symptomatology on exposure to cold (swimming); the ice-cube and cold-water immersion tests were repeated with incremental exposure times (1 min, 3 min, 5 min). Both tests were negative after 1 and 3 min, but resulted in mild local oedema after an exposure time of 5 min.

DISCUSSION

Cold urticaria, as a frequent variant of physical urticaria, is a strikingly chronic disease, and the majority of patients suffer from cold-induced symptoms for years (4). Generalized weals due to aquatic activities are commonly seen on these patients, and in a proportion of more than 40% shock-like reactions will develop (5). In the latter patients, a cold stimulation time test of less than 3 min indicates the severity of cold urticaria, as was seen in our patient while he received ACE inhibitor therapy.

Data from the literature suggest that histamine – in contrast to other variants of urticaria – may not be the principal mediator of the vascular response to cold challenge in ACU. In 1968, DeLaus & Winkelmann (6) reported that bradykinin was produced as a mainly inflammatory mediator in the cold-provoked weals of 11 patients with cold urticaria. Later on, participation of the kallikrein-kinin system in the formation of cold-induced weals has been suggested by various authors (7, 8). Because treatment with ACE inhibitors was recently shown to increase weal and flare reactions to cutaneous applied bradykinin (9), we decided to change the antihypertensive therapy in our patient. ACE inhibitor therapy has been associated with elevated plasma kinin levels (10), and we believe this elevation was responsible for life-threatening attacks in this patient with long-standing ACU.

The mainstay of ACU therapy is awareness, avoidance of the inciting stimulus "cold", and finally it may be symptomatic by applying antihistamines (1, 6). However, identifying and avoidance of drugs known to trigger or potentiate mediator effects are essential in preventing more severe adverse events in ACU patients. We therefore recommend avoidance of ACE inhibitor therapy in patients with cold urticaria – analogous to avoidance in patients with hereditary angioedema, who are known to have elevated bradykinin levels (11).

REFERENCES

1. Kontou-Fili K, Borici-Mazi R, Kapp A, Matjevic LJ, Mitchel FB. Position paper. Physical urticaria: classification and diagnostic guidelines. Allergy 1997; 52: 504–513.
2. Mathelier-Fusade P, Aissaoui M, Bakhhos D, Chabane MH, Leynadier F. Clinical predictive factors of severity in cold urticaria. Arch Dermatol 1998; 134: 106–107.
3. Kränke B, Mayr-Kanhäuser S, Aberer W. Helicobacter pylori in acquired cold urticaria. Contact Dermatitis 2001; 44: 57–58.
4. Kozel MMA, Mekkes JR, Bossuyet PMM, Bos JD. Natural course of physical and chronic urticaria and angioedema in 220 patients. J Am Acad Dermatol 2001; 45: 387–391.
5. Wanderer AA, Grandel KE, Wassermann SI, Farr RS. Clinical characteristics of cold induced systemic reactions in acquired cold urticaria syndrome: recommendations for prevention of this complication and a proposal for a diagnostic classification of cold urticaria. J Allergy Clin Immunol 1986; 78: 417–423.
6. DeLaus FV, Winkelmann RK. Kinins in cold urticaria. Arch Dermatol 1968; 98: 67–74.
7. Michaelsson G. Chronic urticaria. Acta Derm Venereol 1969; 49: 404–416.
8. Martens BPM, Berrens L. Enzyme activation and inhibition induced by cold provocation in a patient with cold urticaria. Acta Derm Venereol 1975; 55: 121–125.
9. Anderson MW, DeShazo RD. Studies of the mechanism of angiotensin-converting enzyme (ACE) inhibitor-associated angioedema: the effect of an ACE inhibitor on cutaneous responses to bradykinin, codeine, and histamine. J Allergy Clin Immunol 1990; 85: 856–858.
10. Pellacani A, Brunner HR, Nussberger J. Plasma kinins increase after angiotensin-converting-enzyme inhibition in human subjects. Clin Sci 1994; 87: 567–574.
11. Nussberger J, Cugno M, Amstutz C, Cicardi M, Pellacani A, Agostoni A. Plasma bradykinin in angiooedema. Lancet 1998; 351: 1693–1697.

Association of HIV Infection, Pyoderma Gangrenosum and Psoriasis

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Sir,
Pyoderma gangrenosum usually occurs in immunocompetent individuals suffering from ulcerative colitis, M. Crohn, M. Bechterew or lupus erythematosus. Pyoderma gangrenosum has also been described in immunosuppressed patients with haematologic malignancies, hypogammaglobulinemia or IgA-deficiency (1, 2). Only a few patients with HIV-associated pyoderma gangrenosum have been reported to date (3–5). We here report a HIV-positive patient with simultaneous exacerbation of pyoderma gangrenosum and psoriasis.

CASE REPORT

A 42-year-old Caucasian man presented to our department with a 5-week history of an ulcerated skin lesion on the right lower leg. He was tested positive for HIV in 1992, most likely infected through illicit use of intravenous drugs. He had no abdominal pain, arthritis or bloody stools, nor had he ever had any HIV-related opportunistic infections. Clinical examination revealed a deep ulceration on the right lower leg, 10–15 cm in diameter, with violaceous, overhanging borders (Fig. 1). He also presented with multiple erythematosquamous papules on the knees, elbows, abdomen and lower back (Fig. 2). Biopsy samples taken from the affected sites were consistent with the diagnosis pyoderma gangrenosum and psoriasis vulgaris, respectively. Bacterial cultures taken from the center of the ulceration at the right lower leg grew *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Laboratory examinations revealed 251 CD4+ lymphocytes per µl (25%), 614 CD8+ lymphocytes per µl (62%), a CD4/CD8 ratio of 0.41 and a virus load of 65,000 copies/ml of HIV RNA. Rheumatoid factor, antinuclear antibody, TPHA, VDRL, toxoplasma antigen, cryptococcus antigen and hepatitis A, B, C antigens were all negative. No other additional haematological, biochemical or immunological abnormalities were demonstrated. We initiated HAART (highly active antiretroviral therapy) consisting of zidovudine 300 mg/lamivudine 150 mg and nevirapine 200 mg twice daily. Psoriasis was treated with topical mometasonfuroat and calcipotriol. The initial treatment also included antibiotic therapy with cefuroxim 250 mg twice daily. Topical therapy of the ulcers with twice daily antiseptic baths (povidone iode solution) was started. When vascularization and granulation of the pyoderma gangrenosum lesions had developed, we performed transplantation of cultured autologous keratinocytes. A full-thickness skin specimen (1.5 cm^2) was taken from the groin. Keratinocytes were isolated from the skin specimen and cultured for 3 weeks. For transplantation, the expanded keratinocyte cultures were seeded in a fibrin gel that was evenly applied on the ulcerative lesion on the right leg (6). Wound management was performed with an outer dressing gauze and elastic bandage. Both skin diseases almost completely cleared within 5 to 6 weeks.

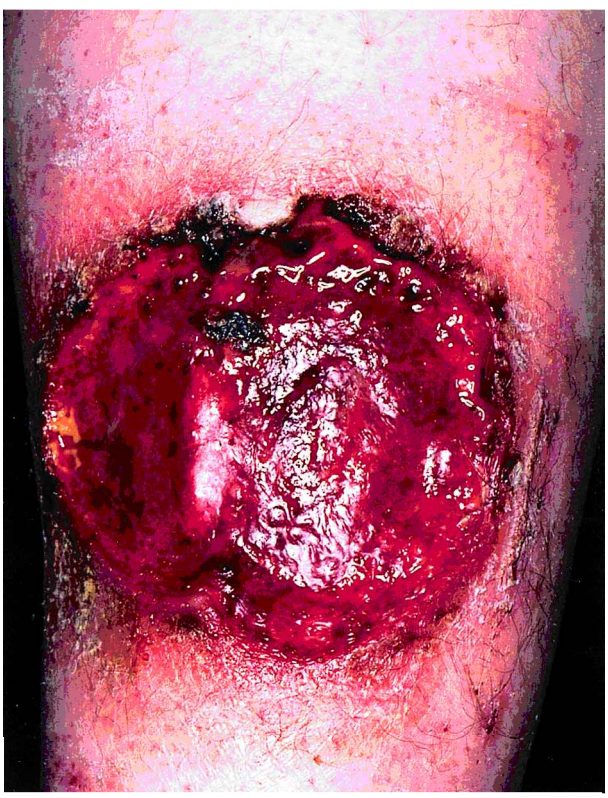

Fig. 1. Pyoderma gangrenosum of the right lower leg in a patient with HIV infection.

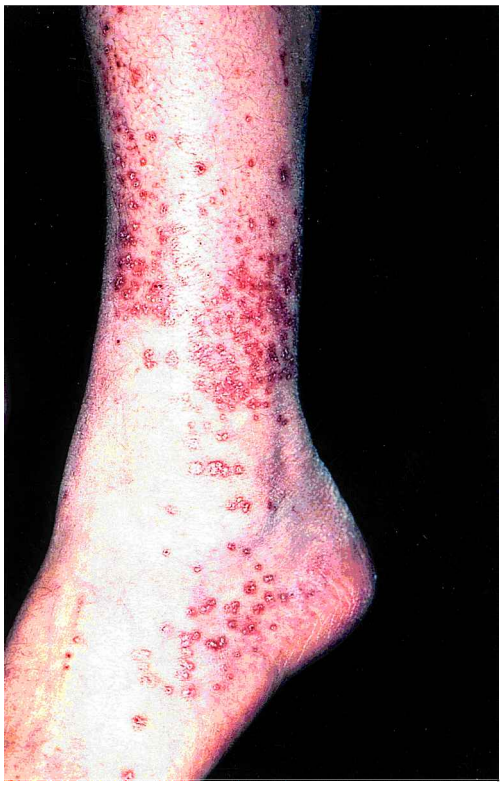

Fig. 2. Psoriasiform eruptions on the left lower leg.

DISCUSSION

Pyoderma gangrenosum usually occurs in immunocompetent persons, but has also been noted in immunosuppressed patients with malignancies or primary immunodeficiency. It typically involves the lower extremities, whereas the perineum has been the most common site in patients with HIV infection. Most of the reported HIV-positive patients with pyoderma gangrenosum, as well as in our patient, had a CD4/CD8 ratio between 0.40 and 0.70. Opportunistic infections

had not occurred in any of these patients. Bacterial and viral infections are well-known trigger factors for psoriasis (7). HIV infection is associated with psoriasis, with an overall prevalence of 5–6% (8). This association appears paradoxical, because psoriatic inflammation is mediated by activated T cells and neutrophil chemotaxis. In psoriatic lesions, epidermotropism and disease-associated changes in the T-cell receptor repertoire have been detected in CD8 lymphocytes (9). The activation and proliferation of CD8 lymphocytes may therefore facilitate the development of psoriasis in HIV-infected individuals. This hypothesis is supported by the observation of improvement of psoriasis in patients after initiating HAART (10, 11).

In our patient, pyoderma gangrenosum and psoriasis rapidly improved within 6 weeks after initiating HAART. Cutaneous dendritic cells play a central role in the control of cutaneous immune reactions. Langerhans' cells express CD4 molecules, HIV co-receptors and various cytokines (12, 13). Taking this into consideration, one might speculate that the improvement of both skin diseases was caused by restitution of (cutaneous) immune system under HAART.

REFERENCES

1. Hickman JG, Lazarus GS. Pyoderma gangrenosum: a reappraisal of associated systemic diseases. Br J Dermatol 1980; 102: 498–502.
2. Powell FC, Collins S. Pyoderma gangrenosum. Clin Dermatol 2000; 18: 283–293.
3. Paller AS, Sohn EE, Garen PD, Dobson RL, Chadwick EG. Pyoderma gangrenosum in pediatric acquired immunodeficiency syndrome. J Pediatr 1990; 117: 63–69.
4. Clark HH, Cohen PR. Pyoderma gangrenosum in an HIV-infected patient. J Am Acad Dermatol 1995; 32: 912–914.
5. Graham JA, Hansen KK, Rabinowitz LG, Esterly NB. Pyoderma gangrenosum in infants and children. Pediatr Dermatol 1994; 11: 10–17.
6. Limova, MT. Treatment of pyoderma gangrenosum with cultured keratinocyte autografts. J Dermatol Surg Oncol 1994; 20: 833–836.
7. Christophers E. The immunopathology of psoriasis. Int Arch Allergy Immunol 1996; 110: 199–206.
8. Badger J, Berger TG, Gambia C, Koo JY. HIV and psoriasis. Clin Rev Allergy Immunol 1996; 14: 417–431.
9. Chang JC, Smith LR, Froning KJ, et al. CD8+ T cells in psoriatic lesions preferentially use T-cell receptor Vβ 3 and/or Vβ 13.1 genes. Proc Natl Acad Sci USA 1994; 91: 9282–9286.
10. Fischer T, Schworer H, Vente C, Reich K, Ramadori G. Clinical improvement of HIV-associated psoriasis parallels a reduction of HIV viral load induced by effective antiretroviral therapy. AIDS 1999; 13: 628–629.
11. Duvic M, Crane MM, Conant M, Mahoney SE, Reveille JD, Lehrmann SN. Zidovudine improves psoriasis in human immunodeficiency virus-positive males. Arch Dermatol 1994; 130: 447–451.
12. Lappin MB, Kimber I, Norval M. The role of dendritic cells in cutaneous immunity. Arch Dermatol Res 1996; 288: 109–121.
13. Dezutter-Dambuyant C, Charbonnier AS, Schmitt D. Epithelial dendritic cells and HIV-1 infection *in vivo* and *in vitro*. Pathol Biol 1995; 43: 882–883.

Pellagra-like Skin Lesions Associated with Wernicke's Encephalopathy in a Heavy Wine Drinker

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Sir,
The endemic form of pellagra associated with poverty and inadequate diet is manifested clinically by the "three Ds" diarrhea, dermatitis and dementia, and occasionally by death (1). Pellagra results from a tissue deficiency in niacin or in its precursor, the essential amino acid tryptophan (2). Sporadic cases are due to chronic alcoholism, dietary lack of natural sources of niacin (liver, fish, lean meat, poultry, yeast and cereal grains), malabsorption, certain chemotherapeutic drugs, or carbamazepin (1). Wernicke's encephalopathy is due to thiamin deficiency and is usually seen in alcoholics who suffer from malnutrition. We present here a case with a suspected combination of these two deficiencies.

CASE REPORT

A 40-year-old woman was admitted to the Neurological Department early in August with rapidly evolving ataxia of gait and diplopia. She had had 3 attacks of dizziness during the previous 6 months and a sun-induced rash on her lower legs that during the previous 3 weeks had spread to her arms, hands and head. Neurologically, she displayed atactic gait, horizontal nystagmus and myoclonic jerk. Laboratory tests showed pathological liver functioning. Serology for hepatitis B and C and HIV was negative. Blood sugar and zinc values were normal. Ultrasound revealed liver steatosis. She reported drinking considerable amounts of wine in the previous few weeks. Since Wernicke's encephalopathy was suspected, vitamin B was injected i.m. (thiamine chloride, pyridoxine chloride and cyanocobolamine, 0.1 g daily each). After about 24 h the patient's neurological symptoms disappeared. Two days after admittance to the hospital she was referred to the Dermatological Department for her rash. She displayed redness, superficial scaling and blisters on her lower legs, whereas her