 mg/day for 2 weeks. The urticaria activity score (UAS) of 7 days of initial treatment scored 34 out of maximum score of 42 (table. 2). Attempt of up dosing loratadine into 20 mg/day was made (10 mg morning + 10 mg evening) and after 1 week of treatment, the lesions still occurred. Further attempt of up dosing loratadine into 30 mg/day (20 mg morning + 10 mg evening) gained good result, with no symptom nor lesions occurred. After 4 weeks of loratadine 30 mg/day, attempt of lowering the dose into 20 mg/day also gained good result with no lesions occurred. Finally after 4 weeks of loratadine 20 mg, further attempt of lowering the dose into 10 mg/day resulted in failure of preventing wheal formation. Loratadine 20 mg/day was reinitiated and are continued until now, for 6 months after the first regimen (figure 3). No drowsiness, no arrhythmia nor change in ECG or other side effects of the drugs were found during the treatment. All laboratory results remained within normal range after 6 months of treatment. No usage of systemic steroid during the whole course. UAS at the final visit scored 0 (minimum). Figure 4 shows the progress of urticaria

activity in this patient. Early retirement as an athlete and starting a non-athlete career are considered by the patient to eliminate eliciting factors.

DISCUSSION

Cholinergic urticaria, an inducible form of urticaria, is currently not classified as a physical urticaria anymore, because its symptoms are induced by an increase in the body core temperature and not by an exogenous physical trigger acting on the skin. Whereas, physical urticaria is a heterogeneous group of inducible conditions that includes cold contact urticaria, symptomatic dermatographism/urticaria factitia, heat contact urticaria, delayed pressure urticaria, and vibratory urticaria/angioedema. Physical urticarias are induced by exogenous physical triggers acting on the skin, including thermal (cold, heat), electromagnetic radiation (solar radiation) and mechanic triggers (friction, pressure, vibration).³

To differentiate cholinergic urticaria from exercise induced urticaria and physical urticarias, provocation testing should be performed. Provocation testing for this patient were performed in a three steps approach. First step is a moderate physical exercise, appropriate to the patient's age and general condition, undertaken on a treadmill or stationary bicycle. If the exercise provocation test is positive, the second step which is a passive warming test should be done at least 24 hours later by hot bath of approximately 42° C for 15 minutes. This is to differentiate cholinergic urticaria from exercise induced anaphylaxis, which the latter condition will yield negative result for the passive warming test. The third step is to differentiate with physical urticarias and to find other eliciting factors. This had been done by performing various provocation testing for physical urticarias, prick tests, and laboratory examinations.^{1,3}

Table 2. Assessment of disease activity using urticaria activity score (UAS)⁶

Score	Wheals	Pruritus
0	None	None
1	Mild (< 20 wheals/24 h)	Mild (present but not annoying or troublesome)
2	Moderate(20–50 wheals/24 h)	Moderate (troublesome but does not interfere with normal daily activity or sleep)
3	Intense (> 50 wheals/24 h or large confluent areas of wheals)	Intense (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep)

Sum of wheal + pruritus score: 0–6.

UAS are the sum score of 7 consecutive days, to determine disease activity and response to treatment of chronic urticaria patients. Range of total weekly UAS: 0–42.

Treating urticaria in which the identified eliciting factors cannot be eliminated is intriguing. In this case, cholinergic urticaria was mainly elicited by exercise, which is a significant matter since the patient is a professional running athlete. Often, attempt must be made to control the disease in such conditions. There are some studies showing the benefit of a higher dosage of antihistamines in difficult-to-treat urticaria.^{4,5} Current guideline also suggest updosing of nsAH up to 4 times.⁶ The choice of nsAH should be made in consideration of effectiveness, safety, and side-effects. Loratadine was chosen in this case because of effectiveness in managing the signs and symptoms of urticaria, comparable with other nsAH, even though is less effective at the same dose than cetirizine for inhibition of histamine wheals.⁷ The safety of loratadine for chronic conditions had been described,⁸ and the side effects of the drug is considered lower than cetirizine especially regarding sedative properties.⁹ This is also supported by no report of drowsiness and no abnormalities of laboratory results were found during the treatment. The treatment approach in our case resembles the hardening regimen,¹⁰ thus attempt to lower the dose of nsAH can be successful. Systemic steroid was not given to the patient because of legal consideration regarding doping regulation in sports.

We describe a case of a running athlete with cholinergic urticaria induced by exercise and passive warming. This case was particularly challenging because the inability to eliminate the eliciting factors and the successful therapeutic approach of updosing regimen of antihistamine.

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